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MUSGRAVE

TRYPANOSOMA AND TRY-PANOSOMIASIS

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DEPARTMENT OF THE INTERIOR.

BUREAU OF GOVERNMENT LABORATORIES.

BIOLOGICAL LABORATORY.

TRYPANOSOMA AND TRYPANOSOMIASIS, WITH SPECIAL REFERENCE TO SURRA IN THE PHILIPPINE ISLANDS.

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LETTER OF TRANSMITTAL.

BUREAU OF GOVERNMENT LABORATORIES,
OFFICE OF THE SUPERINTENDENT,
Manila, P. I., July 4, 1903.

SIR: I have the honor to transmit herewith a report on "Trypanosoma and Trypanosomiasis, with special reference to surra, in the Philippine Islands," by W. E. Musgrave, M. D., Acting Director of the Biological Laboratory, and Moses T. Clegg, assistant bacteriologist, Biological Laboratory.

Very respectfully,

PAUL C. FREER,
Superintendent of Government Laboratories.

Hon. DEAN C. WORCESTER,
Secretary of the Interior.

LETTER OF SUBMITTAL.

BUREAU OF GOVERNMENT LABORATORIES,
BIOLOGICAL LABORATORY,
Manila, P. I., July 4, 1903.

SIR: In compliance with your request of July 1, 1902, I have the honor to submit herewith a report on "Trypanosoma and Trypanosomiasis, with special reference to Surra in the Philippine Islands."

Very respectfully,

W. E. MUSGRAVE, M. D.,
Acting Director Biological Laboratory.

Dr. PAUL C. FREER,
Superintendent of Government Laboratories.

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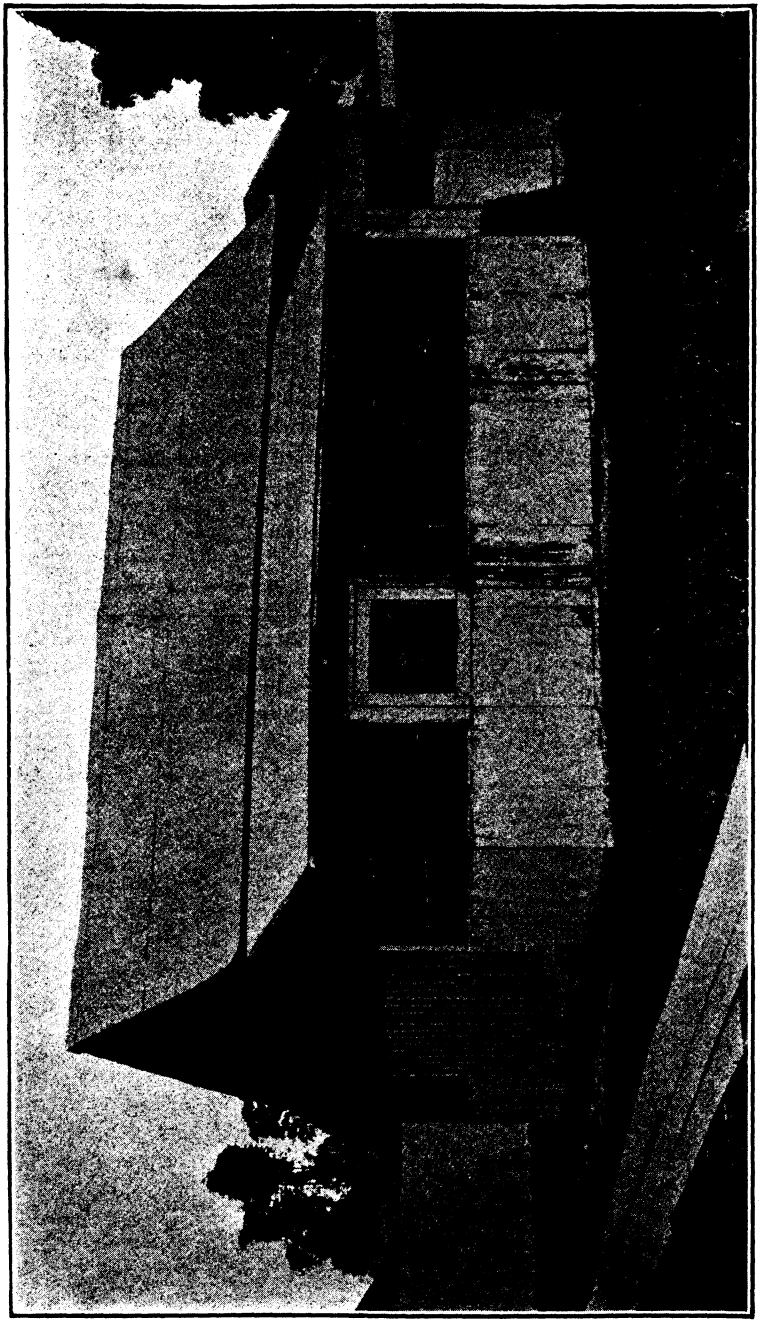

FIG. 1.—Insect-proof stable constructed for our experimental work.

INTRODUCTION.

Before entering upon a discussion of the text of this paper, a few remarks regarding the facilities at our disposal appear advisable.

Figure 1 illustrates a specially constructed insect-proof stable in which all experiments necessitating extraordinary precaution were performed. To obtain satisfactory results such a structure is an absolute necessity. This stable is screened on all sides, the stalls are separated by wire netting, and each is provided with a door of the same kind. On each side there is an additional hall entirely screened and with a single outside door. At one end an insect-proof operating room was built and provided with a protected entrance to the different stalls.

Because of these precautions, experiments have been conducted by us with an absolute certainty of results; and owing to a lack of facilities similar to ours, many of the conclusions contained in reports relating especially to the transmission of the disease do not appear to have been based upon accurate observations.

Discussions of the transmission of the disease by feeding, based upon observations made without protecting animals from insects, do not, of course, lead to a final settlement of the question; and so with many other conclusions in the voluminous literature relating to this subject.

In reviewing literature we have tried in each instance to give credit to the person to whom due, but in this we may sometimes have failed. The works of Voges, Lingard, Kanthuck, Durham, and Blandford, Laveran and Mesnil, Rabinowitch and Kempner, Wasielewski and Senn, Schat, Schilling, Bruce, and many others, have been freely used.

We desire to express our obligations to Miss Mary Polk, librarian of the Bureau of Government Laboratories, for her assistance in editing bibliography and preparing the index, and to Mr. C. J. Arnell, stenographer and translator, and Mr. Charles Martin, photographer of the Bureau of Government Laboratories, for valuable assistance.

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BIOLOGICAL LABORATORY, *Manila, P. I., July 4, 1903.*

TRYPANOSOMA AND TRYPANOSOMIASIS.

I. DEFINITION.

The disease is a specific infection of many of the lower animals, and occasionally of man, caused by Trypanosoma. It occurs in epidemic form over large areas of tropical countries, and is usually more severe during the rainy season. It is characterized by a period of incubation, followed, in most animals, by a remittent, intermittent, or, less frequently, relapsing fever; by the presence of Trypanosoma in the circulating blood, which in some animals are numerous in proportion to the temperature; by progressive anemia and emaciation; by a catarrhal condition of the mucous membrances of the eyes and nose; by roughness of the hair, which in many instances, falls out; and by subcutaneous edema, more commonly of the posterior extremities, genitals, and belly. In the later stages paresis of the posterior extremities is very common. The mortality among most animals of economic importance is 100 per cent.

There are found in most animals at post-mortem, in addition to the evidence of severe anemia, certain changes in the spleen, the most constant being enlargement and a peculiar mottling. Taken with the other principal lesions, such as lymphatic hyperplasia; peculiar, yellowish, gelatinous subcutaneous and suberous infiltrations; an enlarged liver and the accumulation of fluid in the serous cavities, it makes an anatomic picture which is rarely excelled in chronic diseases peculiar to man.

II. NOMENCLATURE AND CLASSIFICATION.

A list of the various names used to designate Trypanosomiasis in different parts of the world has been compiled from literature as follows:

Adjoe.
Andar-tap.
Anémie pernicieuse.
Berbad.
Beschalkrankheit.
Beschalseuche.
Blaschenausschlag.
Bovine surra.
Buffalo surra.
Camel surra.
Canine surra.
Dog surra.
Doaia.
Dourine.
Equine relapsing fever.
Equine surra.
Equine syphilis.
Exantheme coitale.
Fish surra.
Flagellose de equina.
Galtah.
Galtia.
Glossinose.
Horse pox.

Horse surra.
Juckkrankheit.
Khanhog.
Khusk-zaharbad.
La mouche.
Leuma equorum.
Mal de caderas.
Maladie á trypanosome.
Maladie benigne du coit.
Maladie de la tsétsé.
Maladie de Soemedang.
Maladie du coit.
Maladie du prurit.
Maladie vénérienne du cheval.
Marri.
Nagana.
Nikalgaya.
N'gana.
Nygana.
Oae.
Pernicious anemia of horses.
Peste de cadeiras.
Pferdestaupe.
Phenta.
Phenta-ka-darad.
Phera.
Pheta.
Phetra.
Phitgaya.
Photra.
Polynevrite infectieuse du cheval.
Poona.
Purama.
Rat surra.
Relapsing fever of equines.
Sar.
Sara.
Schleuchende fieber.
Sokra.
Sukal.
Surra.
Surra americain.
Surrakrankheit.
Tap.
Tap-dik.
Tape-dik.
Taraf.
Tebersa.
Tibarsa.
Trypanosomose.
Tsétsé-fly disease.
Tsétsékrankheit.
Tumby-a.
Tumby-baba.
Wabai-ki-bokhar.
Zaharbad.
Zherbad.
Zuchtlähme.

In this report the term "Trypanosomiasis," as suggested by Salmon and Stiles, is used, being in a general sense comparable to the terms "filariasis" and "uncinariasis." Following this classification further, according to the animal infected, we would have Trypanosomiasis of man, Trypanosomiasis of horses, Trypanosomiasis of cattle, etc. Such a nomenclature would apply satisfactorily, whether the infecting parasites are identical or not, and also regardless of the manner and place of infection. For example, the term Trypanosomiasis of horses would apply equally well to nagana contracted by the bite of an infected tsétsé fly in South Africa and to surra produced by the hypodermic injection of infected Trypanosomiatic blood in Manila.

If the parasites causing the diseases known under the old names have been or are shown to be different, there could be no very great necessity for interfering with the better part of the established nomenclature. *Surra* would then be the Trypanosomiasis of horses and of other animals due to an infection with *Tr. evansii,* nagana would be the Trypanosomiasis of horses and of other animals due to an infection with *Tr. brucei,* etc.

On the other hand, if these parasites are shown to be the same, or, probably more correctly, until they are shown to be different, there

does not appear any valid reason why any of the names except that of surra, accepted by Evans, the original discoverer of the pathogenicity of the parasite in animals, should be retained.

Without entering in detail upon a discussion, which will be taken up later in the report, regarding the identity or nonidentity of *Tr. evansii, Tr. brucei, Tr. rougetti* (equiperdum), and *Tr. elmassianii* (equinum), and hence the identity or nonidentity of surra, nagana, dourine and mal de caderas, there is considerable difference of opinion, and also considerable inconsistency in some of the writings, especially with reference to some of the diseases discovered and named since Evans's original report.

Numerous writers on Trypanosomiasis base their diagnoses on the presence of *Tr. brucei,* and, after carefully describing the parasite, state that they do not know whether or not it is identical with *Tr. evansii.* How can such writers, not having previously studied either of the parasites, state that it was not *Tr. evansii* rather than *Tr. brucei* they were working with? If they are positive that the parasite is *Tr. brucei,* then they affirm it to be different from *Tr. evansii.* It is obvious that, if these parasites are identical, *Tr. brucei* is not entitled to a place in the nomenclature of Trypanosoma, for *Tr. evansii* was known and described years before Bruce performed his work. Bruce himself, in his original report, considered his parasite probably identical with *Tr. evansii.*

Some eminent authorities criticise Koch and many other writers for stating that *Tr. evansii* and *Tr. brucei* are identical, without offering detailed proof of their statements. Such criticism seems to us unjust. The proof demanded is that they are different parasites, and until this proof is furnished, writers, in our opinion, are perfectly entitled to consider the Trypanosomiasis of horses and a number of other animals as being due to an infection with *Tr. evansii.*

The practical importance of deciding this question is forcibly brought home to workers in the Philippine epidemic, a fact which has already been emphasized by other writers. We have to deal with an extensive epidemic of Trypanosomiasis in several species of domestic animals, particularly in horses, and the parasite causing the disease seems to be the same in all. This parasite answers the description given of *Tr. evansii, Tr. brucei,* and others, and it is necessary either to introduce a new name or to classify from description. We have decided, after a careful review of all available literature pertaining to the subject, that we are dealing with *Tr. evansii* redescribed by Bruce as the causative agent in nagana and named *Tr. brucei* by Buffard and Schneider, and also described and given other names by various authors. To be consistent with this statement, "surra" would be the only allowable popular name for the disease caused by this parasite, the numerous other names becoming mere synonyms.

In those forms of the disease due to other species of Trypanosoma other names would of course be allowable; but, with the possible exception of dourine, we have nowhere else met so much confusion and such a multiplication of names as is found in the group of which *Tr. evansii* is the cause.

III. HISTORIC.

Caladrini, according to Voges, in 1842 wrote letters describing a disease in South America, which has subsequently been determined to be Trypanosomiasis (mal de caderas), and since that time has been discussed under various names and by several authors.

Sivori and Lecler are satisfied that this disease existed in South America before 1850, while Lacerda states that mal de caderas was imported to the mainland about 1850 from Marajo, an island at the mouth of the Amazon River, and from there spread rapidly over Brazil, thence to Paraguay, probably about 1860, quickly covering almost this entire country and killing thousands of horses.

Dourine has been known in various places since the latter part of the eighteenth century, but curiously enough was one of the last varieties to have its etiology elucidated. In 1858 Livingstone wrote of the tsétsé-fly disease in Africa, at that time old and well known to the natives.

Surra was first brought prominently before the scientific world in a report published by G. Evans in 1880. He accurately described the disease, which had been known for generations to the natives of India, and proved the causative role of Trypanosoma in this infection. Since the publication of Evans's report a great deal has been written regarding Trypanosomiasis, as a glance at the bibliography will show.

The disease annually destroys millions of dollars' worth of animals in India, Africa, and South America. Some of the more recently infected countries are the Island of Mauritius, Java, and the Philippines.

The Island of Mauritius was free from Trypanosomiasis up to the South African war, but during that conflict many animals from infected countries were sent into Africa and some of them found their way into this island. A severe epidemic developed, destroying so many of the animals that the planting and gathering of crops became an impossibility.

In 1900 surra broke out among the cattle, carabao, and horses of Java, since which time it has there been endemic. As soon as the disease was discovered in Java vigorous plans to prevent its spread were instituted and with marked success, if the small losses of that country are compared with the frightful havoc among horses and cattle which have been reported from other infected regions.

In 1886 Bignami and Celli mentioned a parasite resembling *Tr. lewisii* which they found in the blood of a patient suffering from malarial fever. Nepveu, in 1898, reported the presence of Trypanosoma in the blood of

seven patients, six of whom were suffering from malaria and the seventh was healthy. He described and illustrated the parasite. During 1902, Dutton, Ford, and Manson reported Trypanosoma in human beings, and in 1903 Manson and others reported a number of cases.

The first published report which we have of Trypanosomiasis in the Philippines was by Smith and Kinyoun in 1901. The history of the epidemic in this country has been reported by Musgrave and Williamson in a preliminary published as Bulletin No. 3, Bureau of Government Laboratories. This report was read before the Manila Medical Society and brought out considerable discussion. The only point at issue was our statement that the disease was introduced here in 1901. We have investigated as far as possible the arguments brought forth that surra was here prior to that time, but have found nothing to justify any change in our original statement. The subject is not of great importance one way or the other, except for its historic interest. There is one thing absolutely certain, that the disease *was* introduced at that time, and, whether this was its original appearance or not, the frightful epidemic which has raged here is positively connected with this infection. Our statements regarding the manner of its spread were absolutely convincing at the time of the publication of the preliminary report, and additional work along these lines has since confirmed the conclusions there given.

During the past month we have had proof of the reimportation of the disease, this time in a cow received from Java.

Since its introduction the infection has been spreading throughout the Archipelago, and at the present time areas in which it is prevalent are reported from almost the entire group of islands.

IV. ETIOLOGY.

GEOGRAPHIC DISTRIBUTION.

The geographic range of the various forms of Trypanosomiasis is shown in the following table:

Continent.	Country.	Province, territory, division, district, etc.	Form.	Reported by—
Asia	India	Bengal	Surra	Lingard.
		Berars	do	Do.
		Bombay Presidency	do	Do.
		Burma	do	Lingard, Steel.
		Cashar	do	Do.
		Kohat	do	Lingard, Gunn.
		Konkan	do	Do.
		Kumaon Province	do	Do.
		Naga Hills	do	Do.
		Manipur	do	Do.
		Northwest Provinces	do	Do.
		Punjab	do	Lingard, Evans.
		Rajputana	do	Do.
	Annam	Cochin China (Tonkin).	Surra	Blanchard, Mollereau.
		Indo-China (Nha Trang).	do	Carogeau.
	Korea		do	W. G. Campbell.

Continent.	Country.	Province, territory, division, district, etc.	Form.	Reported by—
Asia	Persia		Surra	Haig.
	Syria		Dourine	Nocard and Leclainche.
	Java	Bantan	Surra	Paszotta.
		Cheribon	do	Do.
		Deli	do	Vrijburg.
		Rembang	do	Penning.
		Semarang	do	Do.
		Soemedang	do	Hubenet, De Does.
		Tegal	do	Paszotta.
	Philippines		do	Smith and Kinyoun, Slee, Curry, Salmon and Stiles, Strong, Musgrave and Williamson.
Africa	Algeria		Dourine	Chauvrat, Nerche, Signol, Viordot, Lacquerrain.
	Abyssynia		Surra	Bruce, Hallen.
	English East Africa		Nagana	Story.
	Egypt		Surra	Lingard.
	German East Africa		Nagana	Koch.
	Kongo		do	Scloss.
	Madagascar		Surra	Lingard.
	Mauritius		Nagana	Edington.
	Morocco		Dourine	Bruce, Nocard and Leclainche.
	Nubia		Nagana	Hallen.
	Somaliland		do	Brumpt.
	Soudan		do	Schilling, Dupuy, and Pierre.
	Togo		Surra	Koch, Schilling.
			Nagana	E. Martin.
	Tripoli		Dourine	Nocard and Leclainche.
	Transvaal		Nagana	Theilor.
	Zambesi		do	Livingstone.
	Zululand		do	Bruce.
	Malarial zone (see map).		do	Do.
Europe	Bohemia		Dourine	
	France		do	Weber and Nocard, Legrain.
	Germany	Celle	do	Haverman, Hausmann, and Pfannenschmidt, Voges.
		Trakehnen	do	Hertwig.
	Hungary		do	Nocard and Leclainche.
	Spain		do	Weber and Nocard.
		Pyrenees (Navarre)	do	Nocard and Leclainche.
	Turkey		do	Do.
South America	Argentine	Catamarca	Mal de caderas.	Sivori and Lecler.
		Chaco	do	Do.
		Corrientes	do	Do.
		Formosa	do	Do.
				Voges.
		Misiones	do	Sivori and Lecler, Voges.
		Santa Fe	do	Do.
	Bolivia	Matto Crosso	do	Do.
	Brazil		do	Rebourgeon.
				Sivori and Lecler.
	Chile		do	Voges.
	Marajo Island		do	Lacerda.
	Paraguay		do	Thompson.
				Sivori and Lecler.
	Uruguay		do	Do.
North America	United States		Surra	Lingard.
			Dourine	Nocard and Leclainche, Reports of the Bureau of Animal Industry.
Australia			Surra	Lingard.

Fig. 2 gives a schematic representation of the infected areas, drawn from Scheube's map, fig. 3, illustrating the regions of the world in which malaria prevails. Fig. 3 is reproduced to show the relation in geographic distribution of Trypanosomiasis and malaria.

The table and maps given above illustrate the wide geographic distribution of Trypanosomiasis and its special prevalence in the tropical and subtropical zones. New points of infection are being reported from time to time. Neither the table nor the map are complete, and both may contain some inaccuracies owing to the conflicting reports and the fact that some of the references given are not available.

CLIMATIC CONDITIONS.

All the different forms of this disease are infections incident to the periods of wet weather. This statement is made in all discussions of the subject which we have been able to review. The reasons given for the fact are varied, but the true explanation, namely, that biting flies are much more numerous during this season than during any other, is confirmed by nearly all recent writers. Not only this, but the rainy season offers another and equally important condition, which will be fully discussed under modes of transmission—i. e., the dark, cloudy days with great relative humidity make it possible for the fly mechanically to carry the infection for a much longer time. We have shown conclusively that bright sunlight quickly destroys the Trypanosoma; and even if the proper flies *were* more numerous during dry weather, this factor alone would greatly limit their ability to carry infection.

To sum up, the transmission of the disease is greatest exactly under the climatic conditions most favorable to insect life and to the insect's ability to carry the living infection. *Such conditions occur in low-lying, marshy lands during the dark, cloudy days of the rainy season.*

Trypanosomiasis prevails to a limited extent under other circumstances, but we have reason to fear epidemics only when those above described are realized.

We know of no other predisposing causes for surra. All species of animals within certain geographic zones may contract the disease by experimental methods. As will be shown, natural infection is a mechanical processs, so that no reason exists against the supposition that all animals are susceptible to the usual methods of transmission.

A number of writers have stated that a greater percentage of foreign horses coming into an infected zone than of native animals contract the disease. Of 80 horses observed by Lingard, 16 per cent died during the first year, and 70 per cent during the first seven years while under observation. Australian horses were found by him to be more susceptible than the native horses of India.

In our experience in Manila, Australian, Chinese, and American horses do not appear more susceptible than native ponies. In several instances

we have been able to observe the infection in large stables containing both native and American horses, and under these conditions one appeared to contract it as readily as the other. The greatest percentage affected in either case is always found in large groups of animals; and as American horses are more frequently collected in large stables, a superficial deduction from this fact might be misleading. In reality, the higher percentages we have encountered have occurred in stables containing native ponies.

Lingard considers both sexes to be equally susceptible. We have had no opportunity either to confirm or to disprove this statement, as nearly all the horses in Manila are males. Sex certainly plays no part in the communication of the disease in other animals, and there is no reason to suppose it would do so in horses.

In 1885 Steel stated that white and grey mules are more susceptible to surra than darker-colored animals; and, among others, Laveran and Mesnil believe this to be the case with horses as well. They attribute this phenomenon to the supposed fact that flies bite light-colored animals more readily than dark ones. This fact is questioned by some authors, although it is true that on the former animals the flies may be more noticeable than on the latter. We have been unable to verify this statement. White and grey animals have not been infected in greater proportion than others, nor do they more readily attract biting flies. As a matter of fact, our statistics of the Philippine epidemic show them to be less frequently attacked. No importance can therefore be attributed to color as a factor in the spread of the disease.

In general, no material difference in the percentage of infection in horses of varying ages has been found. The greater proportion of animals in Manila are older than four years. Our investigation of rats has shown us that the older animals contain Trypanosoma more often than the younger ones. The difference is probably not due to the greater susceptibility of the former, but is accounted for by the fact that, like dogs, they are prone to fight, and hence very frequently have wounds, particularly about the head, which naturally favor the entrance of the parasites.

TRYPANOSOMA.

HISTORIC NOTE.

In this discussion the species of Trypanosoma have been followed in part at the expense of the chronologic order of publications.

Valentin (1841) discovered hematozoon, and Glugge (1842) parasites, the former in trout (Salmo fario) and the latter in the blood of frogs. Both were probably Trypanosoma, Doflein considering Glugge's description sufficient for the recognition of the genus. In 1843 Gruby observed a flagellate infusorium in frogs, naming it *Tr. sanguinis*; and despite the previous work of others, he has generally been credited with

its discovery, his work being subsequently confirmed by a number of investigators.

Lankester (1871) discovered a sausage-shaped parasite in the blood of frogs, naming it undulina. Gaule (1880) made some further observations on those bodies, which he considered protoplasmic portions of the blood corpuscles separated for a short period of independent life and more prevalent in very dry, warm weather. Leucocytes were seen to be converted into flagellates and then back to leucocytes. Blutschli and Lankester, commenting on Gaule's work, stated, independently, that the conversion of ameboid bodies into flagellates and the reconversion of flagellates into bodies resembling white corpuscles did not prove the latter to be leucocytes. Grassi (1882) observed in frogs a parasite which was named paramecioides.

Blanchard (1890) confirmed Gruby's work and gave the following synonyms: *Paramecium loricatum* Mayer, 1843; *Ameba rotatorium* Mayer, 1843; *Globularia radiata* Wedl, 1848; *Paramecium costatum* Chaussat, 1850; *Undulina ray* Lankester, 1871; *Paramecioides costatus* Grassi, 1882; and *Hematamonas* Mitraphamow, 1883.

Danilewsky (1885) described at least six varieties of parasites in the blood of frogs. He noted the change in the blood at rest from the flagellate to the ameboid stage, as had already been mentioned by others. Ameboid forms were seen to segment into 64 spores, which gradually assumed nomad forms and divided by longitudinal division. Transverse division also was occasionally seen. Flugge (1896) stated that these parasites very closely resembled *Tr. lewisii.* Multiplication consisted in longitudinal and transverse division and spore formation, the latter sometimes being preceded by an ameboid stage. He gave the length as 80 microns and mentioned that the parasites were provided with undulating membranes and flagella. He said that they were found in frogs, tortoises, fish, birds, oysters, chickens, and geese. In general structure they resembled Trypanosoma. Their pathogenic action was not known.

Kominski (1901) again called attention to the probability of an increase in the occurrence of *Tr. sanguinis* Gruby with the age of the animals. They were found at all seasons of the year, and were more common in males than in females. No disease in frogs was produced, and there was no evidence of the mode of transmission in these animals, even when they were kept together for months.

Eberth (1861) discovered in the intestines of birds a parasite which was named by Kent *Tr. eberthi,* but which in all probability was a trichomonas.

Lewis (1879 and 1880) described Trypanosoma found in the rats of India. In a second paper published in 1884 he considered these Trypanosoma identical with *Tr. evansii.* Opie, Flugge, and some other

writers give the credit for discovering *Tr. lewisii* to Osler, but we have been unable to verify the reference, and Osler does not indicate that such is the case in his article on the hematozoon of malaria (B. M. J. March 12, 1887), in which he reviews the work of Lewis and others on the Trypanosoma.

Butschli (1880) found flagellates in the intestinal canal of a nomatode (*Tribolus gracilis*) and also in the intestines of domestic flies. Including flagella they measured about 33 microns in length and were sometimes observed in stellate colonies.

Wittich (1881) discovered in the blood of hamsters a Trypanosoma which he considered identical with *Tr. lewisii*. This observation was confirmed by Koch. Wittich's work was done in Germany on 12 hamsters imported from Africa. He states that his organism answered in all respects to Lewis's description of the Trypanosoma of rats in India. Eleven of his hamsters died; but he did not consider trypanosoma to have played any part in the malady to which they succumbed, although present in all.

G. Evans (1880) discovered Trypanosoma in the blood of horses suffering with the well known surra of India. He proved the causative agency of these parasites in the production of the disease. Steele (1885) confirmed Evans's work, and named the parasite *Spirocheta evansi*. Crookshank (1886) made a report on these parasites, confirming Evans's and Steele's work. He considered these Trypanosoma identical with Mitraphanow's Trypanosoma of carp.

Kent (1881) discovered "herpetomonas" in the intestines of the domestic fly. His parasite had no undulating membrane and was probably not a Trypanosoma.

Certes (1882) found in the digestive tube of an oyster a parasite which has been named *Tr. balbianii*. The general description follows that of Trypanosoma, but slight differences of internal structure were noted. Undulating membrane and flagella were present, but nucleus, nucleolus, and vacuole were not observed. In a later paper he demonstrated a nucleus. He considered this Trypanosoma closely related to Mitraphamow's "hematomonas" (Trypanosoma) of fish. Laveran and Mesnil (1901) found these parasites rarely in Portugese oysters and frequently in common oysters. They say that the bodies were not flagellates and that the presence of an undulating membrane was questionable. They do not consider Certes's organism a Trypanosoma, but rather a bacteria.

Mitraphamow (1883) described Trypanosoma in mudfish (*Cobatus fossilis*). His parasite was 1 to 1½ microns broad and 30 to 40 microns long. He gave a very careful description of these organisms, which occurred in nearly all the fish examined and were more numerous in hot than in cold weather. He gave the group the name "hematomonas" and described two species.

Moebius (1883) found Trypanosoma in oysters (*Tapes decussata* and

Tapes pullastra). These parasites were studied by Lustrac (1896), who considered them Trypanosoma.

Bignami and Celli (1885) found, in the blood of a patient with malarial fever, parasites very closely resembling the Trypanosoma of frogs, birds, and fish. Nepveu (1898) described Trypanosoma in seven cases occuring in men, six of whom were suffering from malarial fever. Barron is quoted by Laveran as having seen flagellates in the blood of an anemic woman. During 1902, Dutton, Ford, Sambon, Manson, and others have described the occurrence of Trypanosoma in human beings. Dutton first published an account of these parasites, found in the blood of Dr. Ford's patient.

Danilewsky (1890) found a Trypanosoma in the blood of birds, naming it *Tr. sanguinis evansii.* Like Blutschli's parasite it had a long flagellum and an undulating membrane. Division was longitudinal, transverse, or by segmentation from the ameboid stage. No symptoms were produced in the host. Danilewsky thought this was probably due to the high temperature of the birds or the tolerance acquired by generations of infection.

Laveran and Mesnil (1901) found Trypanosoma in three kinds of fish—brochet, sole, and redeye. That found in the brochet closely resembled *Tr. evansii,* etc., and was named by them *Tr. remakii,* after Remak, who they say first observed the parasite in 1842. The Trypanosoma from the sole was also of the same general type, and they designated it as *Tr. soleæ.* Laveran and Mesnil state that Trypanosoma had not previously been observed in salt-water fish, but in this they are probably mistaken, for Flugge (1896) reported finding them in the fish of the Mediterranean Sea. The organism which they found in the redeye had a flagellum at each end; they placed it in a separate genus which they called *Trypanoplasma,* giving the parasite the name *Trypanoplasma borrelii.*

Rouget (1896) described Trypanosoma found in the blood of a horse suffering from dourine (beschalseuche), and for two and one-half years continued the study of this organism in susceptible animals. Wasilewsky and Senn (1899) confirmed Rouget's work, and determined the pathogenic action of this Trypanosoma for the horse, passing it through other animals and back to the horse, reproducing the disease. Voges says that this Trypanosoma was discovered by Chauvrat in 1892.[1] Laveran and Mesnil (1901) proposed the name *Tr. rougetii* for the parasite of dourine. Doflein (July, 1901) named it *Tr. equiperdum,* which is the name used also by Salmon and Stiles.

Elmassian, according to Voges, in 1901 first differentiated the Trypanosoma of mal de caderas in South America; while Voges (1902) very carefully described the parasite, proved its pathogenic action, and named it *Tr. equinum.*

[1] Reference not available.

Theiler, in an article published by Bruce (1902), is credited with the discovery of a new Trypanosoma of cattle in South Africa. Bruce proposed the name *Tr. theilerii*. During the same year Theiler found a different species of Trypanosoma in the cattle of the Transvaal, sendings specimens of it to Laveran, who bases his statement that it is a distinct species particularly on the location of the centrosome near the center of the body, close to and sometimes united to the nucleus. He proposed the name *Tr. transvaaliense* for this parasite.

In 1901 Smith and Kinyoun described a parasite which had been observed by Dr. Jobling in the blood of a sick horse in Manila, and this parasite was afterwards determined to be a Trypanosoma. Later in the same year Smith made some additional notes on the organism, and considered it *Tr. evansii*.

Curry (1902) described the parasite and classed it as a Trypanosoma, but was unable to state whether it was *Tr. evansii* or *Tr. brucei*. His description was the first accurate one of the parasite found here.

TECHNIQUE FOR THE STUDY OF TRYPANOSOMA.

For the determination of the presence of Trypanosoma in the blood, only a fresh preparation such as is used for the examination for malaria is needed. The parasites when numerous are readily observed with a DD. or even an AA. objective and No. 4 ocular Zeiss. If they are scarce, considerable time may be necessary to find one, but once seen the diagnosis is determined, and may be facilitated by staining the specimen by any of the approved methods. For a careful study stained specimens are essential.

Fairly good results are obtained by any of the methods used for staining malarial parasites. Romanowsky's method, or any of its modifications, particularly Wright's, gives beautiful pictures. Laveran & Mesnil have also published directions for an excellent stain for these parasites.

A most satisfactory stain for Trypanosoma is one prepared by Dr. Paul G. Woolley, pathologist in this Laboratory, and published here for the first time with his permission.

Fix smears in absolute alcohol for ten minutes.

A. Eosin (w) (Grubler)	gram	1
Distilled water	grams	1,000
B. Polychrome methylene blue (Unna).		
C. Methylene blue (Med) (Grubler)	gram	1
Distilled water	grams	100
D. Of solution B	parts	2
Of solution C	part	1

Mix and add 1 c. c. of A to each 4.5 c. c. of D.

Stain by immersion for twenty or thirty minutes. Wash with water. Wash for two to five seconds with solution A and blot immediately.

The effects on protoplasm and nuclear material may be regulated by longer and shorter exposure to the eosin solution in the last step.

Salmon and Stiles write of flagellates as follows:

In general, but especially in reference to the lower forms, it may be said that the protoplasm is quite homogeneous; a nearly fluid endoplasm may be recognized surrounded by a peripheral ectoplasm, the latter in turn may be bounded by a more dense layer, like a delicate cell membrane. These three divisions are, however, not always very distinct, but grade almost imperceptibly into one another. The pharynx is a very superficial infundibulum; a permanent anus appears to be absent, but the excreta appear to be expelled from a less resistant point at the posterior extremity, without, however, leaving any trace of their passage. The flagellum represents an organ of locomotion, and there may be one or more present. The pulsating vacuole is near the surface, but does not appear to possess either a distinct membrane or a permanent pore. The nucleus is rounded and appears to be provided with a nuclear membrane and nucleolus. If conditions become unfavorable, as when the medium becomes too condensed by evaporation or too toxic by extreme putrefaction, the flagellate may discard its flagellum, become round, and form a surrounding cyst membrane; upon return of favorable conditions, it may escape from the cyst and, forming a new flagellum, recommence its active life; or it may divide during encystment. The division of the free form in multiplying is usually longitudinal. In some cases, the organism encysts before dividing, then by longitudinal division two organisms are formed; the latter may then escape, form their flagella, and become active; or each daughter organism may reëncyst and divide further; or the mother flagellate, when encysted, may divide into a large number of so-called "spores," each of which, upon escaping, forms it flagellum. There may also be a com-

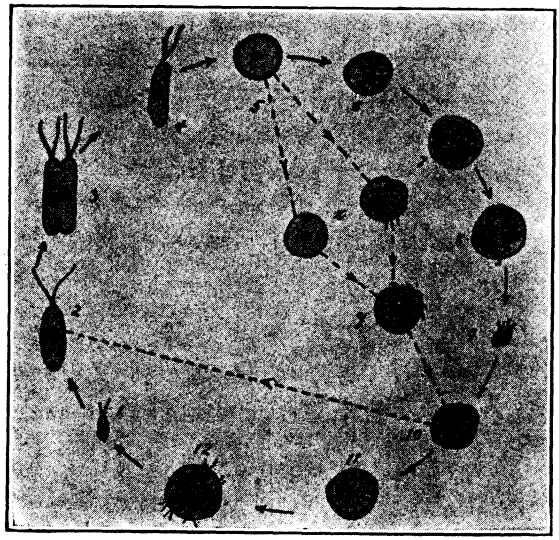


FIG. 4.—Diagram of variations in life cycle of flagellates: 1, A young flagellate; 2, Adult flagellate; 3, Longitudinal division of adult free form; 4, Daughter flagellate; 5, Encystation; 6-8, Division into isogametes; *x*, Division into macrogametes and microgametes, characteristic for some forms; 9, Conjugation of the isogametes; *y*, Conjugation of the micro and macro gametes; 10, Resting stage—zygote; 11-12, Division into young. (After Doflein, 1901, p. 53, fig. 29.)

plete conjugation of the two individuals, followed by encystment and division into numerous young.

The illustration (fig. 4) taken from Doflein is intended to show the variations in the life cycle of the flagellates.

But little is known with reference to that of Trypanosoma, and the majority of writers so express themselves. However, a number have observed in the blood, bodies of various kinds, which they have considered as having to do with the phases in the cycle of development. Voges and others consider the entire life cycle of the parasite to be acted out in the blood, and present very good arguments in favor of their conclusions. Schat is the only author, among those whom we have been able to review, who believes in an intermediate host for the parasites.

He says:

Analogously to what is known to be true in malaria, it appears that the surra parasite also goes through a cycle of sexual development in the body of the fly, and in that of the horse, cow, and donkey an asexual one. The asexual development may be of two kinds, one by the formation of spores and the other by division.

In the blood of horses or cows and in that of our experimental animals we have not observed during the whole course of the investigation a sexual union of the parasites, which is contrary to the observations of Penning and Plimmer and Bradford, who make mention of forms of conjugation.

In this regard we feel justified in supposing that an hypothesis similar to that which Hanson proposed for malaria holds true also in the case of surra—that is, a blood-sucking insect (the stomoxys) serves as a host in this disease also, and that the surra parasite is propagated in the body of this insect outside of the horse and cow.

Fig. 5 taken from this author illustrates his observations.

We are inclined to accept Voges's idea of the life cycle. Trypanosoma have not been found living outside the animal for any considerable length of time; the removal of the animal host from a locality always results in the disappearance of the disease, and attempts permanently to infect media of any kind have usually proved unsuccessful. We have performed a number of experiments with biting flies caught on sick animals, and have failed to convey the disease after twenty-four hours, either by allowing these flies to bite susceptible animals, or by injecting or feeding emulsions of these insects. This of course argues strongly against any but an improbably short cycle in these insects.

Recently Novy has reported the cultivation of *Tr. lewisi* for over a year, without any loss in their virulence, in a media composed of agar and rabbit's blood. Only very brief mention of this report has been received, and we are unable to determine what is meant by "no loss of virulence" in *Tr. lewisii*. The work is interesting, and the results would seem to furnish further evidence that an intermediate host plays no part in the life cycle of Trypanosoma.

FIG. 5.—Illustrating life cycle of Trypanosama (copied from Schat, 1901, Pl. II). Circle A gives a schematicrepresentation of the cycle of a sexual development of the surra parasite through the formation of spores in horses, cattle, and donkeys. Circle B, the changes in the sexual development of the surra parasite through partition, in horses, cattle, and donkeys Circle C, the cycle of sexual development of the surra parasite in the body of the stomoxys fly. Circle A (?), 1, spores introduced into the body of a horse, cow, or donkey through the bite of a fly; 2, The minute conical bodies which result; 3, The young surra parasites which spring from these minute bodies; 4, The matured surra parasite; 5, The ameboid form which results; (?) 6, The formation of spores; 7, The minute conical bodies; 8, The young surra parasite; 9, The matured surra parasite. Circle B, *a*, *b*, *c*, and *d*, represent forms of partition; Circle C 10, Surra parasite in the stomach of the stomoxys; (11), Process of conjugation in the stomach of the stomoxys; 12, The surra parasite produced; 13, 14, Not yet observed, but are probably the subsequent stages of development of the surra parasite in the body of the fly.

GENERAL CHARACTER.

Trypanosoma of all species are in general similar organisms. The family diagnosis, as given by Salmon and Stiles, is as follows:

Flagellate parasitic forms with one chief flagellum directed anteriorly; in some forms a secondary flagellum directed posteriorly; body usually with two angles, and wound more or less in the form of a spiral; one angle of the body provided with an undulating membrane. One nucleus and one centrosome present.

The morphology varies greatly in the same species of Trypanosoma, and also to a greater extent in different species. In general the parasites may be said to measure from 1 to 5 microns in thickness and from 15 to 45 microns in length, including flagellum. They all show very active eel-like movements and some motility. In some species the latter is very slight, the parasites undulating with extreme rapidity, but covering so short a distance as to be easily followed under the microscope; while in others, especially *Tr. lewisii,* the movements are often so rapid in freshly drawn blood that it is impossible to keep the parasite in the field. Some writers have used this variation in motility as a diagnostic point in differentiating the organisms, and in general some importance may be attached to it, but there are so many exceptions, due to conditions which are not understood, that its value in differential diagnosis may partly be disregarded. Variations are occasionally found in one species, often, indeed, in a single preparation, which are nearly as great as those observed between different species.

The flagellum at the anterior end of the parasite, in all forms which we have studied, varies greatly in length. It is always actively motile, pointed, and continuous, with the thickened margin of the undulating membrane ending at or near the centrosome or micronucleus. It may be entirely homogeneous, or it may contain from one to sceveral distinct granules extending well out from the body of the parasite.

The undulating membrane extends along one border of the organism from near the centrosome in the posterior portion to the anterior end of the parasite, from where it continues as the free flagellum. Its breadth and folds vary considerably in the same and in different species of parasites, and also, no doubt, to a considerable extent with the age of the Trypanosoma. Many authors assert that the young forms are entirely free from this membrane.

The nucleus is usually situated in the anterior half of the parasite and varies considerably in size and shape. It is generally oval or round, and assumes other contours with the different stages of division.

The centrosome is usually in the posterior and more blunt end, and appears to have an intimate association with the flagellum and undulating membrane. Its varying distance from the posterior end has been used as a diagnostic point in determining the species; but not much importance can be attached to this, for it has been shown that the posterior end of the Trypanosoma is undoubtedly contractile, so that the distance

from the extremity at which the centrosome is found and also, to a certain extent, the degree of bluntness of this part, a feature which has been so much discussed, depends partly upon its contraction or elongation at the time of fixation for staining and study.

The protoplasm is homogeneous or granular, depending upon the age

FIGS. 6–12.—6, Young adult *Tr. equinum;* 7, Degeneration forms; 8, Young *T. ypanosoma;* 9, Multinuclear adult *Trypanosoma;* 10*a*, Longitudinal division; 10*b*, Transverse division; 10*c*, Multiple division; 11, Irregular form; 12, Two young *Trypanosoma* not yet separated. (After Voges, 1901.)

of the parasite, its environment and no doubt, to a certain extent, upon the species. The granules may vary in number and size from a very few small ones situated in the anterior portion of the Trypanosoma to numerous large ones scattered throughout the protoplasm.

Multiplication.—Voges gives three forms of multiplication, i. e., longitudinal and transverse fission and segmentation. He did not observe conjugation. The chromatin divides into from 3 to 10 segments, which assume irregular shapes and locations, and some of which are often found well up in the flagellum. The nucleus usually divides into equal parts, but may break into several segments. After division the protoplasm may assume various irregular forms. The young nuclei arrange themselves in groups, and the parasite twists and splits by longitudinal or more often by transverse fission. The new division forms are often bowl-shaped, but gradually assume their regular outline. Sometimes a parasite assumes the appearance of a globular mass; nuclei, showing a number of flagella, form around the periphery, and division into several segments occurs.

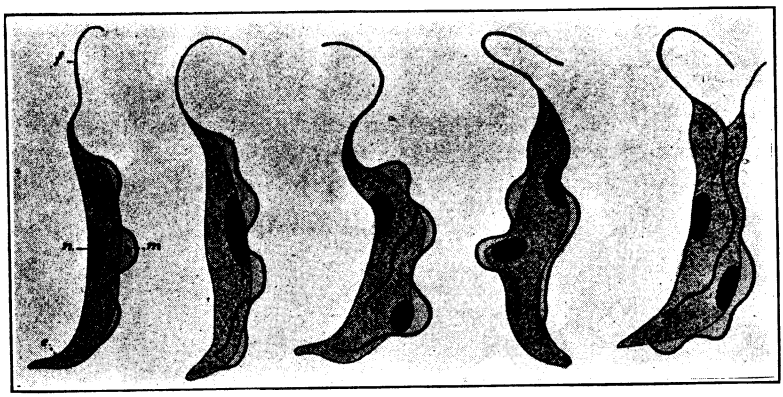
Plimmer and Bradford consider longitudinal and transverse division the more frequent modes of reproduction, although they observed also conjugation, which consisted in the fusion of the micronuclei, followed by an ameboid stage and division by segmentation. The ameboid stage at times occurred independently of conjugation.

Martini, who has recently worked with Trypanosoma obtained from an infected pony imported to Berlin from Togo, gives five stages of multiplication, as follows: First stage: Broadening out of the chromatin grains of the nucleus; flagellum thickens; nucleolus appears to be a thick streak; chromatin granules loosen. Second stage: Two chromatin heaps; two nuclei; pairs remain together; beginning division of the undulating membrane. Third stage: Two distinct membranes seen. Fourth stage: Two flagella, one slightly shorter than the other. Fifth stage: Young Trypanosoma attached only at the posterior end; sometimes one of these is already seen in the process of fission. He did not observe any other forms of multiplication or conjugation.

Schilling did not see multiplication forms in the circulating blood in connection with surra in Togo. He considers the mode of division to be influenced by the number of chromatin granules found in the parasite and to be usually by longitudinal fission. He did not observe ameboid forms or conjugation. He gives two stages in the usual mode of multiplication. In the first one a double undulating membrane is seen, and in the second the whole undulating membrane divides longitudinally and gradually separates the parasite, the posterior end being the last to part. Young forms have no undulating membrane. Daughter parasites are always smaller than the parents.

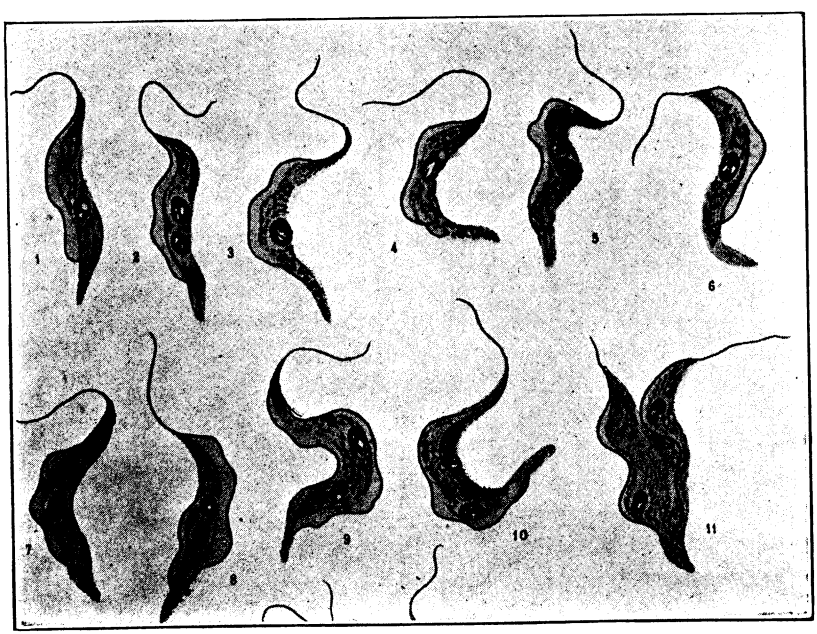
Laveran and Mesnil have studied the forms of multiplication very carefully, and consider that with the Trypanosoma of nagana, multi-

plication in the blood is by longitudinal division only and into young of equal size, which are also nearly as large as the adults. Dividing forms are always present in the blood, and just before division begins the parasite increases in size. The order of division is as follows: (1)

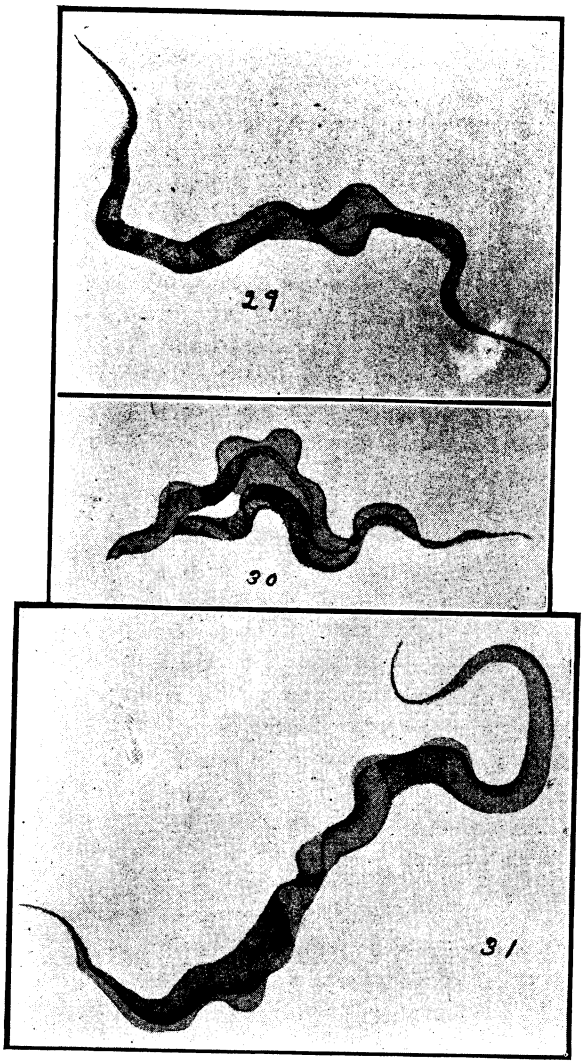


13 14 15 16 17

FIGS. 13–17.—13, *Tr. brucei* (*n*, nucleus; *c*, centrosome; *m*, undulating membrane; *f*, flagellum); 14, Beginning division, showing two centrosomes and partial division of flagellum; 15, 16, 17, Further stages of division. (After Laveran and Mesnil, 1901, figs. 1 to 5.)



FIGS. 18–28.—*T. equinum*, showing various stages of division. (After Sivori and Lecler, 1902, Pl. III.) 1, Trypanosoma with two chromatin corpuscles of the flagellum; 2, Trypanosoma with two nuclei; 3, Trypanosoma with a nucleus, two chromatin corpuscles, and a short flagellum, which starts from the posterior chromatin corpuscle and is united or not to the other flagellum; 4–7, Trypanosoma with a large nucleus, slightly elongated, two chromatin corpuscles; two flagella, one shorter than the other and united to it or not; 8–10, Large Trypanosoma with two separate nuclei; the protoplasm is accumulated toward the poles of the nuclei and is rarer in the middle; two flagella, one longer than the other, or equal and separate; 11, Trypanosoma similar to the preceding, but the flagellated or anterior extremities have begun to separate.



FIGS. 29–31.—*Tr. evansii*, showing dividing forms.

Centrosome, (2) flagellum, and (3) nucleus and protoplasm. The centrosome first elongates and divides into two round bodies, followed by a division of the flagellum. The nucleus increases in size. New nuclei are then formed by direct division. The protoplasm follows the nucleus in separation and may begin at the free end. Two parasites may remain attached at the posterior ends for some time after division, and both may then divide again before separation is complete. These authors have not yet seen the young forms of Kanthuck, Durham, and Blandford, or the ameboid forms of Plimmer and Bradford. They give some variations from the parasite as described by Lewis, but this point will be more fully discussed under "Differential diagnosis of Trypanosoma."

Sivori and Lecler agree with Laveran and Mesnil as to the modes of multiplication illustrated by figs. 18–28.

Rosette formations of Trypanosoma have been extensively noticed, but considerable difference of opinion as to their cause has been expressed. Some consider them as entirely a multiplication phase, others as agglutination, while the majority agree that such formations may be the result of either of these phenomena. There certainly can be no question that these figures occasionally result as a phase of multiplication. Rabinowitsch and Kempner compare them to the segmenting malarial parasite.

The methods of reproduction described comprise those of the most importance and represent the views of many of the writers whom we have been able to review. Schat, as has been seen in the discussion of the life cycle of Trypanosoma, holds some very original opinions. So far as his work has to do with multiplication, he maintains that the asexual, longitudinal division occurs in the blood of infected animals and that the sexual reproduction takes place in certain flies.

In our studies we have never observed conjugation, and in blood under normal conditions reproduction by transverse division or segmentation is very rare. Longitudinal division is by far the most frequent form, and usually takes place in the order given by Laveran and Mesnil. This is not constant, however, for in the same specimen of the parasites taken from the blood of an infected dog, horse, or other animal, we have seen individuals showing this order and others in which the division certainly differed from the course described by these authors. (Figs. 32–35 illustrate this point.) Elmassian, working with the South American disease, has recently reported results similar to ours.

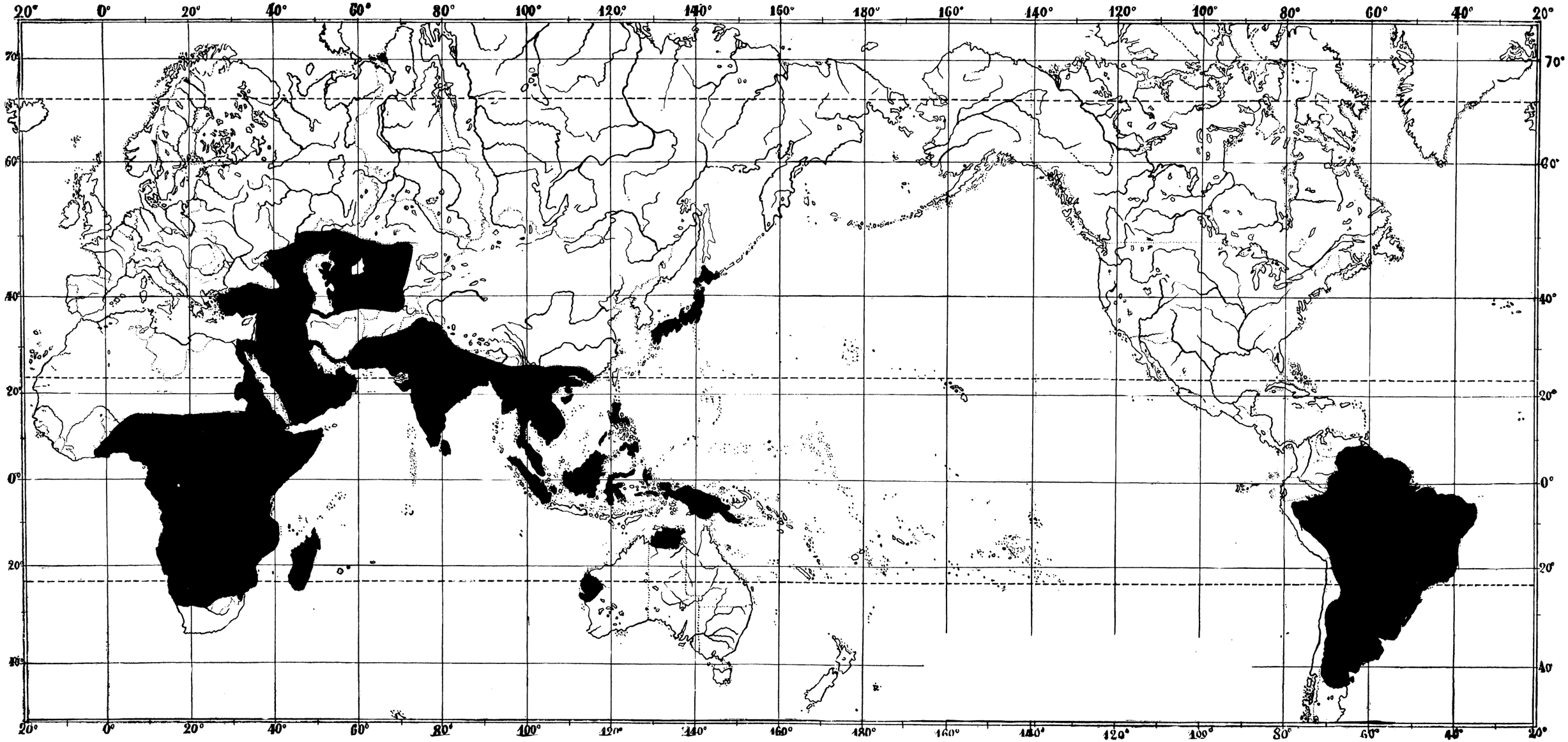


FIG. 2.—Map showing trypanosmatic areas of the world, as compiled from literature. (Scale copied from Schenbe for comparative purposes.)

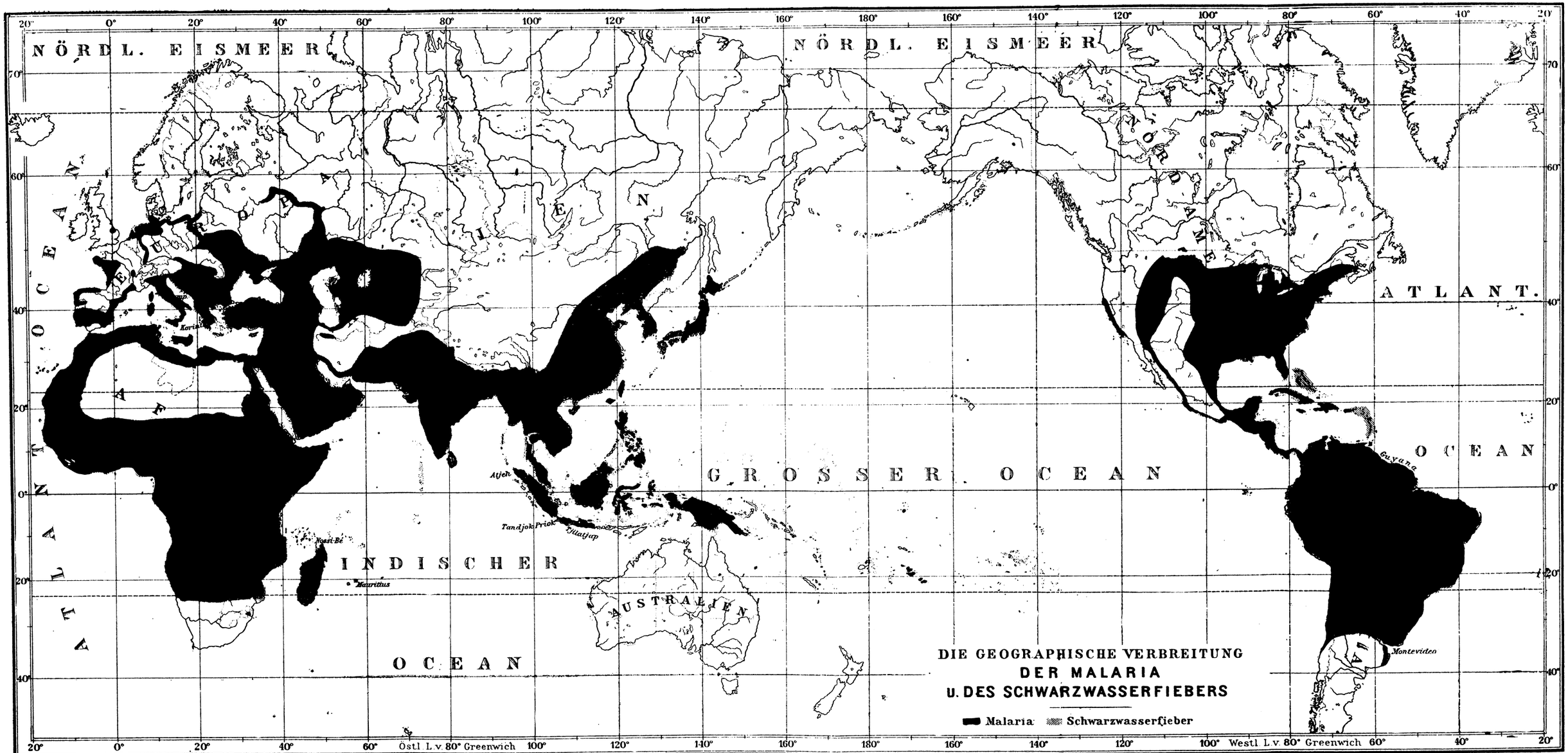
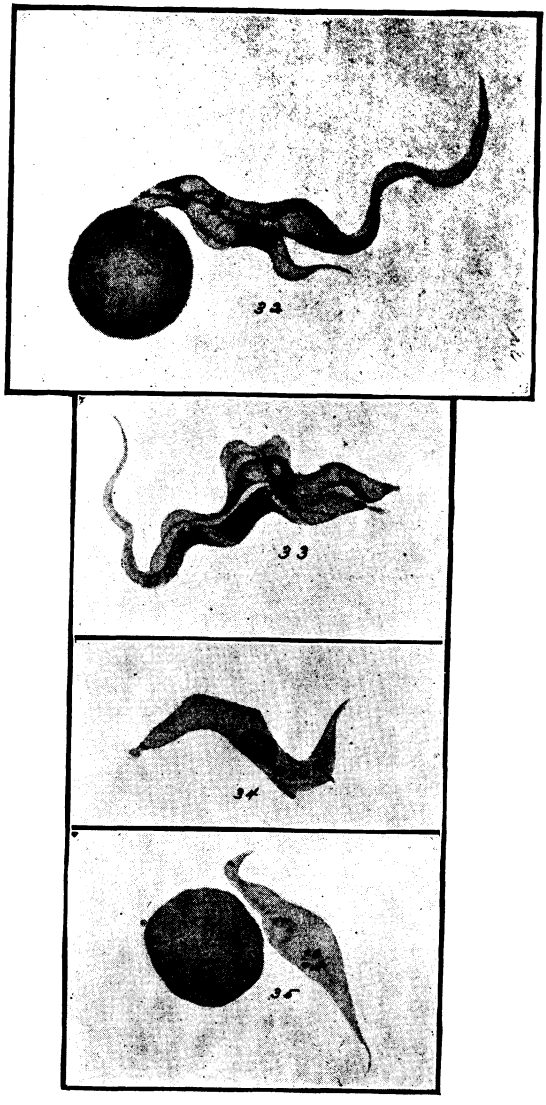


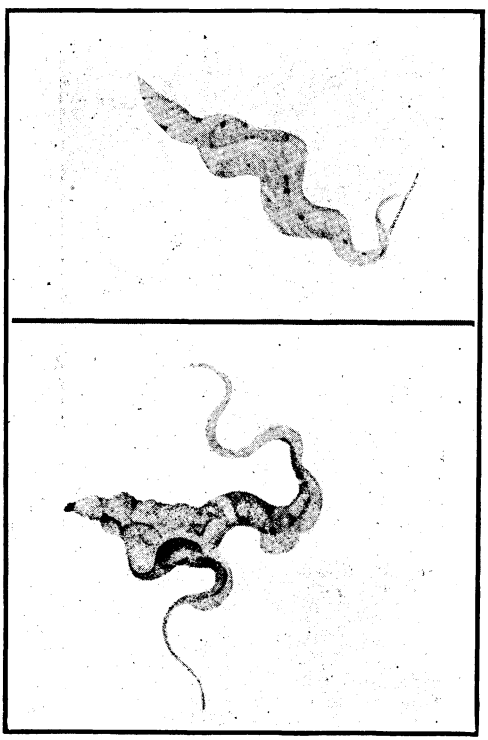
Fig. 3.—Showing malarial regions of the world. (Copied from Scheube.)



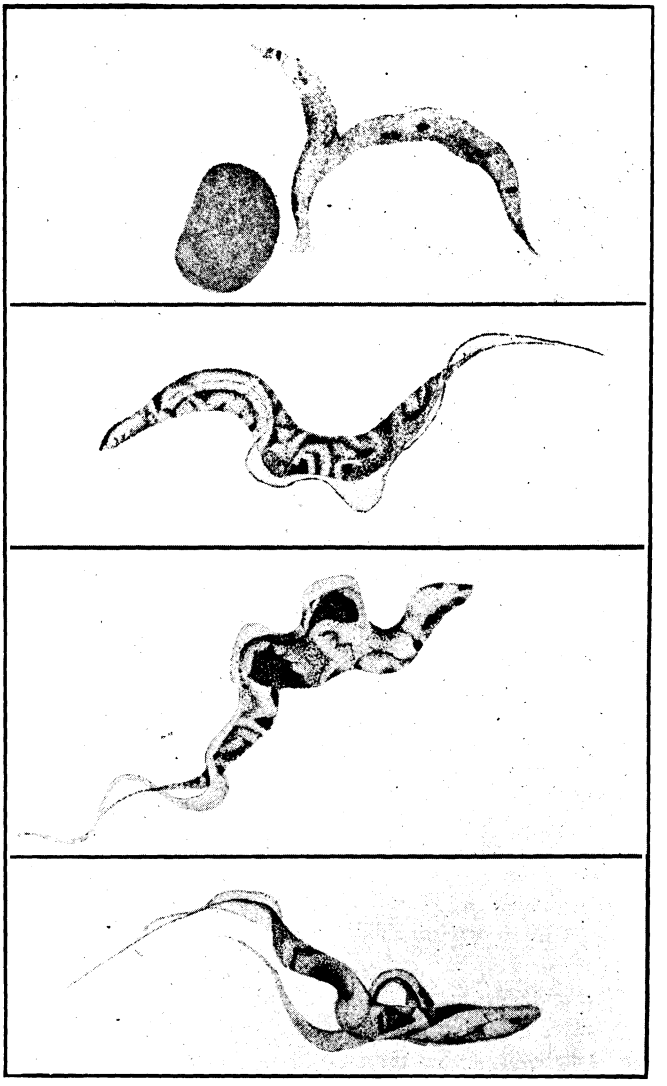
FIGS. 32–35.—Dividing forms of *Tr. evansi*. 32, Irregular division into larger and smaller parasites; 33, Showing division complete except at nucleus; 34, First stage of division, showing thickening of parasite and elongation of nucleus; 35, First stages of division, showing thickening of parasite and loosening of nucleus.

The parasites, just before beginning division is evident, usually becomes thicker, but sometimes this stage is not perceptible. When it occurs it may proceed to such an extent that the transverse diameter of the Trypanosoma will measure from 5 to 7 microns before any other evidence of division can be observed. (Fig. 35.) From this point the picture is not constant. In many forms the next change to be noticed is a division of the nucleus into two or more parts. The centrosome usually divides first, although in some instances the flagella show beautiful division extending well down into the undulating membrane, without the slightest apparent change in either the centrosome or the nucleus.

Schilling's statement that the mode of multiplication depends upon the number of granules which the parasite contains appears to us deserving of careful consideration. Longitudinal division in an individual containing numerous large granules is rarely seen. These parasites assume numerous shapes and often arrange themselves as if segmentation were in progress (figs. 36–41), and in the majority of cases they are the ones that produce the involution forms.



FIGS. 36, 37.—*Tr. evansii* showing various dividing forms.



FIGS. 38–41.—*Tr. evansii* showing various dividing forms.

Agglutination.—Several observers have noted the bunching together of Trypanosoma under certain conditions, and have described the phenomenon as agglutination. Some, as has already been mentioned, consider this to be a multiplication phase, while others suppose it to be the natural position assumed by the parasites just before dying. The process has not been seen at all by some of the most careful investigators.

Laveran and Mesnil regard the agglutination of Trypanosoma as a phenomenon similar to that produced in bacteria and believe it to be brought about by a number of conditions. Among their reasons for this conclusion they mention the continued motility of the parasites after clumping and the fact that the reaction is most marked with weak

FIG. 42.—Showing a peculiar phase of multiplication (*Tr. evansii*).

specific sera and less so with strongly fortified ones. Rabinowitch and Kempner, however, were unable to obtain agglutination with their specific serum. According to Laveran and Mesnil, the reaction may be obtained both with living and with dead organisms, and it does not stop the motility of either the individual or the aggregation of parasites.

The reaction always begins in the same way. Two parasites are seen to join by their posterior ends (fig. 45) and from a number of these, rosettes are built up, the posterior ends of the individuals pointing toward the center and their bodies extending outward like the spokes of a wheel. (Figs. 43–46.) Such masses may, under certain conditions, group themselves and form secondary axes. (Figs. 44 and 47.)

Agglutination often occurs in defibrinated blood containing Trypanosoma and kept on ice. The serum obtained from a rat partly immunized by the injection of blood containing Trypanosoma, when mixed with infected defibrinated blood, causes agglutination.

Parasites which have been killed or paralyzed by formol, chloroform, or a specific serum are agglutinated by the same agencies which produce the reaction in the living organism.

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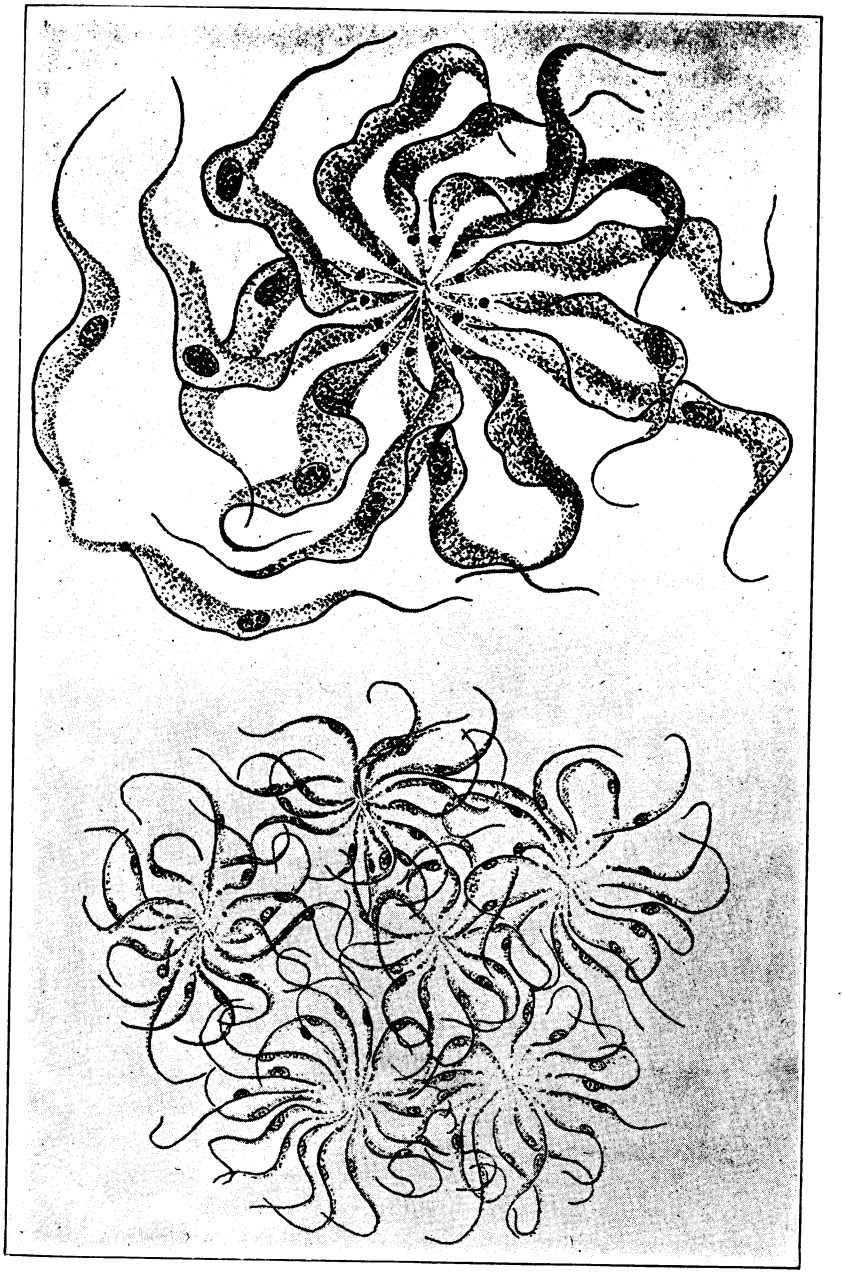

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FIGS. 43–44.—Showing union of two *Trypanosoma*. 43, Primary agglomeration; 44, Secondary agglomeration. (After Stiles and Salmon, 1902, Pl. II.)

Agglutinations often are not permanent, and under certain conditions, according to Laveran and Mesnil, "disagglomeration" takes place. In this the secondary formations are first broken up, and the primery rosettes disunite or lose a part of their elements. They consider this "disagglomeration" to be in inverse ratio to the agglutinating value of the serum employed.

Normal rat's blood has no agglutinative action, but when fortified by inoculations does gain this power. Five to ten c. c. of Trypanosomatic blood injected into a rat will produce a serum capable of agglutinating Trypanosoma in defibrinated blood in a dilution of 1–5 to 1–50.

One of Laveran and Mesnil's rats, which in seven months had received 13 inoculations of blood containing Trypanosoma, gave a serum which in a dilution of 1–10 so paralyzed the Trypanosoma that rosettes were not formed.

Serum exposed to a temperature of 55° to 58° C. during one-half to three-fourths of an hour did not lose its power to agglutinate, but was materially weakened. Exposure to 63° to 65° C. for half an hour completely destroyed its agglutinative properties.

Adult guinea pigs were immunized by several injections of infected blood. Their serum had a feeble agglutinative reaction for *Tr. brucei.* With a similar serum from young guinea pigs no agglutinative reaction was obtained. The serum of a pigeon, guinea pig, or frog did not show an agglutinative reaction for *Tr. lewisii,* but that of a sheep, dog, or rabbit gave a slight one for these parasites. With sera from the horse and the chicken agglutinations were more definite and occurred in dilutions of 1–2 to 1–10.

Of all the animals examined, the serum from the horse was the most active and that of the chicken second, but in both of these the reaction was greater for red blood cells than for Trypanosoma. Human serum did not agglutinate *Tr. brucei,* but the sera of guinea pigs and of pigs, which have no curative properties, gave beautiful agglutinations when mixed with trypanosomatic blood. This would seem to prove that agglutinating and curative properties are separate and distinct. Agglutinations once formed had a tendency to disagglutinate in most sera as well as in other substances. In the rabbit this was accomplished at the end of several hours. They persisted best in the sera of the dog and the sheep. Rats immunized by repeated injections of *Tr. lewisii* showed but feeble agglutinative reaction with their own parasites.

According to Rost, surra blood mixed with goat serum in the hanging drop in a moist chamber killed the Trypanosoma in two and one-half minutes, sometimes with agglutination; control parasites were all dead in twenty-three hours.

Sivori and Lecler, in a preparation of horse's blood containing numerous Trypanosoma, sometimes observed two, three, and even six individuals or more, united at their posterior extremities and arranged in a

45 46

47

FIGS. 45–47.—Trypanosoma of Surra americain, showing phases of agglomeration. 45, Two *Trypanosoma* united at posterior extremities, in a preparation made from the peritoneal exudate of a guinea pig twenty-four hours after intraperitoneal inoculation; 46, Rosette formation produced by mixing equal parts of infected blood of one horse and serum of another some time before death from Surra americain; 47, Large agglomeration seen immediately after making the mixture above mentioned. (After Sivori and Leeler, 1902, pl. 5.)

radiate figure. The center of the figure was sometimes near a red corpuscle or a leucocyte. The parasites so united preserved their motility. In the blood of a young cat, containing numerous Trypanosoma and prepared in a hanging drop, there were visible at the end of an hour 8, 10, or 12 agglomerated parasites. Many of these agglomerations separated after a certain length of time.

Laveran and Mesnil write:

The Trypanosoma of nagana sometimes unite; under certain conditions they form primary agglomerations in rosettes; rarely large secondary agglomerations, which are common in blood containing *Tr. lewisii*, are observed.

These Trypanosoma united two by two would suggest conjugation, but this interpretation is not admissible, as the agglomeration is not observed in pure, fresh blood, and is produced only under conditions which may be called abnormal. The number of individuals which agglomerate is exceedingly variable.

In *Tr. bruccii*, as in *Tr. lewisii*, the agglomerations may be seen to separate after varying lengths of time.

We have seen agglomerations of Trypanosoma in the pure blood taken from the heart, after one-half to one hour, in the peritoneal exudates, after an injection of blood rich in Trypanosoma into the peritoneum of rats or mice, and in blood mixed with physiologic water after being preserved for twenty-four hours on ice or heated for half an hour at 41° C.

On mixing, in equal parts, the defibrinated blood of a rat or mouse, rich in Trypanosoma, and the serum of a horse, we have obtained beautiful persistent agglomerations. The Trypanosoma separated at the end of a few hours. On mixing one part of the serum of a horse and ten parts of blood no agglomerations were produced. The serum of the blood of a pig also gave beautiful agglomerations.

The serum of a sheep, mixed in equal parts with the blood of a rat or mouse, rich in Trypanosoma, gave, in one case, a beautiful agglomeration; in another the agglomerations were not so beautiful and less persistent. The serum of a deer gave small nonpersistent agglomerations.

The serum of human blood did not show itself either agglutinative or microbicidal.

The following sera mixed in equal parts with the blood of a rat or mouse, rich in *Tr. bruccii*, did not show any agglutinative properties: The serum of a rat, normal or immunized against *Tr. lewisii*, and agglutinative for these Trypanosoma, the serum of a normal chicken, the serum of a chicken inoculated several times with *Tr. bruccii*, the serum of a normal goose, and the serum of a goose inoculated several times with blood rich in Trypanosoma of nagana.

If there is added to a few drops of blood rich in *Tr. bruccii* a drop of water slightly acidulated with acetic acid, Trypanosoma are seen to agglomerate and change their forms rapidly. On adding a drop of water slightly alkalized with soda no agglomeration occurs.

Trypanosoma when dead still tend to agglomerate, but the process then takes place very irregularly.

Hefferan, commenting on Laveran and Mesnil's statements regarding agglutination of *Tr. lewisii*, doubts the correctness of their observations, giving her reasons for so doing. (Centralb. f. Bakt., etc., bd. 8, No. 22, May 26, 1902.)

Curry noted that parasites in infected monkeys' blood mixed with

human blood lost their motility in twenty minutes and agglutinated. Chicken's blood mixed with infected monkey's blood gave similar results.

Schilling states that in cattle immunized with the peritoneal exudate of dogs inoculated with infected blood, the serum killed the Trypanosoma on the fourteenth and fifteenth days, and in the hanging drop in from thirteen to twenty-five minutes; but he has little to say of agglutination.

On reviewing the work done on the agglutination of Trypanosoma, it will be seen that results have been uncertain and inconstant, the subject being left in an unsatisfactory state.

Hefferan's criticisms of Laveran and Mesnil's work in this line, and the statement of Rabinowitch and Kempner that no agglutinations were obtained with their specific serum makes the value of other results doubtful.

So far our work has developed nothing convincing. We have seen the rosettes and other described figures of agglutination, but they have been too inconstant and have occurred under too many conditions to be of any very great significance. Circumstances under which these figures have at one time appeared have at other times produced no results; and they have even occurred under conditions which are not supposed to favor agglutination.

Our results in the agglutination of *Tr. evansii* by various substances described as producing this phenomenon have been at variance with much of the recent work done along this line and more in accord with Rabinowitch and Kempner's conclusions. We have not observed a single condition which constantly gave agglutination figures. Such results were obtained occasionally with various substances, but reactions indistinguishable from these sometimes occur in infected blood without any additions.

Cow No. 158 was immunized up to 3,000 c. c. doses of infected blood and failed to produce a serum which would agglutinate Trypanosoma with any degree of constancy. Similar results were obtained with chicken and human serum as well as with those secured from numerous other sources. Various mixtures of these sera were likewise unsatisfactory. Several chemicals, such as thymol, turpentine, and chloral, would occasionally give what appeared to be agglutination; but no regularity could be observed.

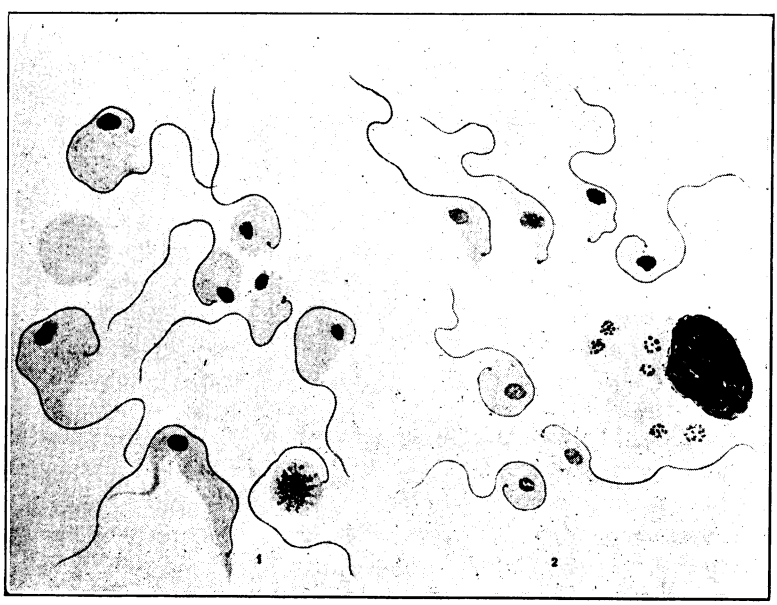
After weighing all evidence in the case and applying our own results, we must conclude with several others that the so-called phenomenon of agglutination is of no value from a *diagnostic point of view; and if it is in reality an agglutination, it is too uncertain in its occurrence to serve as an index of immunity or susceptibility.*

Involution forms.—Involution forms are produced by surroundings unfavorable to the life of the parasite. Laveran and Mesnil mention

among the conditions which favor their production (1) the blood of rat rich in Trypanosoma, mixed with the serum of some other animal and kept for several hours in a hanging drop; (2) blood containing Trypanosoma and heated to 41° to 42° C. for one hour or more; (3) infected blood injected into the abdominal cavity or the conjunctiva of birds and withdrawn after one to three hours; (4) parasitic blood placed in an ice box or in some other way subjected to freezing, and (5) rat's blood containing Trypanosoma and treated with arsenic, etc.

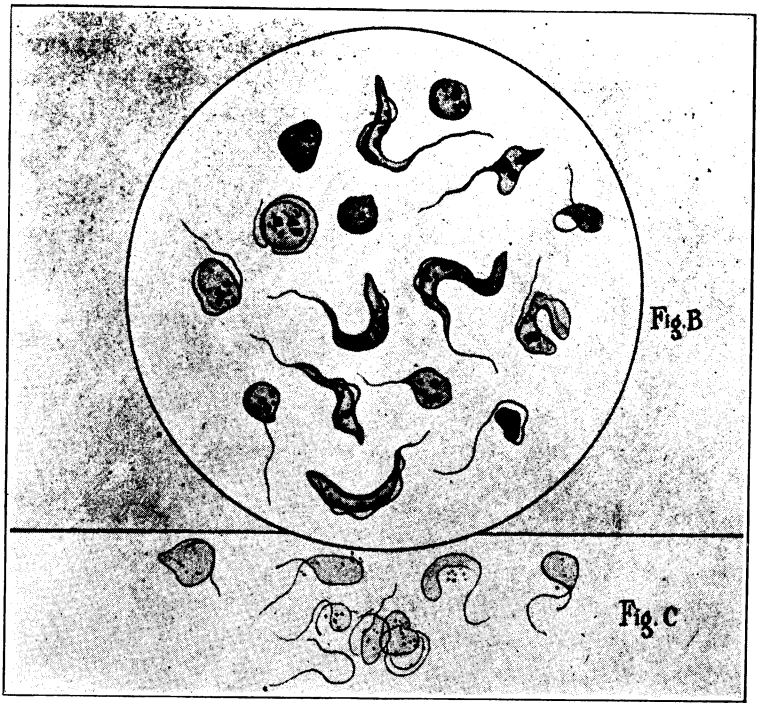
The same authors give the following as the principal type or involution forms. Round, flask-shaped bodies, in stained specimens usually showing nuclei, centrosomes, and flagella. If dividing forms have assumed this shape, two nuclei, two centrosomes, and two flagella may be seen. These bodies may form small agglutinations, and it is probable that the latter are what Plimmer and Bradford called plasmodic forms. Flask-shaped Trypanosoma are not always dead when not moving, as they may still be capable of conveying the disease to rats.

Trypanosoma in dying undergo profound alterations: (1) The protoplasm disappears and takes no color; (2) the shape is indicated only by a faint line of countour; (3) the nucleus stains faintly; (4) the protoplasm and nucleus disappear, leaving nothing but the flagellum and centrosome and forming a knob at one end, and (5) the flagellum may be found alone or attached to the centrosome.



FIGS. 48-49.—Involution forms of *Tr. equinum*. 48, Involution forms seen in horse twenty-four hours after recovery; 49, Involution forms seen in the blood of a horse twenty-four hours after death. Large mononuclear cells containing parts of *Trypanosoma*. (After Sivori and Lecler, 1902, pl. 6.)

Figs. 48, 49, 50, and 51 illustrate some of the involution forms given by various authors and figs. 52 to 59 others which have been observed in our work.



FIGS. 50–51.—50 (Fig. B), *Trypanosoma* of mal de caderas mixed with serum of chicken and preserved on ice for six days, maintaining their vitality; several have assumed abnormal forms; all have their nuclei reduced to large granulations, stained according to Laveran; 51 (Fig. C), *Trypanosoma* in the process of destruction; the free filaments have no centrosomes. (After Lignieres, Recueilde Med. Vet., vol. 10, No. 2, Jan. 30, 1903, Pl. II.)

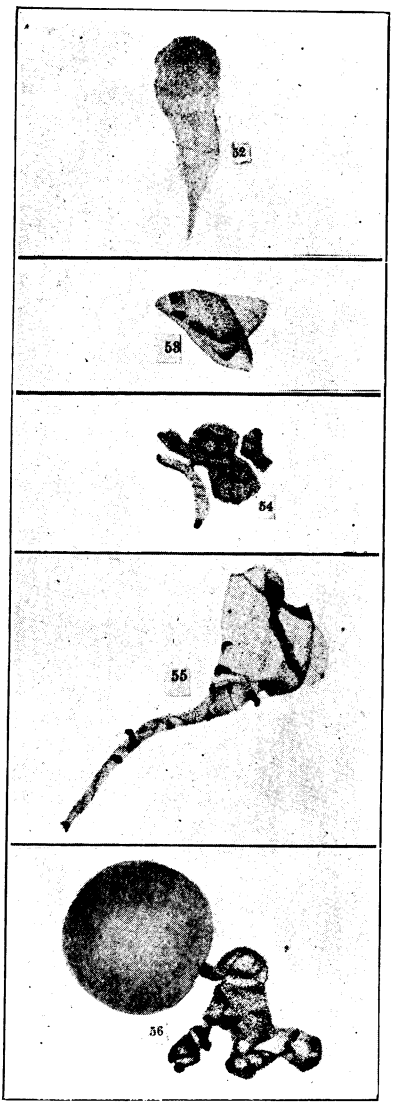
DISTRIBUTION IN THE BODY.

The great majority of writers agree that Trypanosoma in an infected animal are found in all the body juices, and are not present at the same time in enormous numbers in one part of the body with but few in another. Animals having many parasites in the blood, when killed show them also in the organs; but if they are not demonstrable by microscopic examination in the former, they are also not found in the latter. The blood of animals suffering from the disease is always infectious by animal inoculation, although there are periods during its course when the parasites can not be found for days by microscopic examination. Plimmer and Bradford, and others state that the lymphatics near the point of inoculation first show the parasite, and that the animal's blood may be infectious for two days before the parasites are found therein.

There are, however, a number of writers who do not accept the general

statement given above, but who believe the parasites to be more numerous in certain organs, such as the lymphatics and the bone marrow, than in others. Martini regards the spleen, lymphatics, bone marrow, and, to a less extent, the liver and kidneys, as the places for the destruction of trypanosoma.

Elaborate experiments have been performed to show whether or not reproduction occurs in any special organ, but practically without success. It has repeatedly been shown that a hyperplasia of the lymphatics



FIGS. 52–56.—Various involution forms of *Tr. evansii*.

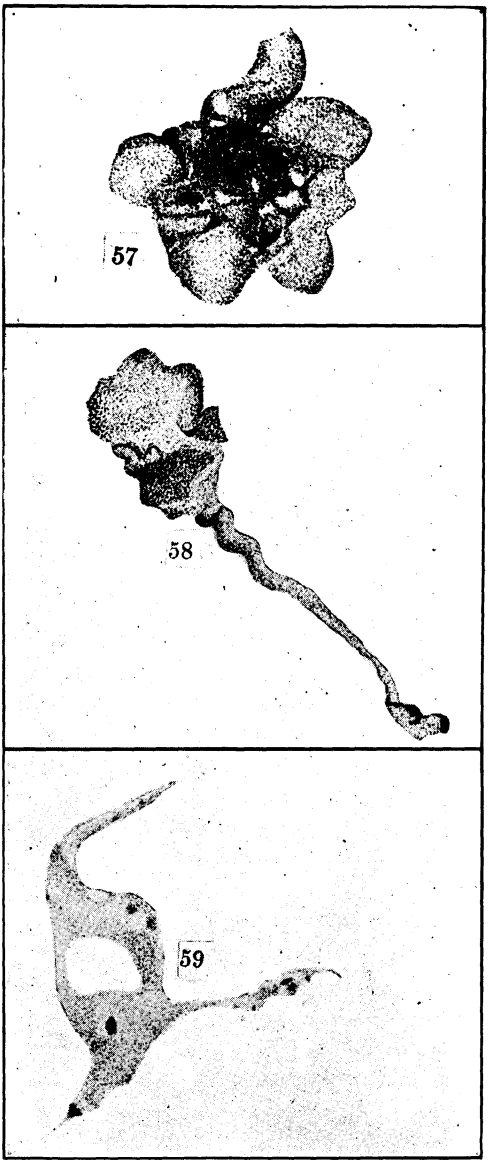


FIG. 57–59.—Various involution forms of *Tr. evansii*.

occurs to a greater extent in an animal inoculated after splenectomy than in one on which this operation has not been performed.

Here again we revert to Voges's statement that the whole cycle of the parasite is acted out in the blood; and it would seem that the experiments conducted to determine the place of multiplication in the body tend to

support this statement. It is certainly true that the Trypanosoma are pretty evenly distributed in the body juices and that similar forms are found in all parts.

It seems to be a very generally accepted opinion that Trypanosoma inoculated into the peritoneal cavity undergo a considerable multiplication before entering the circulating blood, and by some this time has been considered as constituting the true period of incubation.

Parasites in the dead body.—Trypanosoma live only a short time in the body after death. Within two hours signs of degeneration begin; the parasites shrink, assume irregular shapes and then disappear. Motile parasites are not usually found two hours post-mortem. Ample work fully demonstrating this important point has been done. In exceptional cases living parasites have been found as late as sixteen hours after death; but this condition is rare. Our work in this line has consisted in determining the longest time post-mortem during which the blood could be proved infectious by inoculation into susceptible animals. Results are conclusive that this is rarely greater than twenty-four hours. However, in one instance blood has been found to convey the disease forty-eight hours after death.

When an animal, in the blood of which trypanosoma are present, dies, the parasites are then found in all the organs; and conversely, where none appear in the former, they are also absent in the latter. They are generally distributed, and multiplication forms do not appear in exceptional numbers in any one organ; however, they are usually somewhat more numerous in the spleen, liver, and lymphatic glands than in the bone marrow, and are seldom present in the medullary canal. They are found in the serous fluids and exudates of the joints, but rarely in the urine.

Schilling's results were somewhat exceptional. He says that "Trypanosoma were not found in the spleen when positive in the blood, and the peritoneal exudate and bone marrow showed parasites of a budding form;" and again, "that Trypanosoma might be absent from the fluids and tissues, but were constantly present in the bone marrow. The number of parasites in the spleen varied greatly, but there was never a great accumulation or multiplication of forms." He draws the conclusion that multiplication of parasites occurs in certain organs, while others destroy them.

TRYPANOSOMA OUTSIDE OF THE BODY.

Although Trypanosoma in a natural condition are not known outside the body and propagate only to a limited degree in any known artificial media, yet under favorable conditions they can be kept for a considerable time outside the body, a fact which has been believed to afford certain diagnostic points for different species. Berg kept Trypanosoma of fish for six days in blood at 12° C., and Mitraphanow from three to

four days in salt solution. Laveran and Mesnil showed that during warm weather living forms of *Tr. lewisii* were found in blood which had been maintained at room temperature for four days. Once during cold weather motile parasites added to chicken's or pigeon's blood in a hanging drop were observed after eighteen days. Kept on ice and in blood mixed with physiologic water, they were observed during thirty to fifty-two days, the blood at the end of this time being virulent. They withstood 41° C. very well, but when heated to 50° C. for five minutes were all killed.

Voges states that outside the body Trypanosoma of mal de caderas disintegrated rapidly, blood usually being noninfectious after from three to four days. However, he noted one exception where infection occurred with blood which had been kept aseptically for fourteen days. Several writers have tried to attenuate Trypanosoma with formalin, heat, and several other means, but entirely without success. The parasites were either all killed so that no infection resulted, or they were as virulent as in control blood. *Tr. equiperdum* (elmassianii) continued motile for forty-eight hours at a temperature of 36° C.

Laveran and Mesnil state that when human serum and blood containing Trypanosoma were mixed in equal parts in a hanging drop the Trypanosoma showed feeble action in one-half to one hour, and generally were not motile at the end of two to three hours. Kanthack, Durham, and Blandford determined *Tr. evansii* to be destroyed by complete drying; they also demonstrated four days as the greatest length of time during which they could live in aseptically drawn blood. Laveran and Mesnil, Voges, and others have shown that the blood of an animal infected with Trypanosoma was not capable of transmitting the disease after twenty-four hours.

Martini states that the warm stage does not increase the life of Trypanosoma in vitro. He noted a bunching of parasites in dead bodies, and considered this a form which they assumed on dying.

Laveran and Mesnil state that the serum of immune deer mixed in the hanging drop with infected blood showed no parasiticidal action, and this was found to be true with most other sera. Infectious nagana blood exposed to a temperature of 41° C. for one hour showed deformed and nonmotile parasites, but was still capable of transmitting the disease. Exposure to a temperature of 41° C. and 44° C. for a short time killed the Trypanosoma and the blood was no longer infectious.

Many chemical substances quickly destroy the parasites outside the body. Laveran and Mesnil report that they were rapidly killed by the newer silver salts, and that a 1 per cent solution of Toluidin blue attenuated them somewhat, as was shown by the prolonged incubation period. Sivori and Lecler consider the life of the parasite in vitro to be variable, depending upon the conditions produced, but never reaching four days.

Schilling noted that Trypanosoma were soon destroyed by a 60 per cent solution of bile.

Bruce showed that dried blood was infectious after twenty-four hours in one out of three experiments, with an incubation period of sixteen days. In two cases it was not infectious at the end of forty-eight hours. Aseptically drawn, virulent blood was infectious for four days, and after seven did not produce the disease.

Laveran and Mesnil state that the movements of Trypanosoma are retarded by cooling and accelerated by warming the blood in which they are contained. They were not immediately killed by a temperature of 50° C. to 55° C. below zero. Their experiments were as follows:

Experiment I.—Rat blood with many *Tr. bruceii* diluted with potassium citrate solution and kept at 18° C. for one-half hour. One and one-half hours after returning to room temperature it still showed many normal looking motile Trypanosoma. Mice injected in the conjunctiva with this blood died in the usual time with Trypanosomiasis.

Experiment II.—Similar dilutions of blood exposed twenty minutes to 15° C. and eight minutes to 25°–30°. After two hours warmed blood showed normal looking motile Trypanosoma and was infectious in the usual time for mice.

Experiment III.—Similar solution of blood exposed for one-half hour at 15° C. and five minutes at 50°–55° C. After two hours the thawed and warmed blood contained normal looking and motile Trypanosoma and was infectious for mice in the usual time.

Experiment IV.—Same as No. 3, except that the freezing and thawing was repeated. It was still pathogenic for mice, but was slightly slower in its action.

These authors demonstrated that blood infected with *Tr. brucei* heated three hours at 40° C. or one hour at 42° was still virulent. Blood infected with *Tr. brucei* heated twenty minutes at 40° to 44° C. killed nearly all the Trypanosoma, and when heated to 44° to 45° C. all the parasites were quickly destroyed.

Blood taken aseptically and mixed with citrate solution at room temperature, according to Laveran and Mesnil, was virulent for three days, and Trypanosoma lived longer in a mixture of blood and serum than in blood alone. In the defibrinated blood of a rat mixed with the serum of the host, motile Trypanosoma were still observed after three days.

Human serum and that of refractory animals was not considered less adapted to the preservation of Trypanosoma than that of more susceptible animals. *Tr. lewisii* lived longer on ice than at room temperature; but this was not true of *Tr. brucei.* Blood containing *Tr. brucei,* after being kept on ice for three to five days, was often noninfectious, though it still contained slightly motile Trypanosoma. Involution forms quickly ap-

peared in blood kept on ice, their morphology differing in no respect from that of the involution forms produced by other causes.

We have experimented extensively with the object of determining the length of life in vitro of the Trypanosoma with which we have been able to work, and on the whole have obtained results similar to those arrived at by most recent writers on other Trypanosoma.

Our experiments made to determine the action of heat and cold on parasites confirm, in the main, the conclusions drawn by Laveran and Mesnil, including the differentiation of *Tr. lewisii* by its ability to live longer than *Tr. evansii* in the ice box. We failed to find any constancy in the agglutinations these authors describe. They did occasionally occur, following exposure to conditions especially adverse to life; but they were not constant and also took place in the hanging drop. We can not attach to this phenomenon the importance given it by some authors.

Several specific sera mixed in the hanging drop in equal parts with blood rich in Trypanosoma gave no appreciable results, with the possible exception of the mixtures containing antiplague and antirinderpest sera. The Trypanosoma were usually nonmotile in the plague serum at the end of forty minutes, and in the rinderpest serum sometimes as early as thirty minutes. In two out of five experiments made with the latter, the blood was noninfectious for rats at the end of one hour. In most of the experiments made with serum the parasites lived as long as in the control drop, and in some instances much longer.

A 1–500 solution of quinine mixed in equal parts with blood containing Trypanosma arrested the motility of the parasites in from five to ten minutes. With a 1–1,000 solution of methylene blue the Trypanosoma lost their motility from five to twenty minutes earlier than in the control. They are less affected by solutions of alcohol, glycerin, or ether.

No perceptible action was produced an the Trypanosoma by mixing the infected blood with equal parts of the following substances: A 1–1,000 solution of acetozone; 1–1,000 solutions of the soluble eosins; alcohol; potassium acetate; potassium chlorate; potassium cyanide; salt solution; picric acid; oxalic acid; and the chlorides of magnesium, calcium, and barium. Indeed, in many of these solutions the parasites remained active longer than in control.

The Trypanosoma were quickly destroyed by mixing infected blood in the hanging drop with equal parts of the following substances: A 1–1,000 solution of arsenious acid; a 1–1,000 solution of turpentine; a 1–1,000 solution of corrosive sublimate; a 1–500 solution of chloral hydrate; a 1–500 solution of carbolic acid; a 1–500 solution of formalin; a 1–1,000 solution of potassium permanganate; and a 1–200 solution of quinine.

CLASSIFICATION.

Authors differ considerably in the classification of this family of the *Protozoa*.

Doflein (1901) divides the genus *Tr. Gruby* into three subgenera, as follows:

1. Major flagellum present 2
   Major flagellum absent, or very short and thick ..... *Trypanosoma*
2. Undulating membrane continued posteriorly in a flagellum so that 2 flagella are present ..... *Trypanomonas*
   Posterior flagellum absent, undulating membrane ending on or before end of body ..... *Herpetosoma*

Laveran and Mesnil (1901) have shown Doflein's *Trypanomonas* to be a distinct genus and have given it the name *Trypanoplasma*, with *Trypanoplasma borreli* as a type species.

Salmon and Stiles criticize Doflein's classification and divide the family *Trypanosomidæ* into two genera—*Trypanosoma and Trypanoplasma*. With a few minor changes this classification is adopted tentatively in this report. However, as will be seen by following the discussions, we are strongly of the opinion that at least two of the parasites of mammals and probably others are identical with *Tr. evansii*, and in reality the names of these should fall as synonyms of *Tr. evansii*.

PROTOZA, class *Mastigophora*, subclass *Flagellata*, order *Monandida*, family *Trypanosomidæ*, genus *Trypanosoma* Gruby.

Trypanosoma: One flagellum present extending from the centrosome along the undulating membrane and becoming free at the anterior extremity.

Trypanoplasma: Two flagella, one extending anteriorly and the other posteriorly.

Trypanosoma rotatorium Mayer, 1843, L. & M., 1901.

Synonyms.—*Amœba rotatoria* Mayer, 1843, July; *Paramœcium loricatum* Mayer, 1843, July; *Paramœcium cestatum* Mayer, 1843, July; *Trypanosoma sanguinis* Gruby, 1843, November; *Globularia radiata sanguinis* Wedl, 1850; *Undulina ranarum* Lankester, 1871; *Herpetomonas* Kent, 1880; *Paramecioides costatum* Grassi, 1881; *Paramecioides costatus* Grassi, 1883; "*Trypanosoma sanguinis* Gruby" of Lanessan, 1882; "*Globularia radiata* Wedl, 1849," of R. Blanchard, 1885; *Hæmetomonas* Mitrophanow, 1883; *Trypanomonas ranarum* Danilewsky, 1885; "*Spirochæte* of Steele," 1885; "*Hemotomonas*" of Blanchard, 1888; "*Trichomonas sanguinis*" of Crookshank, 1886; *Trypanosoma ranarum*, 1889; *Trypanosoma costatum* Danilewsky, 1889; *Trypanosoma costatum ranarum* Danilewsky, 1889; *Trichomonas ranarum* (Lankester) Danilewsky, 1889; *Trichomonas batrachorum* Danilewsky, 1889; "*Trypanosomos* Gruby" of Laveran, 1895; "*Trypanosomum*" Chauvrat, 1896; "*Trypanosome* Gruby" of Buffard and Schneider, 1900; "*Paramœcium loricatum* Mayer" and "*Paramœcioides costatus* Grassi" of Laveran and Mesnil, 1901.

Trypanosoma avium Danilewsky, 1885, of birds.

Synonyms.—*Trypanosoma avium* Danilewsky, 1885; *Trypanosoma fusiforme* Danilewsky, 1889; *Trypanosoma minus* Danilewsky, 1889; *Trypanosoma majus*

Danilewsky, 1889; *Trypanosoma sanguinis avium* Danilewsky, 1889; *Trypanosoma costatum* Danilewsky, 1889; *Trypanosoma major* Danilewsky, 1889.

? *Trypanosoma eberthii* Kent, 1880, of fowls (intestine).

Synonyms.—*Trypanosoma eberthi* Kent, 1880; "*Trypanosoma eberthi*" of Lanessan, 1882; (?) *Cercomonas gallinarum* Davaine, 1877; (?) *Cercomonas gallinæ* Rivolta, 1880; *Trypanosoma eberthi* of Lecerlq, 1890; *Trychomonas columbarum* Kruse, 1896.

Trypanosoma cobitis Mitrophanow, 1883, of mudfish.

Synonyms.—*Hæmatomonas cobitis* Mitrophanow, 1883; *Trichomonas cobitis* (Mitrophanow) Crookshank, 1886; *Trypanosoma piscium* Danilewsky, 1885; *Trypanosoma (Herpetosoma) cobitis* (Mitrophanow) of Doflein, 1901; *Hæmatomonas cobitidis* Luehe, 1902.

Trypanosoma carassii Mitrophanow, 1883, of fish.

Synonyms.—*Hæmatomonas carassii* Mitrophanow, 1883; *Trichomonas carassii* (Mitrophanow) Crookshank, 1886; *Trypanosoma piscium* Danilewsky, 1889; *Trypanosoma fusiforme* Danilewsky, 1889; *Trypanosoma (Herpetosoma) carassii* (Mitrophanow) 1883, Doflein, 1901.

Trypanosoma soleæ Laveran and Mesnil, 1901, of soles.

Trypanosoma balbianii Certes, 1882, of oysters.

Synonyms.—*Trypanosoma balbiani* Certes, 1882; *Trypanosoma balbianii* (Certes) Balbiani, 1888; "*Trypanosoma balbianii*" of Danilewsky, 1889.

Trypanoplasma danilewskyi Labbe, 1891.

Synonyms.—*Trypanomonas danilewskyi* Labbé, 1891; *Trypanosoma (Trypanomonas) danilevskyi* (Labbé) Doflein, 1901.

Trypanoplasma borrelii Laveran and Mesnil, 1901.

Trypanosoma lewisii Kent, 1880, of rats.

Synonyms.—*Herpetomonas lewisi* Kent, 1880; "*Herpemonas lewisi* Kent," 1880; *Trichomonas lewisi* (Kent) Crookshank, 1886; *Herpetomonas lewisii* Danilewsky, 1889; *Trypanomonas murium* Danilewsky, 1889; *Trypanomonas lewisii* (Kent) Labbé, 1891; *Trypanosoma lewisi* Kent; *Trypanosoma* Kanthack, Durham and Blandford, 1898; *Trypanosoma rattorum* Boerner, 1901; *Trypanosoma (Herpetosoma) lewisi* (Kent) Doflein, 1901.

Trypanosoma evansii Steel, 1885, of surra.

Synonyms.—*Spirocheate evansi* Steel; "*Spirochæta evansi* Steel," 1885, of Crookshank, 1886; *Hæmatomonas evansi* (Steel) Crookshank, 1886; *Trichomonas evansi* (Steel) Crookshank, 1886; "*Homotomonas evansii*" Blanchard, 1888; "*Trichomonas sanguinis* Crookshank" of Balbiani, 1888; "*Spirochetæ evansii*" of Nariman and Vaz, 1893; "*Spirochetæ evansii* Steel" of Laveran, 1895; "*Trypanosomum evansi* (Steel) Chauvrat," 1896; *Trypanosoma evansi* (Steel) Pease, 1897; *Trypanosoma evansii* Pease, 1897; *Herpetomonas lewisii* Steel, of Danilewsky, 1889; *Trypanosoma (Herpetosoma) evansi* (Steel) Doflein, 1901; "*Trichomonas sanguinis evansi* Crookshank" of Doflein, 1901.

Trypanosoma brucei Plimmer and Bradford, 1899, of tsétsé disease.

Synonyms.—*Trypanosoma brucii* Plimmer and Bradford, 1899; "*Trypanosoma brucei*" of Schneider and Buffard, 1900; *Trypanosoma (Herpetosoma) brucei*

Plimmer and Bradford, of Doflein, 1901; *Herpetomonas brucei* (Plimmer and Bradford) Laveran and Mesnil, 1901.

Trypanosoma nepveui, of man.

Synonyms.—Trypanosoma gambiense Dutton, 1902; *Trypanosoma fordii* Maxwell, Adams, 1903; *Tr. ugandiensii,* 1903.

Trypanosoma rougetii Laveran and Mesnil, of dourine.

Synonyms.—Trypanosoma equiperdum Doflein, 1901, July; *"Trypanosoma" (Herpetosoma) equiperdum* Doflein, 1901; *Trypanosoma (Hæmatomonas) equiperdum* Doflein of Luehe, 1902.

Trypanosoma equinum Voges, 1901, of mal de caderas.

Synonyms.—Trypanosoma equinum Voges, 1901; *Trypanosoma equinum* Voges of Railliet, 1901; *Trypanosoma elmassiani,* 1902.

Trypanosoma theillerii Laveran and Mesnil, 1901, of cattle.

Trypanosoma transvaaliense Theiler, Laveran and Mesnil, 1902, of cattle.

Trypanosoma rotatorium Mayer, 1843.—The length of this parasite including the flagellum (which is 10 to 12 microns long) is usually

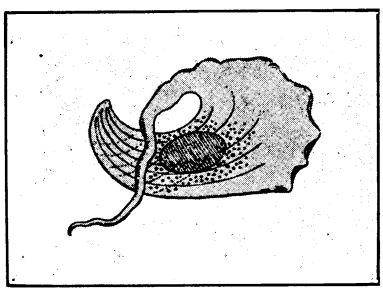
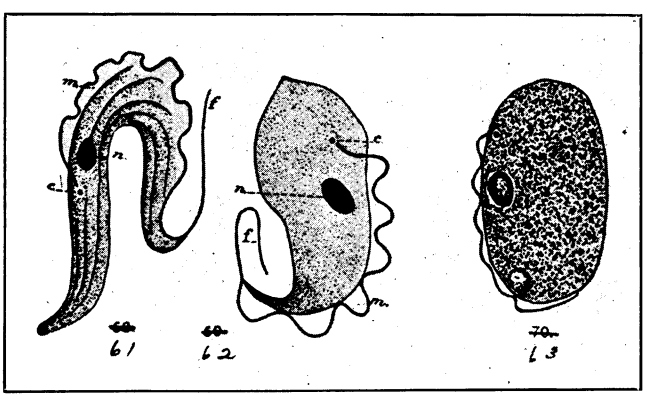


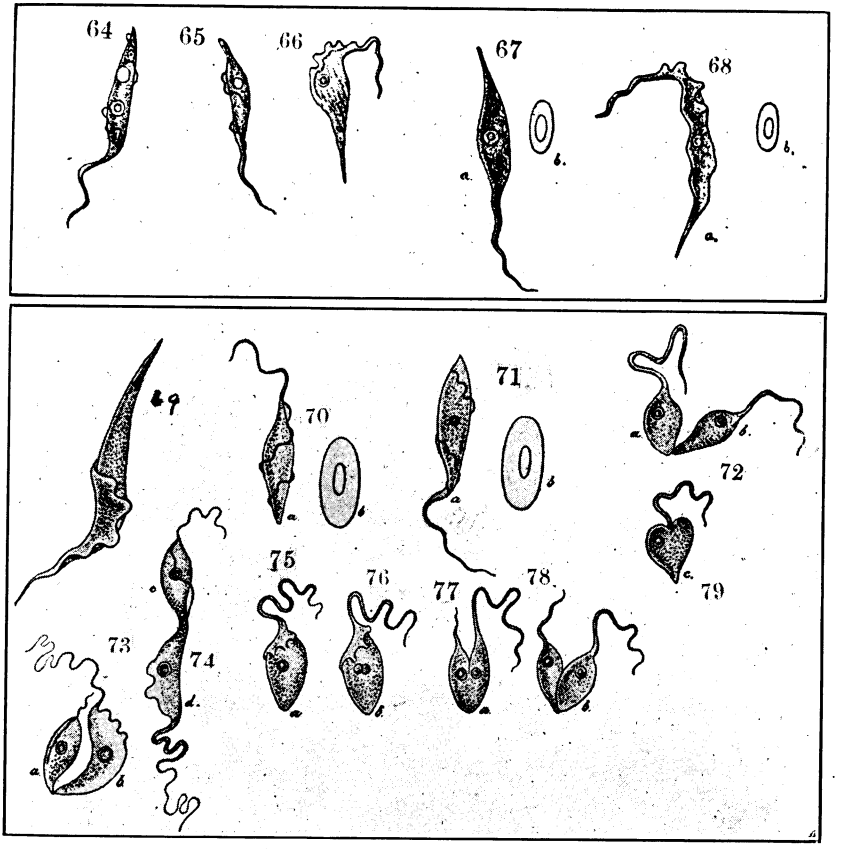
FIG. 60.—*Tr. sanguinis* Gruby. (After Doflein, 1901, fig. 32.)



FIGS. 61–63.—Showing different forms of *Tr. rotatorium.* , Flagellum; *m,* Undulating membrane; *n,* Nucleus; *c,* Centrosome. (After Laveran and Mesnil, 1901, figs. 1–3.)

given as being about 40 to 80 microns, while the breadth is 5 to 10 microns. Doflein says it has a broader body and undulating membrane than most of the other *Trypanosoma*. It has a granular protoplasm and a large clear nucleus. One end is somewhat blunt and the other is provided with a short flagellum.

Salmon and Stiles in their specific diagnosis of this parasite, after giving the dimensions, state that "the body is compressed, semilunate,



FIGS. 64-79.—Various forms of *Trypanosoma* of birds. (After Salmon and Stiles, 1902, figs. 53-64.)

twisted; the convex border membranous and undulating; the posterior extremity of the body portion pointed and curved inward, the opposite one produced into a long tag or tail like appendage, which almost equals in length the remainder of the body; surface of the body coarsely striate longitudinally; endoplasm or parenchyma slightly granular; endoplast ovate, central."

Habitat: Blood of frogs (*Rana esculenta, Rana temporaria,* and *Rana arborea*).

According to Doflein the mode of transmission is not fully determined, and this statement is confirmed by Laveran and Mesnil. There may be more than one species of this parasite, but so much of the work regarding it is unsatisfactory that for the present it seems advisable to consider it a single species. It apparently has no special pathologic significance, and for that reason is of but little importance in this paper.

We have examined the blood of a large number of several varieties of frogs here, but have failed to find this or any other *Trypanosoma.*

Trypanosoma avium Danilewsky, 1885.—Salmon and Stiles give as its specific diagnosis: "*Trypanosoma* 18 to 60 microns long; body cylindrical, compact, fusiform, and homogeneous; anterior extremity gradually attenuate, and continuing directly into a long or short flagellum; flagellum intimately united with the undulating membrane, which extends from the flagellum to the posterior extremity; nucleus spherical in equator or anterior half of body."

There have been found in literature several references reporting *Trypanosoma* in birds, but most of the descriptions are inadequate. We have examined a large number of birds of several varieties in the Philippine Islands, but we have failed to find *Trypanosoma* in their blood and have been entirely unable to infect them with the *Trypanosoma* with which we have worked.

Trypanosoma eberthii Kent, 1880.—Salmon and Stiles and others doubt the correctness of the classification of this species; Doflein believes that two or three species have been confused in its description.

It is described by Doflein as half-moon in shape, the concave side being the body of the parasite and the convex the undulating membrane, which has numerous small folds. The protoplasm is homogeneous and contains a nucleus. One end of the body is blunt and the other is tapering and continues into a short, motionless projection. Kent says that the membranous border is often spirally convoluted around the thicker central portion, the entire body under such conditions assuming an auger-like aspect.

Habitat: Glands of Lieberkuhn, cecum and ileum of chickens, doves (?), ducks, and geese. Rivolta and Pfeiffer, according to Doflein, found this organism or a similar one in poultry diphtheria.

In the few chickens, pigeons, and small birds which we have examined in Manila these parasites have not been found. It seems more than likely that some of the *Trichomonidæ* have been mistaken for *Trypanosoma;* as it is doubtful that so strict a blood parasite would be found in the intestinal canal of birds.

Trypanosoma balbanii Certes, 1889.—Doflein gives the length of this parasite as 50 to 180 microns and the breadth as 1 to 3 microns. Salmon and Stiles give the length as 50 to 180 microns and the breadth as 1 to 30. It is described by Doflein as an elongated parasite with slender

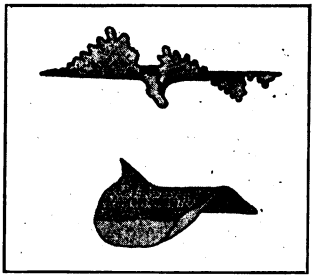


FIG. 80.—*Tr. eberthii.* (After Doflein, 1901, fig. 33.)

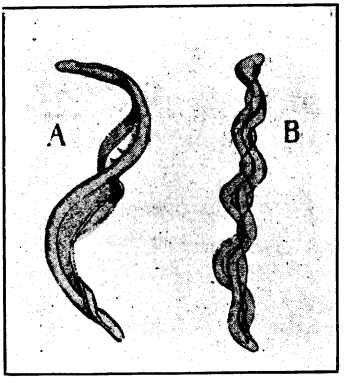


FIG. 81.—*Tr. balbianii* Certes. (After Lustrac.)

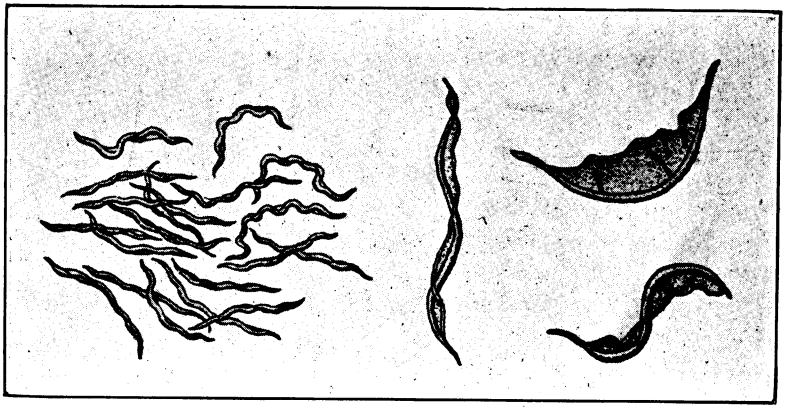


FIG. 82.—*Tr. balbianii* Certes. (After Salmon and Stiles, 1902, figs. 76–79.)

body and slender undulating membrane. Certes, Lustrac, and others have observed longitudinal division, which Lustrac says begins in the undulating membrane. Laveran and Mesnil do not consider this parasite a member of the family *Trypanosomidæ*.

Habitat: Intestines of oysters (*Ostra edulis, Ostra angulata, Grypha angulata*) and mussels (*Tapes decussata, Tapes pallustra*).

Pathogenesis: Not known.

Neither this nor any other Trypanosoma has been observed by us in the examination of a large number of oysters of the Philippine Islands.

Trypanosoma cobitis Mitrophanow, 1883.—A very active and motile Trypanosoma, 30 to 40 microns long by 1 to 1.5 microns broad. Doflein says that one end tapers abruptly and the other gradually, ending in a flagellum 10 to 15 microns in length. The undulating membrane is distinct in prepared specimens. The protoplasm is homogeneous, except, according to Doflein, in multiplication and degenerating forms, where it may be granular.

Habitat: Blood of mudfish (*Cobitis fossilis*).

Pathogenesis: Described experiments have failed to convey the infection from fish to fish or from fish to animals, by inoculation.

Trypanosoma carassii Mitrophanow, 1883.—Doflein says that it is very similar to *Tr. cobitis,* but more flattened; that the undulating membrane is better developed and the body more uniformly pointed at both ends and larger than that of *Tr. cobitis.*

Habitat: Blood of fish (*Carassius vulgaris*). Doflein observed it or a very similar parasite in the tench (*Tinca vulgaris*).

Pathogenesis: Not known. The *Trypanosoma* which Doflein observed were found in sick fish.

The fish of the Philippine Islands are apparently free from this *Trypanosoma.*

Trypanosoma remaki Laveran and Mesnil, 1901.—Trypanosoma 28 to 30 microns in length and very slender. Two sizes and possibly two varieties. Very closely resembles *Tr. lewisii,* actively motile, with undulating membrane, both ends tapering with a long flagellum at the anterior end, protoplasm finely granular. The larger forms measure 45 microns in length and 2 to 2.5 microns in breadth, and stain somewhat better than the small variety.

Habitat: Blood of pike (*Esox lucius*).

Pathogenesis: Not infectious by inoculation.

We have not succeeded in finding *Trypanosoma* in the blood of fish in the Philippine Islands, although several varieties of both salt and fresh water fish have been examined.

Trypanosoma soleæ Laveran and Mesnil, 1901.—A *Trypanosoma* resembling *Tr. lewisii,* 40 microns in length, very actively motile, structure in general like that of the other members of the family, posterior

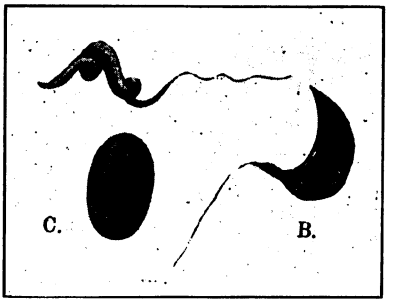


FIG. 83.—*Tr. cobitis* Mitrophanow. (After Mitrophanow.)

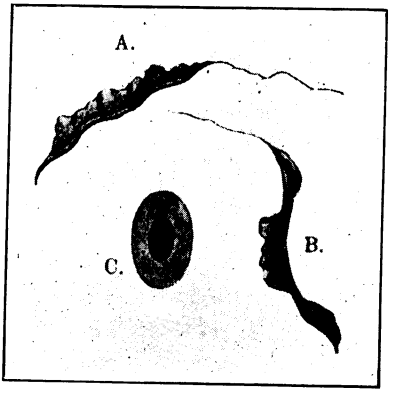
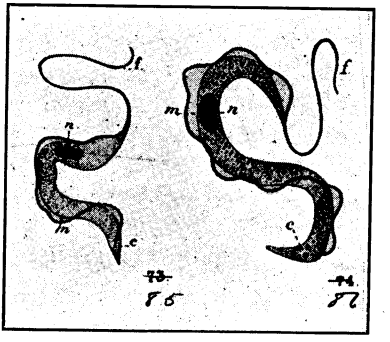


FIG. 84.—*Tr. carassii* Mitrophanow. (After Mitrophanow.)



FIGS. 85–86.—85, *Tr. remakii* parvum; 86, *Tr. remakii* magnum; *f*, Flagellum; *m*, Undulating membrane; *c*, Centrosome; *n*, Nucleus. (After Laveran and Mesnil, 1901, fig. 3.)

end not so sharp, nucleus oval, centrosome present and undulating membrane well developed.

Habitat: Blood of sole (*Solea vulgaris*) of France.

Pathogenesis: Laveran and Mesnil did not succeed in infecting other animals with this *Trypanosoma.*

Trypanoplasma borreli Laveran and Mesnil, 1901.—Laveran and Mesnil describe this parasite as a *Trypanoplasma,* with two flagella, both extending from the centrosome and one going to each extremity, the anterior one bordering a well-defined undulating membrane and extending into a free flagellum 15 microns in length. The total length of the parasite with flagella is about 50 microns and the breadth 3 to 4 microns. One end is more pointed than the other and very motile. This parasite changes its form, sometimes resembling an ameba. Two chromatin masses lie close together near the junction of the posterior and anterior parts of the body, one of these masses resembling a nucleus and the other a centrosome.

It is to be noted here that Labbé (1891) had already seen a *Trypanoplasma* with two flagella in the blood of leeches and that Kunster (1898) had mentioned a similar organism found in the blood of a guinea pig. Fig. 89 is Labbé's illustration of the parasite observed by him in leeches in 1891.

Habitat: Found by Laveran and Mesnil in the blood of the redeye (*Leuciscus erythropthalmus*) of France.

Pathogenesis: Not infectious by inoculation.

Trypanosoma Lewisii Kent, 1880.—Gros in 1845, Chaussat in 1850, and later other authors found remarkable parasites, which for a long time were the cause of controversy, in the blood of rats and hamsters. While some considered them as amebæ, flagellates, etc., there were others who did not recognize them as independent organisms, but as spermatazoa, or, as Siebold, even considered them small patches that somehow had been torn loose from the walls of the circulatory and lymphatic systems.

After a long pause interest in this organism was again aroused, and a large number of articles dealt with the subject, without mentioning or recognizing the earlier works. Lewis (1879 and 1880), Wittich (1881), Robert Koch (1881), Crookshank (1887) published several treatises on *Tr. lewisii* to which Kent in 1882 gave its name; but he placed it in the genus *Herpetomonas,* which according to diagnosis at present accepted possesses no undulating membrane. Labbé, Danilewsky, and Mitrophanow also dealt with this species, while all investigators of surra likewise refer to it. Interest was awakened through the investigations of surra and tsétsé fly disease, and has recently been increased by the observations of Koch, Rouget, and others, but especially by the important works of Rabinowitch and Kempner, Wasielewski and Senn,

and Laveran and Mesnil, which explain the methods of multiplication and widen our knowledge considerably.

Rabinowitch and Kempner, as well as Wasielewski and Senn, have

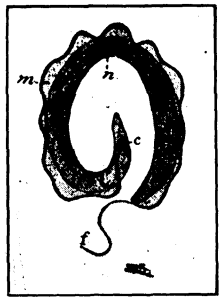


FIG. 87.—*Tr. soleae*; *f*, Flagellum; *n*, Undulating membrane; *c*, Centrosome. (After Laveran and Mesnil, 1901, fig. 3.)

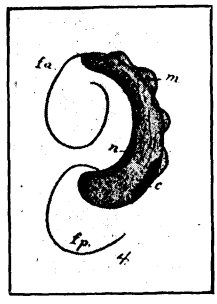


FIG. 88.—*Trypanoplasma borreli*. (After Laveran and Mesnil, 1901, fig. 4.)

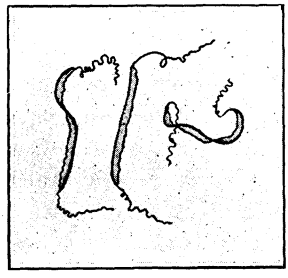


FIG. 89.—*Trypanoplasma danilewskyi*. (After Salmon and Stiles, 1902, fig. 83.)

studied multiplication forms with a considerable degree of thoroughness. Their investigations agree on essential points. According to them there are three kinds of multiplication; two forms of division,

and one form of multiplication through segmentation, a division into numerous rosette-shaped sprouts lying side by side.

Whether conjugation takes place is yet unknown, but to Doflein it appeared that such a process precedes the multiplication by division into sprouts. Some pictures of Rabinowitch and Kempner point to such a course. This, however, is still very problematical, especially since the life history of *Trypanosoma* is not fully understood.

Senn, for example, considers the ordinary division as budding, since, according to his statement, the mother parasite is always larger than daughters produced by her. The individuals are seen rapidly to increase, especially after a new infection, impetuously dividing themselves. The divisions are often multiple, and the mother is seen to separate into two, three, four, and even eighteen daughters. Senn considers the rosette formation to be the result of a division into several individuals, and not as a special form of multiplication; but since the complete life cycle of the species has not been positively determined, this is also a mere theory.

In any case, separation into two parts is the typical form of longitudinal divisions; and the apparent deviations in prepared specimens explained by the delicacy of the protoplasm, which on being killed assumes the most varied forms. As yet resting forms have not been observed.

Habitat: This species lives in the blood of rats (*Mus rattus, Mus decumanus, Mus refuscens*) and probably in that of the hamster (*Cricetus arvalis*). Thus far it has been observed in Europe (Germany, England, France, Italy, and Russia), in Asia (India, Japan, and the Philippines), and in Africa (Dutch East Africa and Algiers).

Pathogenesis: The parasite is found in the blood of animals attacked by the disease. In the case of rats it sometimes produces sickness and death, but it is generally found in apparently healthy animals. Wild rats are often found infected with it, but in tame ones, especially in the white variety, its occurrence is rare, although these as well as white mice are susceptible to the disease. In many instances 25 to 29 per cent, but in others a much smaller percentage, of wild rats has been found infected. Under certain conditions epidemics seem to break out.

Whether the *Trypanosoma* which appear in hamsters and those found in rats are identical can not yet be stated positively.

This parasite is very common in rats in numerous localities, both in the Trypanosomatic zone and in countries which have apparently always been free from the disease in domestic animals. For the purpose of study it is one of the most easily obtainable, and because of its non-pathogenic significance and its very close relation to the more virulent forms is one of the most important of the genus. The history and synonyms recognized by leading authors have been given above.

Salmon and Stiles give as the specific diagnosis:

Eight to 10 microns long by 2 to 3 microns broad; 24 to 25 microns long by 1.4 microns broad (Laveran and Mesnil, 1901); a very refrangent granule (near centrosome) in place of which a clear vacuole is seen in stained preparations. "Animalcules exceedingly minute, attenuate and vermicular under normal conditions, but highly polymorphic and capable of assuming a variety of contours; flagellum single, terminal, two or three times the length of the extended body; no contractile vesicle * * * as yet detected."

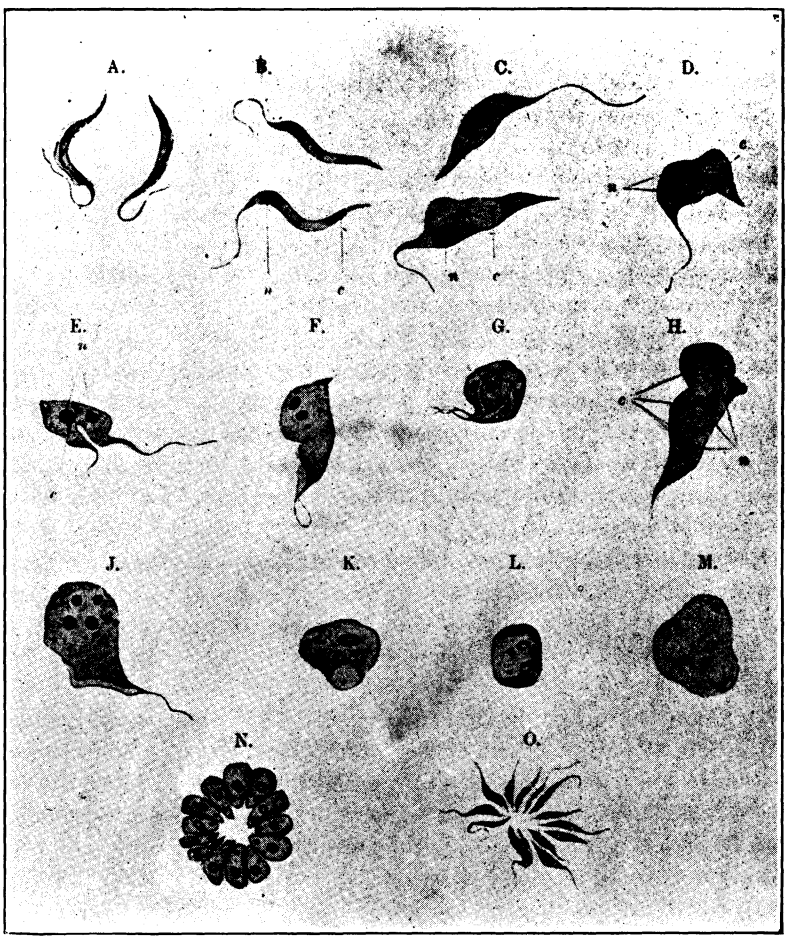


FIG. 90.—*Tr. lewisii* Kent. A, Adult living parasites; B, Adult stained parasites; C–F, Stages of longitudinal division; G, multiple longitudinal division; H, Beginning multiple transverse division; I–M, Other forms of division; N–O, Rosette forms of division; *n*, Nucleus; *c*, Centrosome. (After Rabinowitsch and Kempner.)

Doflein's description, translated, reads as follows:

The *Trypanosoma* of rats is lance-shaped and reveals a very finely granular protoplasm, around which a thin hyaline but clearly visible endoplasm lies. From the latter spring the flagellum and the undulating membrane. The flagellum is

almost as long as the body itself, and springs from the posterior end of the parasite with a central nucleus-like structure considered as its origin, and then continues as a thickening of the edge of the undulating membrane, first becoming free at the anterior end of the parasite and wriggling about in the medium surrounding it. In the anterior part of the parasite is found the somewhat large nucleus, staining deeply and filled with a dense chromatin network. A contractile vacuole has not been seen. The length of *Tr. lewisii* varies between 8 and 10 microns and the breadth between 2 and 3 microns.

As is true of other parasites, *Tr. lewisii* undoubtedly shows variations in size. Individuals are found not measuring more than 15 to 20 microns in length by 1 to 2 microns in breadth. On the other hand, specimens are seen which may be fully 30 microns long and 3.5 microns broad. The average measurements of adult parasites observed in Manila rats, obtained from hundreds of specimens, are 25 microns long by 2.5 microns broad.

On the whole the motility of this parasite in the hanging drop is probably greater than that of any other *Trypanosoma*. The active, darting motion observed is not characteristic of all specimens, and we have been unable to determine the responsibility of outside influences for these variations.

In addition to *Tr. lewisii* Manila rats certainly harbor *Tr. evansii*, and we have not yet satisfied ourselves that there is not a third species in some of them. This makes observations of *Tr. lewisii*, based upon the examination of the *Trypanosoma* found in rats, more difficult, and in the past has probably been responsible for the lack of harmony in results obtained.

Numerous comparisons of diagnoses made of rat *Trypanosoma* by morphological characteristics and by those determined by animal experiments with the same organisms have fully convinced us of the futility, in many cases, of depending upon microscopic data for the diagnosis of *Tr. lewisii* or of other *Trypanosoma*.

The most trustworthy and important diagnostic point for this parasite, besides the animal test, is the fact already brought out by others, particularly by Laveran and Mesnil, that it lives so long in the ice box, where in solutions of blood in potassium citrate *Tr. lewisii* retain their activity for days and always longer than *Tr. evansii* which on various occasions have been tested side by side with them. They not only retain their activity longer, but also remain infectious for rats for a much greater length of time.

This is not true, however, when compared with the possible third variety of rat *Trypanosoma* mentioned above. These are excessively motile, remaining so for a long time in the ice box, where they maintain their infectiousness. The supposition that these *Trypanosoma* belong to a separate species has been gradually evolved from experimental data. There have been times when we have felt confident we were working with *Tr. lewisii*, only to find the parasites infectious for dogs,

monkeys, etc., after two or three days in the ice box. At present this point has not been satisfactorily determined and must be left to a future discussion.

Of this we are sure, that *Trypanosoma* corresponding in every respect to the descriptions given of *Tr. lewisii*, including their noninfectiousness

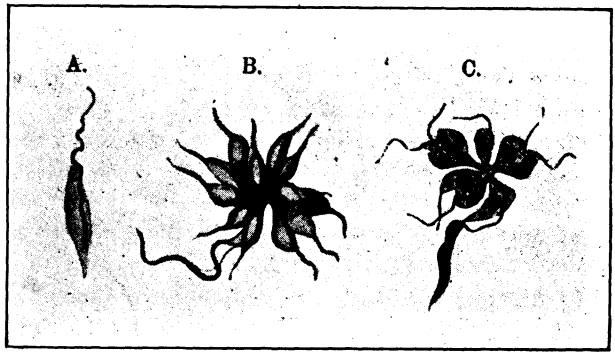


FIG. 91.—*Tr. lewisii* Kent. A, Adult parasite; B, Multiplication forms in fresh specimen; C, Multiplication forms in stained specimen. (After Wasielewsky and Senn.)

for other animals, may be found in the blood of Manila rats. In addition to those *Trypanosoma* correct in every essential for *Tr. evansii* occur in those rodents, as well as parasites which microscopically resemble *Tr. lewisii* but are infectious for other animals, producing disease and death.

Trypanosoma evansii Steel, 1885.—A motile *Trypanosoma* 20 to 30

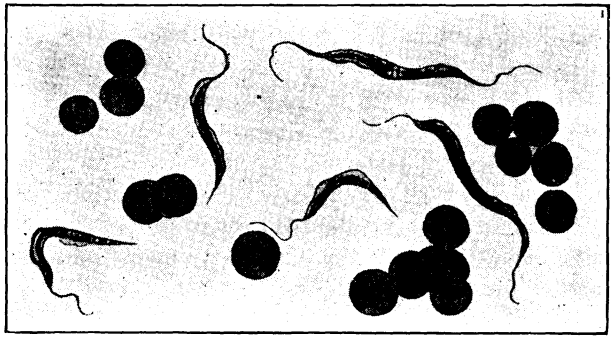


FIG. 92.—*Tr. evansii.* Two of them in process of division. (After Crookshank.)

microns in length by 1 to 2 microns in breadth, somewhat blunt at the posterior end and gradually tapering at the anterior end. The undulating membrane is well defined, beginning at or near a small body (centrosome) in the posterior portion of the parasite and extending forward as a free flagellum.

This *Trypanosoma* is provided with a nucleus and a granular protoplasm.

We have classified the parasite causing *Trypanosomiasis* in the Philippine Islands as *Tr. evansii*. This is the name adopted for the original organism causing the disease in domestic animals, and the one in the Philippine Islands answers the descriptions of this *Trypanosoma* as well as those of some of the other parasites later to be discussed.

It is a *Trypanosoma* from 20 to 35 microns long by 1 to 3.5 or 4 broad, including the flagellum. The gradually tapering anterior end is provided with a long flagellum, which in the living parasite has a very active motion and is a free continuation of the thickened border of the undulating membrane. It extends backward along this membrane to its end, about one-third to three-fourths the length of the parasite, and terminates at or near the centrosome (micronucleus). The undulating membrane extends from the posterior portion of the parasite along one border to the anterior, where it gradually tapers into the free flagellum. This membrane, active in the living parasite, in fixed specimens is found to be more or less folded, giving it a ruffled or fluted appearance. It is usually homogeneous, but sometimes contains granular matter apparently identical with that found in other parts of the parasite. The posterior end of the parasite is more or less blunt. In the living state this part is undoubtedly contractile, a fact which accounts at least in part for the varying degrees of bluntness seen in fixed specimens. Too great importance has been attached to the shape of this extremity, which in the parasites observed by us varies too much to be very significant as a diagnostic point.

The *protoplasm* of the parasite alters considerably with conditions, one of which is probably the age of the organism. In some it is almost homogeneous, as viewed with a Zeiss 1/12 objective, ocular 4. It is usually granular, especially in the anterior portion, the granules being either small or large but more often a mixture of the two kinds. A number of the larger chromatin granules, which may measure as much as 1 micron, are often seen near the centrosome, again in the anterior portion, and sometimes well up into the flagellum. We have observed them a few times in the undulating membrane.

The *nucleus* is situated somewhat anteriorly to the center and is oval or round and of good size. A nucleolus is not usually observed. The nucleus takes a characteristic stain and is homogeneous or slightly irregular in structure; but we have been unable to bring out the beautiful effects of karyokinetic division illustrated by some authors.

The *centrosome* is situated in the posterior portion, its distance from the posterior end varying from one-fourth to one-third the length of the parasite, depending no doubt upon the degree of contraction of this part at the time of fixing. It is chromatic, and within small limits varies in size. It is intimately associated with the beginning of the undulating

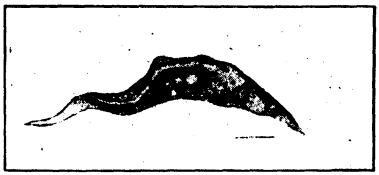
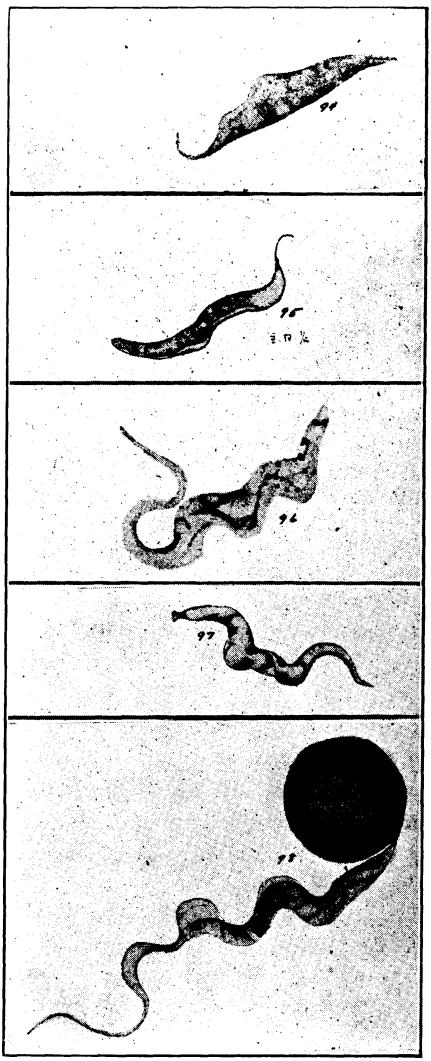


FIG. 93.—*Trypanosoma* showing particularly folding of undulating membrane.



FIGS. 94-98.—Various irregular forms of *Tr. evansii.*

membrane and flagellum, and while difficult to demonstrate satisfactorily, is probably the head of the flagellum.

In fresh specimens the parasite has an eel-like motion, owing to the vibration of the undulating membrane and flagellum and to a less extent to the action of the entire parasite. The actual motility varies in some specimens, and while it is generally not great, it may be quite extensive. These variations are difficult to explain, the more so since they occur in specimens prepared from the same animal but at different times. For the study of structure, fixation and staining are necessary. The various methods which have been published for showing the motion of the living parasite in such a way as to reveal the structure are unsatisfactory.

Habitat: The habitat of this *Trypanosoma* has already been given, but we wish to add Manila rats to the list. This fact merits especial emphasis in the consideration of measures for the control of the incurable malady caused by the parasite.

Pathogenesis: It is pathogenic for nearly all animals, as will be seen when the discussion of susceptible animals is reached.

Trypanosoma brucei Plimmer and Bradford, 1889.—Laveran and Mesnil describe it as a *Trypanosoma,* 26 to 27 microns long by 1 to 1½ microns broad. In horses and asses it may reach 26 to 30 microns in length. The size, however, varies but little. It is a motile, worm-like organism, with an undulating membrane extending into a long flagellum at the anterior end. The posterior end is variable—round, tapering, or cone-shaped. The motility is not great. The structure is not well marked in fresh specimens, but in stained ones it closely resembles that of *Tr. lewisii.* It contains large, deeply staining granules, especially in the anterior end. The nucleus near the middle of the body is elongated and contains deeply staining granules. The centrosome is near the posterior end, and is a round corpuscle staining more intensely than the nucleus and often surrounded by a clear zone in stained specimens. The flagellum, free in the anterior end, continues along the undulating membrane and stops near the centrosome, appearing, however, to be separated from it by the clear zone above mentioned. In involution forms flagella often appear to have direct connection.

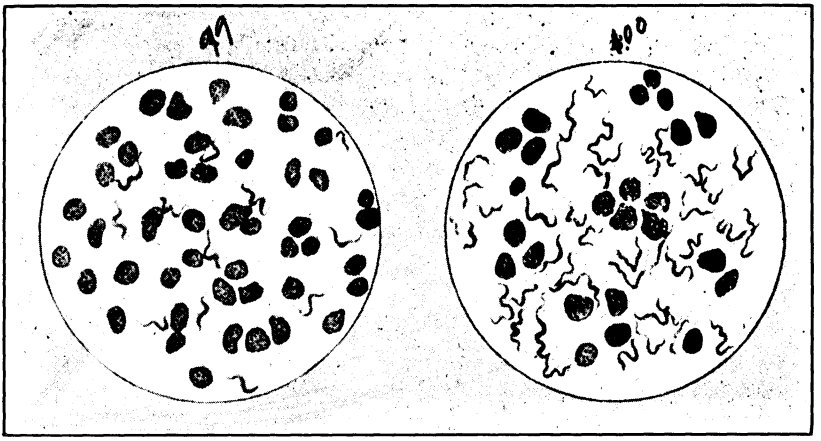
Bruce says that this parasite as found in the dog is thicker, shorter, and the posterior end more rounded than in other animals. In the horse the dimensions are nearly double, with the posterior end tapering.

Plimmer and Bradford consider the parasite to vary in size and length with the period of the disease and the species of the animal, being the largest in the rat at the time of death.

Salmon and Stiles give as the specific diagnosis of this *Trypanosoma:*

Twenty-five to 30 microns long, 1.5 to 2.5 microns broad. As compared with *Tr. lewisii* the posterior extremity of *Tr. brucei* is not so sharp, the undulating

membrane is broader and more plicate, the protoplasm colors more easily and more deeply, and the movements are less active. The protoplasm contains granules, which accumulate principally in the anterior half, some of which are as large as the centrosome, and they color the same as the centrosome; centrosome divides before the nucleus.



FIGS. 99-100.—*Tr. equiperdum.* 99, In the blood of a rat four days after inoculation; 100, Same eight days after inoculation. (After Doflein, 1901, fig. 40.)

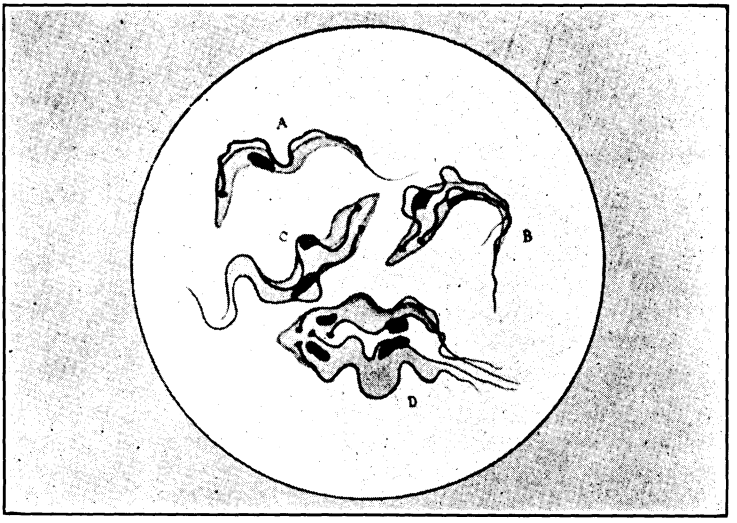


FIG. 101.—Trypanosoma of dourine in the process of evolution, clearly showing the centrosomes. (After Lignieres, 1903.)

Habitat: It is found in the blood of several species of domestic as well as wild animals. This point is more fully discussed in a chapter devoted to this subject.

Pathogenesis: It is infectious upon inoculation for nearly all animals.

Trypanosoma rougetii Laveran and Mesnil, 1902; Trypanosoma equiperdum Doflein, 1901.—Rouget describes this parasite as a motile, worm-like *Trypanosoma*, 18 to 26 microns long and 2 to 2.5 microns broad, with an undulating membrane and a long anterior flagellum. The posterior end is tapering or blunt and contains a small, shining globule which does not stain. The protoplasm is granular. He considers it identical with other *Trypanosoma* of domestic animals.

Nocard, who worked with this parasite, considers it and the disease produced by it identical with other *Trypanosoma* and Trypanosomatic infections.

Buffard and Schneider maintain a close relationship between this parasite and the others, but they are not sure of their identity.

Habitat: Blood and lesions of horses and asses suffering from dourine.

Pathogenesis: Naturally infected animals are horses and asses. Infection may be transferred by inoculation to dogs, rabbits, white mice, and several other animals.

Trypanosoma nepveui.—Whether or not this is a distinct species is hardly determinable from the descriptions thus far given, but the work of those having cases of Trypanosomiasis in man under observation will probably settle this point. All *Trypanosoma* described as occurring in cases of human Trypanosomiasis are included tentatively in this species for convenience.

Nepveu first described a *Trypanosoma* in human blood as follows:

> This Trypanosoma presents all the characteristics of the genus. It has a homogeneous colorless membrane, one border of which is thinner than the other, and hyaline, with characteristic undulating movements. This membrane bears a nucleus and a fine flagellum, situated anteriorly, the undulations of which follow in rapid succession. * * *
>
> In conclusion, Trypanosoma must be classed among the parasites of human blood. I am unable at present to give a more complete description of this variety, and therefore refrain from giving it a special name. It will therefore be best first to establish the similarities and differences between this parasite and the congeneric parasites of animals and also to complete the observations on its morphology and life history.

Dutton, who has found a *Trypanosoma* in Forde's case in South Africa, describes the parasite as follows:

> In contrasting the parasite with similar parasites in animals it approaches most nearly in its morphology *Tr. brucei.* It is the smallest of all described mammalian *Trypanosoma;* its average length is 22 microns, including the flagellum; its breadth is greater in proportion to its length than in other parasites. The posterior part as measured from the micronucleus to the extreme tip is short and characteristic for this parasite.
>
> The micronucleus and its associated vacuoles are always large and well marked. The "set" in fixed specimens differs from that of other species, as has already been pointed out.
>
> Dr. Laveran, who has very kindly examined some blood films taken from the

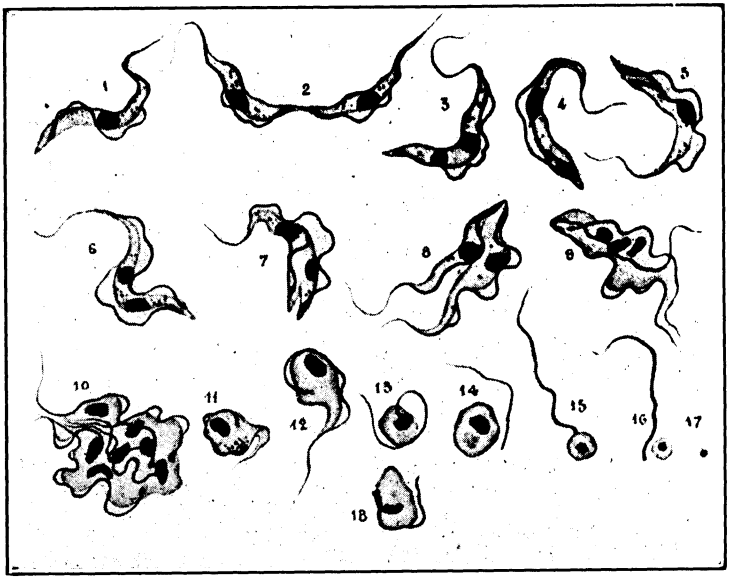


FIG. 102.—*Trypanosoma* of mal de caderas without centrosomes distinguishable by staining according to Laveran or Romanowsky. (After Lignieres, 1903.)

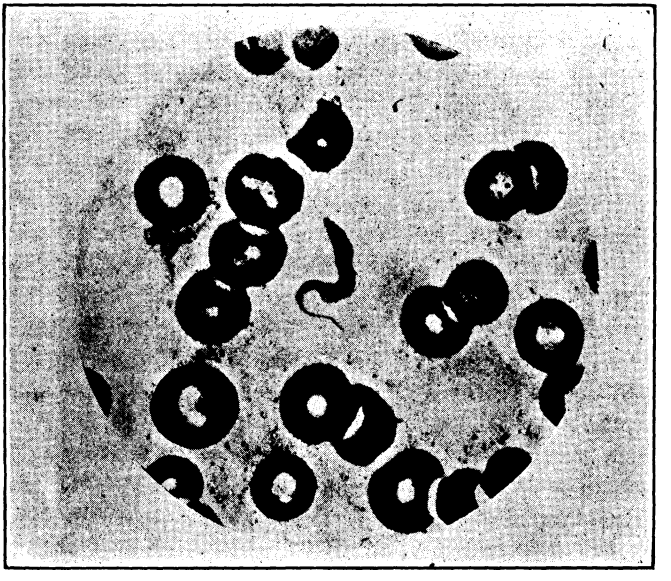


FIG. 103.—Showing *Trypanosoma* found by Dutton in the blood of a European. (After Forde, in Jour. Trop. Med., Sept. 1, 1902.)

patient, informs me that if the morphological characters are alone considered, he would regard my specimen as a new species; it differs from *Tr. brucei* in the length of the flagellum and in the small number of chromatin granules in the protoplasm.

Having as yet not had the opportunity of transferring the parasite in the blood from man to other animals as has been so completely done in nagana by Bruce in Africa; Kanthack, Durham and Blandford, and Plimmer and Bradford in England; Laveran and Mesnil in France; and to a less extent in surra by Evans, Steel, Lingard, Van Dyke Carter; and in dourine by Rouget, Nocard, and others; I am quite unable to contrast the pathogenicity and the morphological appearance of the human parasite in lower animals with the other species. It is to be remembered that no case has ever been recorded in man in the districts in which animal infection is so common, although man is exposed to the same risk in infection; for instance, the tsétsé fly (*Glossina morsitans* Westwood), which was proved by Bruce to carry the infection of nagana from animal to animal, bites travelers, natives, and others, as well as animals.

The consideration of these facts and the discovery of a parasite—evidently of the genus *Trypanosoma*—in the blood of a patient presenting symptoms markedly similar in very many points to those of the two or more diseases of lower animals which have been definitely proved to be caused by the presence of different species of the genus *Trypanosoma* forces one to the conclusion that the parasite found in this patient is a new species, and is also the cause of the disease from which the patient is suffering. I would therefore suggest the name *Trypanosoma gambiense*.

Until more work has been done, it is advisable to use caution in classifying this *Trypanosoma* as a separate species. It is done in this report tentatively, but the chances are that careful work will decide it to be identical with some of the others. There are several reasons for this assumption. The cases so far reported are from areas where the disease is prevalent in animals, and these cases are few in number and somewhat scattered. There are probably many cases which have not been detected, but we can not believe them sufficiently numerous to perpetuate the species without a host in some of the lower animals. It seems much more likely that there are changes in the patients which somehow interfere with the natural resistance for the well-known parasites.

Trypanosoma equinum Voges, 1901; Trypanosoma elmassianii, 1902. The length of this parasite, according to Voges, is two or three times and its width one-third to one-half the diameter of a red blood cell. The anterior end is provided with a flagellum about as long as the body of the parasite and extends backward about two-thirds the length of the body as a somewhat thickened margin of a distinct undulating membrane. The posterior end of the parasite is about one-third the length of the flagellum and is contractile and somewhat beak-shaped.

Its motion resembles that of an eel, but the actual motility is not great, the whole body taking part in an excessively active wriggling motion and the flagellum and beak ends moving in opposite directions. The motion is due to the undulations of the membrane, which run in both directions. The flagellum is the anterior extremity, but the parasite may move in the

opposite direction. There is a nucleus toward the anterior end, a centrosome near the posterior end, and the protoplasm is granular. In young parasites (rarely found) a larger speck (nucleus) is seen near the anterior and a smaller chromatin mass near the posterior end. The

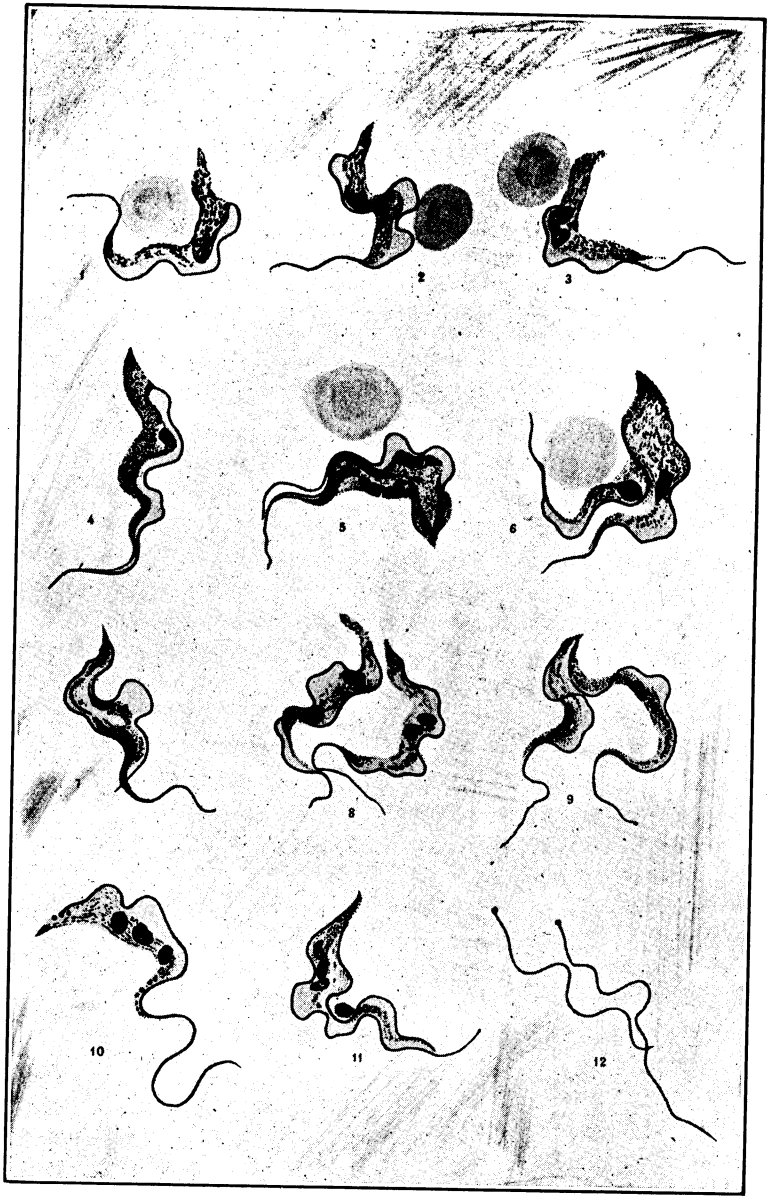


FIG. 104.—*Tr. equinum.* 1–6, Forms of multiplication in the blood of a horse; 7–9, Same in the blood of a guinea pig; 10–11, polynuclear forms in the blood of a guinea pig in a state of gestation; 12, Flagella and centrosomes free in a preparation made from the blood of a guinea pig in a state of gestation. (After Sivori and Leeler, 1902, Pl. IV.)

chromatin mass in stained specimens is sometimes surrounded by a bright area, which in turn is surrounded by a nonstaining border.

Habitat: Similar to that of *Tr. brucei* and *Tr. evansii,* except for cattle, which are said to be immune.

Pathogenesis: Pathogenic for domestic and certain wild animals. Voges considers the cattle of South America immune.

Trypanosoma theilerii (Bruce, 1902).—Bruce has published a note regarding a new *Trypanosoma* discovered by Theiler in the cattle of South Africa. The new parasite is to be distinguished by its size, being almost twice as large as any of the others. It is pathogenic only for cattle.

Laveran and Mesnil have studied this *Trypanosoma* in specimens furnished by Theiler, and they agree that it is a new species. They give its length as 30 to 60 microns and its breadth as 2 to 4 microns. In its

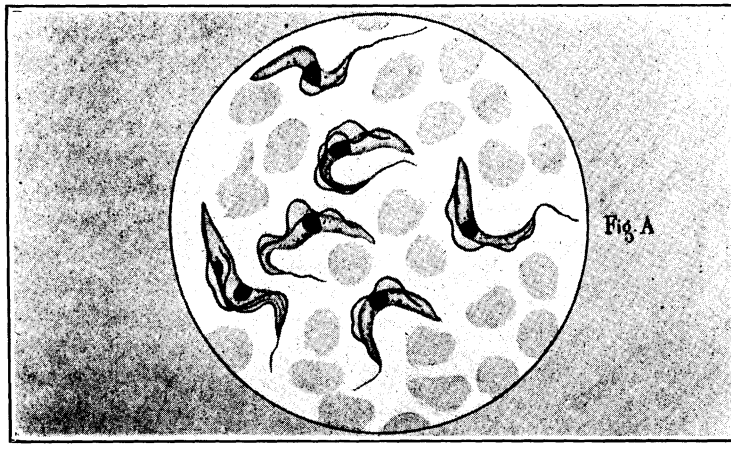


FIG. 105.—*Trypanosoma* of mal de caderas stained according to Laveran. (After Lignieres, Recueil de Med. Vet., 1902, Pl. II.)

general structure and modes of division it does not differ materially from other *Trypanosoma.* They consider one of its diagnostic points the presence of blood cells with basophilic granules in the infected blood.

Habitat: Blood of cattle.

Pathogenesis: Horses, dogs, goats, sheep, deer, rabbits, guinea pigs, rats, and mice are said to be immune to this parasite, but Theiler was able to infect calves by inoculation.

Trypanosoma transvaaliense (Laveran and Mesnil, 1902).—This *Trypanosoma* was discovered by Theiler in the cows of the Transvaal. Its dimensions are variable, the average being 30 microns in length by 4 to 5 microns in breadth. Its characteristic diagnosis is, according to Laveran and Mesnil, who have studied specimens submitted by Theiler, is the presence of the centrosome near the center of the parasite and near and

sometimes united to the nucleus. The altred corpuscles seen in blood infected with *Tr. theilerii* have not been seen with this parasite.

Habitat: Blood of Transvaal cattle.

Differential diagnosis of Trypanosoma of mammals.—Regarding the differential diagnosis of the *Trypanosoma* which are of the greatest importance in the disease of domestic animals, there seems to be considerable difference of opinion; and the work will probabaly not be satisfactorily completed until all the supposed varieties are studied in one country in similar environments.

According to Laveran and Mesnil the distinction between *Tr. brucei* and *Tr. lewisii* is marked. *Tr. lewisii* is thinner and more tapering, and its undulating membrane is smaller and less folded. Its protoplasm colors less deeply. Its chromatin granules are not so large and numerous. Its posterior extremity is always thin and tapering and never has the appearance of a truncated cone. It lives longer on ice than does *Tr. brucei.* However, individuals showing no material differences are found in both varieties. In fresh blood without the presence of dividing forms they are differentiated with great difficulty. In *Tr. brucei* the centrosome always divides first, following which the flagellum, nucleus, and protoplasm separate in the order named. In *Tr. lewisii* division may begin in the nucleus, and before it takes place the parasite sometimes reaches 5 microns or more in breadth.

Tr. equiperdum, according to the same authors, closely resembles *Tr. brucei,* but the morphologic differences between the two are appreciable. *Tr. brucei* has much greater dimensions; its protoplasm colors more deeply and nearly always contains large chromatin granules, which are absent in *Tr. equiperdum,* which is never more than 20 microns in length. However, we have, in the blood of animals, seen *Tr. equiperdum* which so closely resembled *Tr. brucei* that methods of differential diagnosis were unsatisfactory.

Tr. brucei and *Tr. equinum,* according to Laveran and Mesnil, have almost the same length and form. The protoplasm, the nucleus, the undulating membrane, and the flagellum have the greatest resemblance in the two *Trypanosoma,* but this is not true of the centrosomes. The centrosome of *Tr. brucei* colors easily and deeply and measures about $1\frac{1}{2}$ microns in diameter; that of *Tr. equinum* does not measure more than $\frac{1}{3}$ or $\frac{1}{4}$ microns, and colors rose, like the flagellum, and not violet, like the centrosome of *Tr. brucei.* A number of chromatin granules difficult to examine are often found near it. Some observers have came to the conclusion that the centrosome is defective in *Tr. equinum.*

Owing to the fact that the centrosome differ in stained specimens of the blood of mice infected simultaneously with *Tr. brucei* and *Tr. equinum,* they have been able to distinguish the two species of *Trypanosoma.* The forms of multiplication are the same, double partition being the

rule. Large divisions into three or four parts, which are somewhat more common in *Tr. equinum* than in *Tr. brucei,* are sometimes observed.

Martini considers the posterior end of *Tr. brucei* more blunt than that of *Tr. lewisii, Tr. equinum,* or *Tr. evansii.*

Buffard and Schneider and several others believe *Tr. rougetii* to be identical with other *Trypanosoma* producing Trypanosomiasis in domestic animals.

Scheube, Bruce, Rost, Koch, and many others consider *Tr. evansii, Tr. brucei,* and some of the other parasites probably identical.

Ligneres has recently written elaborately regarding the distinctions between the various *Trypanosoma* of mammals. In the main his results agree with those of Laveran and Mesnil already given.

A consideration of this subject resolves itself into two headings: First, a differentiation based upon microscopic observations of the parasites, and, secondly, that based upon their pathogenic action. As might be expected, the more two parasites differ when compared by one of these methods the greater will be the difference between the two as determined by the other.

Tr. lewisii differs morphologically from the parasite of nagana, surra, etc., and these differences are confirmed by their pathogenic action. Concurrence of opinion on the individuality of *Tr. lewisii* as found in different countries is so universal that further attention need not be paid to it.

When we come to consider the identity or nonidentity of *Tr. evansii, Tr. brucei, Tr. equiperdum* (*rougetii*), and *Tr. elmassianii* (*equinum*), we are compelled to obtain our data for all of these parasites except *Tr. evansii* from the work of other authors.

Taking up first the study of morphologic differences, we fail to see any justification for the extremely careful and guarded conclusions of Laveran and Mesnil or the very sweeping ones of several more recent authors. They have disregarded the fact of the variability of these organisms in the same species of animal in the same country, their greater variability and different species of animals in the same and in different countries, and other conditions requisite to identity of environment and to a conclusive comparative study. It must be remembered that we are dealing with organized animal life and that environment has an important influence on its physical condition.

The most important differences which conservative writers generally point out between these organisms are variations in the shape of the posterior extremity, the centrosome and the undulating membrane and the granular condition of the parasite itself.

From careful observations we are confident that the posterior end of *Tr. evansii* is contractile, a condition which a few writers have noted in other parasites. This results in a variation of the shape of this

extremity in *Tr. evansii,* and doubtlessly in other parasites, as great as that given for any two members of the group.

The same statement applies to some of the other differences, such as variations in the undulating membrane and the general morphology of the parasite.

Another important factor which has not been given due consideration is the age of the parasite, as is also the condition with reference to life, of the media from which the preparations are taken for study. In *Tr. evansii* and probably in some of the other parasites the number and size and to a certain extent the location of the granules depend upon the conditions mentioned. The difference in the staining of the centrosome in *Tr. brucei* and *Tr. elmassianii* (*equinum*), first emphasized by Laveran and Mesnil, we are not in a position to comment upon.

Laveran and Mesnil have written very carefully regarding the differentiation of these parasites, and are most conservative in considering differences in pathogenic action, regarding the latter as secondary in importance to the morphologic differences of the organisms. More effusive and less careful writers have drawn emphatic conclusions from pathogenic manifestations alone. There is undoubtedly a great similarity in the pathogenic action of the various *Trypanosoma,* in general the same animals being susceptible and showing similar symptoms and post-mortem lesions. The chief differences are those of degree, and they vary almost as much in different animals of the same species when inoculated with the same *Trypanosoma* as with different *Trypanosoma.* Cattle, for example, have been used to show differences in the parasites, when as a matter of fact in Manila these animals, when inoculated with *Tr. evansii,* show variations as great those noted in literature for any two diseases. We have seen a cow die in twenty-four days from surra (see fig. 127), and all degrees of resistance above this to an almost complete natural immunity have been observed.

After carefully reviewing literature and taking our own observations into account, we do not feel justified in forming a positive conclusion; but it seems to us that proof sufficient to establish the individuality of the *Trypanosoma* causing Trypanosomiasis in domestic animals has not yet been advanced.

V. MODES OF TRANSMISSION AND INFECTION.

Believing, as we do, that the transmission of *Trypanosoma* by biting and stinging insects is the only method deserving consideration from a practical standpoint, we are in harmony with the best thought of modern literature on the subject. To demonstrate that this is the only practical method requires (1) evidence of a host constantly present in infected zones, (2) direct evidence of transmission from this host to the healthy animal, and (3) evidence that in the absence of either the host or the insects the disease is not communicated.

With reference to the presence of the host, we have ample evidence that it is constantly present in the different countries afflicted with *Trypanosoma*. It has been shown that in Africa elephants, camels, cattle, and other animals live for months and sometimes years with this disease, certainly long enough to carry the source of infection from one rainy season to another. Foa, Bruce, and others in this same country have shown conclusively that a certain percentage of the wild animals are infected and that they harbor the parasites with little or no inconvenience to themselves. They have further shown that when these animals are driven from a community the biting flies to a large extent follow them, and in this manner the epidemic which may be raging at the time is almost completely suppresed. In India camels, cattle, and other animals live long enough with this infection to carry the disease from one season to another; in fact, the camel may live for more than three years. Rogers and others believe that in India the cattle, which live for months with *Trypanosoma* in the blood and often completely recover, principally act as the hosts. In South America wild animals and certain species of cattle when infected live for a considerable time and act as hosts in the propagation of the disease. Some of the recent writers in that country have concluded that horses are infected in sufficient numbers to act as hosts.

In the Philippine Islands with an epidemic of two years' duration it has not been found necessary to go outside of the horse family to find a host constantly present. In Manila infected horses are found during the entire year, during the dry season, of course, in small numbers. The wild animals of this country have not been examined, and cattle, while susceptible to the infection, are rarely found to be naturally so.

In literature there is an abundance of incontrovertible evidence to prove the disease to be transmitted from sick to healthy animals by biting insects, and this has been fully confirmed by our work, as will be shown. There is also sufficient evidence to show that, in the absence of either the host or the biting insects, the disease does not spread.

BY CONTAGION.

There is nothing in the nature of the disease or in the manner of its spread that in the slightest degree indicates transmission by contagion. The same may be said also of *congenital* transmission. Observers are unanimous in the opinion that the fetus in utero is not infected. We have performed a number of experiments in this line on dogs, monkeys, rabbits, guinea pigs, and rats. In one dog infected with *Trypanosoma* by inoculation about two weeks before delivery, miscarriage followed on the eighth day. In none of our other animals was gestation interfered with and the young were never found to be infected, although susceptible to infection. In one of our experiments two puppies were allowed to nurse

from an infected mother in an insect-proof stable, and at the time of the death of their mother, eight days after their birth, they were free from infection.

BY COITION.

Almost all writers, referring to dourine, state that it is transmitted by coition, and a considerable number believe this to be the only method of transmission for this disease, while others believe it to be the exception, even in this form of Trypanosomiasis. This method of transmission has been given little consideration in relation to the other forms.

Recently some writers upon this subject have offered at least suggestive explanations. Schilling believes that transmission by coition occurs in those regions free from the usual infecting insects and from other conditions favorable to the propagation of the disease; and the geographic distribution of dourine tends to support Schilling's conclusions. In infected countries, if the infection takes place by coition it is lost sight of in the more frequent methods and could be determined only by careful experimentation.

We have performed a number of experiments looking to the elucidation of this point in the epidemic now raging in this country. Considerable difficulty has been experienced in obtaining direct evidence. Horses are not available for the work, and with the native ponies it has been almost impossible to find at the same time infected animals and those desiring intercourse. In several instances infected blood has been introduced into the vagina of female dogs by the use of a catheter. All these experiments except one have given negative results, and in the positive one infection is attributed to a lesion of the vagina. In those cases in which the mucous membrane of the vagina was injured purposely, infection following the introduction of virulent blood occurred in every case, with an incubation period equal to that following infection through the injured mucosa of the mouth.

We have not observed an absolutely conclusive result following coition. One male dog contracted the disease after intercourse with an infected female; but a small number of biting and stinging insects were present at the same time, so that it was probably transmitted by them. Upon another occasion an infected male goat was seen to copulate with a healthy female, but no infection followed. This was hardly the most desirable kind of an experiment, since the goat in question rarely showed parasites by microscopic examination, though his blood was infectious by animal experiment. Again, the manner in which goats effect copulation would be much less likely to result in infection than in the case of the horse, provided, as has been suggested, it depended upon *traumatism*. It seems more than probable, however, that in many animals, and especially in the case of the horse, infection might often follow sexual intercourse as the result of traumatic injury of the genitals.

It is not uncommon to see a few drops of blood after sexual intercourse between these animals, and it would certainly require no stretch of the imagination to suggest the possible presence of small injuries in the mucosa of the genitals of both animals. It does not appear, however, that much importance should be given to this as a practical means of transmission of the disease. Any disease of horses transmitted only by coition could, of course, be eradicated with the greatest ease.

RATS AS CARRIERS OF THE INFECTION.

In referring to the part played by rats, we come to a much more important subject. To bring out its full significance necessitates a brief consideration of the natural infection of rats with *Tr. evansii,* a point which will be thoroughly discussed under "Trypanosomiasis of rats," and a consideration of the bearing such infection has upon the transmission of surra in animals of economic importance.

Rats in an indefinite way have been blamed for the transmission of the disease. Lingard has made elaborate experiments to show that grain soiled with the excrement of these little pests and eaten by horses played an important part in the spread of the infection. He demonstrated that rat surra was transferable to horses by inoculation; but, owing to his failure properly to protect his animals from insects, his work has received but little consideration. Musgrave and Williamson have shown conclusively that a certain percentage of rats in Manila harbor *Tr. evansii.*

In a preliminary report they say:

> A varying percentage of rats are known to harbor a *Trypanosoma* somewhat resembling the one found in the horse, and it has been conclusively shown that a certain number of rats in Manila harbor the same *Trypanosoma* which causes the disease in other animals. These parasites have been determined both morphologically and in their pathogenic action to be identical with the parasites causing Trypanosomiasis in horses.

With this information we are prepared to consider the part they play in transmitting the disease to domestic animals and in perpetuating the epidemic. Rats frequently fight, and it has been shown that the infection passes from one to another in this way. In addition, the wounds so caused attract biting insects, particularly fleas, which are known to transmit *Trypanosoma* from rat to rat, and, as will be seen later, from rats to other animals. In Manila the number of rats infected with *Tr. evansii* makes it necessary seriously to consider them in discussing means of controlling the disease in this city.

INFECTION OF PASTURES, FOOD, AND WATER.

Infection through the sound mucosa and through the injured mucous membranes presupposes to a large extent as its source infected food and drink. Lingard, the great champion of this method of transmission,

considers the ingestion of stagnant water and of grass from land subject to inundation a source of infection, the latter being a favorable breeding place for low forms of animal life and possibly of *Trypanosoma*.

Salmon and Stiles believe that there is nothing at present known in connection with the life history of any *Trypanosoma* to lead us to look seriously upon grass as a source of infection. We know that *Trypanosoma* die very rapidly under all usual conditions outside of the living body. If they are to be found in either food or drink, they must be in some phase of the life cycle with which we are unacquainted. If food and water should be infected, as Lingard maintains, they would still be harmless in the presence of the demonstrated fact that the disease as we know it is not transmittable through the sound mucosa of the alimentary canal.

In a preliminary report Musgrave and Williamson make the following statement regarding this subject:

> The existence of an extracorporeal stage of *Trypanosoma*, living on grass and on water in marshy places, in this stage taken into the stomach of susceptible animals eating and drinking in these localities, and from this organ or other part of the animal economy passing into the blood in the forms we recognize, is without sufficient evidence to warrant consideration in this paper.
>
> Before leaving this subject, however, for a fuller discussion in a subsequent paper, it is proper to state that *Trypanosoma* quickly die under all tried environments outside of the body of some living creature, and no evidence of their existence in water, on grass, or other similar places can be advanced. Both water and grass have been inoculated with large numbers of *Trypanosoma* and have failed to convey the disease, after days, weeks, or months, when fed to susceptible animals, and also when injected under the skin.
>
> Malaria is similar to Trypanosomiasis in that both are parasitic diseases and both are prevalent in low-lying, marshy lands and during wet weather. Malaria was for ages attributed to the air, the water, etc., of these marshes, and it took years to make the public understand that all these conditions are harmless in producing it, provided the patient is protected from the bite of mosquitoes, so prevalent in these regions.
>
> Take the epidemic of Trypanosomiasis in Manila. At the time of its outbreak, and for some time afterwards, it was confined to the city. The grass and water given the horses was the same which had been fed for years, and no disease resulted.
>
> The disease started from a focus of infection and spread directly with exposure to infected animals, and attacked alike animals fed exclusively on hay and oats and those fed on grass. The disease is prevalent in Manila at the present time and has been so continuously since its introduction. The majority of horses having the disease, under our observation for the past four months, had been fed previously entirely on hay and oats.
>
> In one large stable, with both American and native horses, four of the American horses and mules (fed entirely on dry feed) and two of the native ponies have died of the disease, and one of the two ponies was the only horse of this class in the stable which received dry feed only.
>
> The statement is made that certain districts in India are avoided by cavalry on the march because of the danger in these districts from food and drink through which animals may contract the disease. Similar conditions are found

in South America, but in addition it has been shown that infected districts on this continent are just as dangerous to horses provided with dry food and pure water while passing through them as they are to animals eating forage grown on the spot.

It has been shown by a number of observers that an infected animal taken to a new place becomes a focus for the spread of the disease, provided biting flies are present, no matter whether the territory is marshy or dry.

Since that time the work has been continued, but no evidence has been obtained to show that food, water, or pastures are ever factors in the spread of the disease.

Attempts artificially to infect water and grass have always failed. It is true that when these substances are used as culture media parasites may live for a short time under certain conditions, but multiplication to an appreciable extent does not occur. It is of course possible that infection may occasionally take place in localities where sick and healthy horses graze on the same ground or drink water from the same place, provided both classes of animals have lesions of the mucous membranes or cutaneous wounds on those parts of the legs which come in contact with the grass or the water. It is absolutely certain, however, that if food and water are ever infected to any degree it must be with some form of the parasite not yet known. Even if such places served as culture media for *Trypanosoma,* as we know them, they would still be comparatively harmless to those animals having sound mucous membranes and free from cutaneous wounds.

INFECTION THROUGH THE SOUND MUCOSA.

There is some difference of opinion, especially among recent writers, in regard to infection by food and drink through the sound mucosa of the alimentary canal. Lingard affirms emphatically that the disease is so transmitted, but the great majority of recent investigators state with equal positiveness that the disease can not be so produced.

Kanthuck, Durham, and Blandford attempted to transmit *Trypanosoma* by feeding, performing a number of experiments. At times they were successful, but in most cases they failed. They concluded that the possibility of infection depends upon accidental lesions of the mucous membranes of the upper portion of the alimentary canal. Continuing, they say:

> Of a number of rats fed on the organs of nagana animals only a few acquired the disease, and these invariably showed superficial lesions of the snout and ears, due to lice. When fed upon infected material, they buried their snouts in it and scratched their ears with their blood-stained forepaws. Furthermore, in rats which acquired the disease through feeding, the cervical glands were always enlarged most, a fact which proves that hematozoal infection must have taken place in the head, for, as we shall show, the primary infection travels by the lymphatics.
>
> A cat fed repeatedly on the soft tissues of bodies of infected dogs and cats and subsequently on the bodies of dead rats, died at a time corresponding by

lethal period to an infection at the first meal on rats. We regard it as probable that some splinter of bone caused superficial lesions, through which the hematozoa were enabled to enter.

A rabbit, fed carefully by means of a pipette with large quantities of infected blood, did not show the slightest sign of the disease. Rouget (1896) also failed to infect animals by the mouth.

Evans and Steel believe that surra can be transmitted either by ingestion or by inoculation in dogs, horses, and mules, provided that fresh infected blood is used. With blood kept twenty-four hours or more they did not succeed in conveying the disease.

Writing in 1899, Lingard considered that natural infection with surra might occur in one of four ways: (1) From eating grass and other vegetation grown upon land subject to inundation; (2) from drinking stagnant water during certain months of the year; (3) from the bite of certain species of flies, probably as carriers of the virus; and (4) from the ingestion of corn soiled with the excrement of rats and bandicoots.

Having determined that the *Trypanosoma* of rats in India was the cause of Trypanosomiasis in a certain percentage of other animals, such as the horse, he experimented to prove whether this was of any practical importance in the spread of the disease. He mixed the excreta of rats with grain, which was fed to horses during the dry season in an area free from surra, with negative results. With similar experiments, however, under favorable conditions of moisture and heat, he claims to have obtained positive ones. With regard to these he writes as follows:

> At a later date, during the latter half of the hot season and the rains of 1893, further experiments with the same end in view were carried out in Bombay, where the climate is favorable from its humidity and the disease is enzootic. From these positive results were obtained, the incubation period occupying four months (about June to September); but the incubation period of the disease will probably be found to vary with the amount of moisture in the atmosphere and the amount of materies morbi ingested by the animal. This points to the probability that a number of surra cases in Bombay were contracted through the ingestion of rats' or bandicoots' excreta mixed with the corn.

Salmon and Stiles doubt the accuracy of these results. They say that *Trypanosoma* have not been found in the excrement of either horses or rats, that it is not clear that Lingard used the necessary precautions to exclude fly bites and other factors in his experiments, and that if rats harbored *Tr. evansii* transmission from them would have been as possible by rats and fleas as by their excrement. Voges fed animals with several liters of infected blood mixed into a paste, without results. Laveran and Mesnil also failed to convey the disease through the sound mucosa. Rouget's feeding experiments were negative, but he obtained positive results by dropping infected blood into the conjunctiva. Rogers was unable to convey the disease through the sound mucosa, and says that in

those cases in which infection occurred by feeding there were injuries of the mucous membranes.

Rost writes that grass, grain infected by rat's excreta, and flies must be considered in the etiology. Salmon and Stiles consider ingestion as a possible means of infection, but state that it can deserve no special consideration as a means of transferring the disease from horse to horse.

It appears to us that one of the strongest arguments against the transmission of the disease through food and drink is furnished by Lingard himself. He states that a street-car company which had lost hundreds of horses from surra finally provided their animals with boiled drinking water only and with grass brought from an elevation of 6,000 feet, prohibited the feeding of green vegetables, and also ordered the animals to be isolated, without success. It is to be noted that these stables were situated on a street along which infected horses were traveling, so that the isolation of the company's animals did not protect the healthy ones from flies. The manner of feeding did exclude infection by this means, and seems to us a strong point in determining that food and drink play absolutely no part in the transmission of the disease.

The numerous citations of instances in which dogs contracted Trypanosomiasis by eating the carcasses of animals dead of the disease seem to us to be no argument in favor of its transmission through the sound mucosa. Such animals are always fighting, and the infection might readily take place through wounds, and in addition these animals are usually well provided with biting insects. Curry states that it is not known whether the disease in the Philippines can be transmitted by food and drink.

Our investigations have failed to produce the slightest evidence that infection by food, drink, or otherwise ever occurs through the sound mucosa. Musgrave and Williamson, discussing this mode of transmission, say:

> The great majority of writers agree that infection can not take place through the sound mucosa of the alimentary tract, and that the occasional infection following the administration by mouth of the virulent blood and organs of animals recently dead of the disease are probably due to the fact that these animals had damaged mucous membranes of the mouth or upper part of the alimentary canal, which would, of course, result in infection, just as would occur in any other part of the body by bringing an injured surface into contact with infectious material, or vice versa.
>
> In nearly all feeding experiments large doses of the infective agent have been given, and in this sense they have not approached natural infection, which, from the nature of things and whether administered through the mucous membrane or the skin, would be in small doses.
>
> Lingard attempted infection through the digestive canal by the administration of very small doses of infected blood given frequently in large dilutions of water. One of his horses that had received such treatment, and in addition one dose of 13 c. c. of infected blood, developed the disease on the one hundred thirtieth day after the beginning of the experiment. He fed a second horse 200 minims of

fresh virulent blood at one dose, with an incubation period of seventy-five days. He does not state that these horses were protected from insects during the periods of the experiments, which were made in an infected country, and it is more than probable, considering the incubation periods of one hundred thirty and seventy-five days, that his animals were infected in some other way.

So far as we have been able to discover, there is not in literature any absolute proof of infection through the sound mucosa by feeding.

In this preliminary report but one of our many feeding experiments will be given.

Monkey No. 126—healthy adult male monkey—was isolated, temperature taken and blood examined daily for a week. The temperature remained normal and the blood negative for *Trypanosoma*. After twelve hours' fasting he was fed weekly for six weeks on cooked rice (the usual diet) soaked with fresh warm virulent blood, rich in *Trypanosoma*, from different animals at different feedings. On two occasions he was given to drink infected blood in weak potassium citrate solution, in which *Trypanosoma* live longer than in any other known solution outside of the body.

At the end of six weeks the animal was apparently in good health, temperature had remained normal, and the blood free from parasites. In order absolutely to exclude the existence of infection, a drop of blood was injected subcutaneously into another monkey, which remained well and was afterwards proved susceptible. During the feeding the infected rice would often be stored in his chops and remain there for hours.

After proving the animal not infected at the end of six weeks, a small scratch was made in the mucosa of the mouth and he was again fed as before. The disease developed on the fourth day, as was evidenced by rise in temperature and the presense of *Trypanosoma* in the blood. He ran the regular course of the disease, and died on the eighteenth day after infection.

This work has now been continued for more than a year, involving the use of hundreds of animals. We have experimented with horses, dogs, goats, rabbits, guinea pigs, monkeys, cats, and rats; we have fed them large and small doses of virulent blood and all kinds of preparations of both blood and infected organs. All experiments were performed under circumstances which made accidental infection impossible. Particular attention to this part of the subject was deemed necessary in order intelligently to recommend measures for the control of the epidemic. Our results have given absolutely convincing proof that infection does not occur through the sound mucous membranes by *Trypanosoma*, no matter in what form administered.

INFECTION THROUGH THE INJURED MUCOUS MEMBRANES.

As stated by Musgrave and Williamson in a preliminary report, surra is essentially a wound disease, and transmission through the injured mucous membranes results when infected material is brought in contact with it. When infection occurs through the alimentary tract, it does so through a wounded mucous membrane. Monkey No. 126 was one of the many animals experimented upon to determine this point as well as the possibility of transmission through the sound mucosa. Of course it was easy to prove that infection could occur through an injured mucous

surface; but definitely to show of what importance this would be in the practical transmission of Trypanosomiasis required more work.

It was necessary first to determine what percentage of a number of animals in the natural course of events have sufficient injuries to make possible an infection in a given period of time. Naturally this was found to vary greatly. In dogs and rats injuries are so frequent that in order to obtain animals without lesions to be used in determining the possibility of transmission through the sound mucosa, we were compelled to confine each animal by itself for some time. In horses, cattle, and other animals of economic importance natural lesions of the mucous membranes are more rarely found. In horses used for carriage and draft purposes, lesions in the corner of the mouth caused by the bridle bit are quite frequent. In the case of cattle and carabao, lesions are seen in the nose around the ring which is placed through the septum and which usually has a rope fastened to it. Small wounds might occasionally be produced in the mouth by eating rough dry food.

With injuries present in the mucous membranes, the next question to consider was the manner in which infectious material may be brought in contact with these wounds; and from a practical standpoint (excluding flies) there are not many possibilities. All such means are of course mechanical and readily suggest themselves; they are, changing bridle bits from sick animals to healthy ones, allowing healthy animals to lick sores on sick ones, placing animals to graze upon the same ground, or allowing them to drink the same water, etc.

Here may be introduced a strong argument against the theory that food and water play a serious part in the transmission of the disease. If such were the case, animals with wounds would contract the disease from eating and drinking food and water which had been allowed to stand just as readily as they do when freshly infected material is fed to them; but this is not the case. We have experimented on animals with fresh wounds, feeding them water and grass infected from forty-eight hours to three months previously and kept under all kinds of conditions, but have failed to convey the disease in this manner.

Flies.—Of the biting insects that play a part in the transmission of the disease, certain varieties of flies are of the greatest significance.

Of flies credited with playing an etiologic role in this disease, the tsétsé fly (*Glossina morsitans*) is among the most important.[1]

Schilling states that *Glossina logipalpis* is very prevalent in Togo, as well as *Stomoxys calcitrans* and three species of *Tabani*. He regards all

[1] We had hoped to introduce here a short illustrated description of each species of the flies which have been credited with playing a role in the transmission of *Trypanosoma;* but the pressure of other work has prevented the entomologist to whom the duty was assigned from completing the undertaking. At some future time we hope to be able to do this, when we shall also finish the discussion of some of the points left open in this paper.

these varieties as able to transmit the infection. He proved conclusively that at least two species of these flies can transfer the infection in dogs.

Martini found normal *Trypanosoma* twenty-three hours after feeding the *Stomoxys calcitrans* on infected blood, the insect itself being kept in a room at a temperature of 23° C.; but he did not see dividing forms. On the following day the blood was digested and the parasites could not be observed. On dogs biting experiments with these flies failed. Healthy horses and asses standing next to sick horses, all covered with *Stomoxys calcitrans*, did not contract the disease. Martini's work was performed in Berlin.

Working in Manila, Curry considered the *Stomoxys calcitrans* as the principal agent of transmission and found enormous numbers of them feeding on sick animals. He observed active *Trypanosoma* in the proboscides and stomachs of these flies twenty-four hours after their feeding upon infected blood. He was unable to find *Trypanosoma* in any other species of flies. Rost found *Trypanosoma* in juices squeezed from the horsefly some hours after feeding on a surra animal, and he was convinced that these transmit the disease.

Lingard describes an epidemic in India in which flies were very numerous and no precautions to isolate or destroy infected ponies were taken. Sixty-five animals died in the region in question. During the next season, however, in the same locality and among the same class of horses, the infected animals were isolated and only two deaths occurred. He demonstrated that the body fluids of certain flies contain *Trypanosoma* after feeding on infected animals and that the inoculation of such fluids in susceptible animals causes the disease. He and his assistants examined large numbers of *Diptera* of some ten varieties, during both the dry and the wet season, but *Trypanosoma* were not found in any case except in adult flies which had fed on infected animals.

Sivori and Lecler in South America proved that the *Musca brava*, the *Stomoxys calcitrans*, and the *Taon* can transmit the disease from horse to horse. The relative of these flies, *Ochleretatus obifasciatus*, also showed *Trypanosoma* after feeding on a sick horse, but did not prove capable of transmitting the infection.

Voges states that the disease is transmitted only through wounds, injections, etc. Several varieties of *Tabani* are found in South America, and the *Musca brava* is also prevalent, as well as various species of mosquitoes.

Buffard and Schneider consider *Tabani* as active factors in the transmission of the disease.

Rogers proved conclusively that surra is transmitted by flies which have recently bitten infected animals. Infected flies kept from one to four days did not transmit the disease by biting and were harmless when fed to rats.

Bruce considers the tsétsé fly able to convey the disease for forty-eight

hours after feeding on infected blood. He placed five muzzled horses in areas containing flies, and notwithstanding the fact that they were all prevented from using the food and water found there, they contracted the disease. Suspected flies transferred to a district free from nagana conveyed Trypanosomiasis by biting two dogs after four to seven hours. He found living *Trypanosoma* in the proboscides of these insects forty-six hours after they had fed on infected blood, and in their stomachs one hundred eighteen hours after feeding; but at the end of one hundred forty hours no parasites were present.

Schilling noticed that at a certain place in Africa on one side of a lagoon three kilometers in width, surra and tsétsé flies were prevalent, while on the other side neither could be found.

Without going into further detail, there is an abundance of incontrovertible evidence that the disease is transmitted by a number of species of biting flies, as was the opinion of the natives of India and Africa long before science demonstrated the fact. It has thus far been conclusively shown that the tsétsé fly (*Glossina morsitans*), at least one other variety of *Glossina*, *Stomoxys calcitrans*, *Musca brava* (?), *Taon*, and at least one variety of *Tabani* transmit the disease. All other biting insects have been looked upon with suspicion, but absolute proof of transmission by them has not been furnished.

Is it a mechanical action or is it one phase of the life cycle of the parasite which takes place in these insects? The time limit of infection in all conclusive experiments has been too small to admit of any other construction than that the action is mechanical. This is the conclusion of nearly all modern writers. Schat, whose work has been mentioned above, is the only exception, but his experiments do not confirm his theory that a phase of the life cycle of the parasite takes place in the fly. The time limit of infection for these insects is given by most authors at twenty-four hours, and a few place it as high as forty-eight. Agreeing with Salmon and Stiles, we must say that a phase of the life cycle in insects is certainly not necessary to a definite continuation of the infection, and it is extremely doubtful that it exists.

We have transferred the infection to monkeys by biting flies in experiments so guarded as to make the results absolutely conclusive. We have also transmitted it by means of the common house fly from an infected dog having a wound to a healthy one in a similar condition. Monkeys are difficult to experiment with, for the reason that they take pleasure in destroying all flies coming near them; but we succeeded in performing our experiments by placing one of the animal's legs in a test tube containing flies which had recently been fed on infected blood. These experiments have been repeated, and the transmission of the disease to the horse, dog, monkey, rat, and guinea pig by biting flies has been confirmed. Our work has been conducted with the greatest care and in all cases controlled by animal experiment. In short,

the transmission of the infection in this way has been so frequently shown that further demonstration hardly appears necessary.

With these facts before us, however, we have yet to discuss the very important part of the subject which refers to the rolé which these insects play in the *practical* dissemination of the disease. This of course is difficult to prove by direct experiment without great expense and trouble; but the evidence showing this to be the usual method of transmission is so conclusive as to render such experiments unnecessary.

Summarized, this evidence is as follows: It has been repeatedly shown that biting flies can transmit the infection. It has been proved that animals protected from insects do not contract the disease, but that when protected from every other source of infection but this one Trypanosomiasis occurs with the usual regularity. Finally, no other suspected method of transmission explains why they are found in zones where the disease is epidemic.

Fleas.—Plimmer and Bradford and Rabinowitch and Kempner have shown conclusively that fleas may transmit *Tr. lewisii* from rat to rat; and it has been suspected that they may play a similar role in the more important animals, although this suspicion had not at the time this work was taken up been demonstrated.

With reference to the transmission of the disease by fleas, our own work has been absolutely convincing. Surra has been transferred by these insects from dog to dog, from rat to rat, and from rat to dog. Horses have not been used for this work because of their cost and the apparent uselessness of wasting expensive animals without material gain in information.

Sources of error in this work were eliminated in the following manner: The dogs were placed in an area covered with sand and protected from insects by screens. All but one of the dogs were then taken from the stable, and this one we proved to be free from *Trypanosoma* by animal experiment. A surra-infected dog was then placed near by, but separated from the other one by a screen to prevent them from touching each other but at the same time allowing free passage to the fleas. The healthy dog developed the disease on the sixth day, as evidenced by a rise of temperature and the presence of parasites in the blood. This experiment was repeated a number of times with positive results. The time intervening between the admission of a dog and the first positive evidence of disease (as nearly as the incubation period could be estimated) varied from five and one-half to twelve days.

All animals were then removed from the flea-infected area and only healthy ones introduced after periods of time varying from twenty-four hours to four weeks. Although the fleas in the sand remained quite plentiful, no infection occurred.

Rats, in screened cages placed in this flea-infected area in close prox-

imity to an infected dog, contracted the disease. The dog was then removed and a cage of healthy rats substituted, some of which contracted the disease.

These observations have removed fleas from the doubtful means of transmission and proved them to be a factor to be carefully considered in our efforts at prevention. Fleas are very numerous in Manila, especially so during the wet season, when Trypanosomiasis is most prevalent.

Mosquitoes.—Beyond the bare mention of the possibility that these insects may transmit Trypanosoma, we have been unable to find any records in literature; and because of the lack of time our experiments in this direction have not been as thorough as we desired.

A number of experiments have been performed, all of which have been negative and were carried out with young monkeys and guinea pigs in the following manner: A young guinea pig with parasites in its blood and a healthy one were placed in a large mosquito-proof cage and separated from each other by a coarse wire screen. Mosquitoes were then placed in the cage in large numbers, and more were added when necessary. The experiment was continued for a month without results.

Mosquitoes were allowed to feed upon infected blood and then placed in a large test tube, into which a monkey's arm was introduced and allowed to remain for three hours at a time. The experiment was repeated daily for a week, but no infection occurred.

The mosquitoes used in these experiments were *Anophales, Stegonyia,* and *Culex.* These varieties are all very prevalent in Manila, but do not appear to disturb domestic animals greatly; and for that reason, even if they sometimes carry the infection, as is likely, they deserve only secondary consideration in discussing the spread of surra in horses. It is more than likely that the large gnats found in swampy places and which attack large animals are important factors in the transmission of *Trypanosomiasis.*

Lice.—These little pests repeatedly are mentioned in literature as possible agents in the transmission of the different forms of Trypanosomiasis; but so far as we have been able to determine, there is no direct evidence furnished that such is the case. It certainly appears possible that the disease may be transferred by lice, especially in the case of animals, such as rats and other small animals, suffering from wounds; but as far as the larger ones are concerned, we can hardly consider these insects as a practical means of dissemination for the disease. We have repeatedly performed experiments on monkeys, dogs, and guinea pigs in order to determine this point, but so far they have failed to give positive results; nor have we been able to find *Trypanosoma* in lice caught on the bodies of infected animals.

It has already been pointed out that lice are very numerous on rats

and help to cause small wounds on these animals, especially around the ears. They are also exceedingly numerous on carabaos, but do not appear to produce any injury to these thick-skinned animals.

Ticks.—As in the case of lice, ticks have been blamed by a number of writers as agents in the transmission of the disease. Voges does not believe they play an important role, for the reason that a tick no sooner injures the skin than it absorbs the blood of the surrounding tissue by suction, and as soon as this is accomplished falls to the ground. The feedings of the tick are so far apart that *Trypanosoma* would not likely be carried by them from one animal to another. This logic seems to us to be very satisfactory and has been accepted without experiment.

Enormous numbers of ticks are present in certain sections of the Philippines, and if they were agents in the spread of the disease they would merit very careful consideration.

INFECTION THROUGH OPEN SKIN WOUNDS.

From what has already been said in discussing infection through the injured mucosa, it will readily be seen that skin wounds are a constant source of danger during the prevalence of the disease. Such places entice flies, which can undoubtedly infect wounds with greater ease and certainty than they can uninjured skin surfaces. With the presence of skin lesions there are many additional possibilities to be considered, which may be disregarded in dealing with sound animals. These may vary somewhat with environment, but in no case are they of frequent occurrence. Musgrave and Williamson mention among these agencies the passing of curry combs, brushes, etc., over wounds on sick animals and then over similar places on healthy ones.

With a fuller understanding of rat infection, a more important point may be raised here. This has not been actually demonstrated, but with the knowledge already possessed of the transmission of the disease by fleas, open sores on the lower extremities would be subject to infection by these insects, and in this way it would not be surprising to find them playing an important part in transmission, especially in a country like this, where minor injuries to horses' legs are so common and fleas so numerous.

MISCELLANEOUS.

Lingard has brought out the point that the disease may accidentally be transferred by birds' picking sores on infected animals and following this on noninfected ones.

Railways have been mentioned as factors in the transmission of Trypanosomiasis, and when they become more numerous in some of the infected zones, they will no doubt play an important part in the spread of the infection, since they make possible a more rapid distribution of animals and also a greater dissemination of flies. However, as a means of

transmission deserving consideration from a practical point of view in the Philippines, the possibility is very remote.

Theiler believes that in South Africa the propagation of the disease to a limited extent is influenced by the immunization of cattle against rinderpest with defibrinated blood. In Manila we have had a striking example of this possibility. Dr. Jobling, Director of the Serum Laboratory, received from Java a number of cattle for serum work. One of these developed rinderpest and was bled to death, the blood obtained being used on four serum animals, three of which promptly developed surra and of course became useless for serum purposes. The infection in these cases undoubtedly came from the Java cow and illustrates too well what, as suggested by Theiler, no doubt frequently happens.

In following the discussion of the modes of transmission and infection, it is seen that but few of the headings which have been chosen really have any practical significance; and we may well close this part of the subject with the statement, already emphasized, that *Trypanosomiasis is essentially a wound disease and that infection takes place when materies morbi are brought in contact with an injured surface and in no other way.* The most common agents in bringing this condition about are biting and stinging insects, and of these certain flies and to a less extent fleas are the most important.

The manner of perpetuation.—The manner of perpetuation of a disease of this kind is interesting, since it has a practical bearing upon methods for its control. The eradication of the disease may with propriety be discussed at this point.

Musgrave and Williamson in a preliminary report referring to this question say:

> The manner of perpetuation of an epidemic of Trypanosomiasis in any country is a very important point in considering the prevention and eradication of the disease.
>
> By the very nature of parasites and of parasitic diseases in general, we know that, unless the disease is continuous, the parasite must have a natural host, or there must be a stage in its life cycle in which it can exist for an indefinite period outside the living body; otherwise the infection will disappear.
>
> Many of the large tsétsé-fly areas are absolutely destitute of domestic animals, and probably some of them have never had one within their borders, and yet the flies in these districts are capable of infecting domestic animals. As it has been quite conclusively shown that the fly is not capable of carrying the infection at most but a short time, it necessarily means that there is a source of infection from which the flies are supplied, and the natural inference would be that the native source of infection is the wild animals in which the country abounds. It has already been shown that some of these animals are susceptible to the disease and that others harbor the parasites with little or no inconvenience. It is very probable that, were inoculation methods instead of microscopic blood examinations used for diagnostic purposes, a much larger percentage of these wild animals would be found infected than has generally been supposed.
>
> Conditions in certain sections of South America are very much like those in

Africa, and the indications are that the epidemic is perpetuated there in the same manner.

In India some observers claim that the cow acts as a host for the parasites over the long dry period in which there are not enough cases in horses to continue the infection. The probabilities are that a number of wild animals which exist in at least certain districts of India aid in this continuation. It is claimed that in certain sections of the country there are two varieties of animals which live in the bush, are susceptible to rinderpest and foot-and-mouth disease, but are not known to have "surra," though they are in infected areas. At certain seasons the flies are so numerous that these animals seek the open for protection from them. It would be interesting to test the blood of these animals by inoculation to see whether or not they are free from Trypanosomiasis. In India, camels also may play an important part in carrying the infection from one fly season to the next, as it is stated that these animals may live as long as three years after infection.

From the foregoing, and if the disease continues to spread, it is evident that the wild animals of this country must be considered in dealing with the epidemic. If a certain portion of them are not already infected, it is only a question of time until they will be, and another difficult point in the solution of the problem will thus be produced.

The part that rats play in perpetuating an epidemic has not yet been fully determined, but the fact that at this time, in the middle of the dry season, a considerable number of these animals are found to be infected, and with the knowledge before us that the infection may be transmitted from one rat to another by fleas, which are numerous on rats at all seasons of the year, makes it probable that these animals play a very important part in perpetuating the infection in the Philippine Islands and in other countries.

However, so far as the city of Manila is concerned, it does not appear necessary to leave the horse family to discover how the infection is perpetuated. Now, even during the dry season, one can, almost daily, see a horse, sick with surra, driven along the streets, and biting flies, although not by any means as numerous as during the wet season, are still plentiful enough to continue the infection.

The existence of an extracorporeal stage of the *Trypanosoma*, living on grass and in water in marshy places, in this stage taken into the stomach of susceptible animals eating and drinking in these localities, and from this organ or other part of the animal economy passing into the blood in the forms we recognize, is without sufficient evidence to warrant consideration in this paper.

Before leaving this subject, however, for a fuller discussion in a subsequent paper, it is proper to state that the *Trypanosoma* quickly die under all tried environments outside the body of some living creature, and no evidence of their existence in water, on grass, or other similar places can be advanced. Both water and grass have been inoculated with large numbers of *Trypanosoma* and have failed to convey the disease, after days, weeks, or months, when fed to susceptible animals, and also when injected under the skin.

Since writing the above, much information has been obtained with regard to the part rats play in the spread of the disease, and the evidence makes it important that these pests be taken into account in discussing the perpetuation of Trypanosomiasis.

It is not believed that the rats of Manila were infected previously to the advent of surra, and this is supported by the evidence obtained by an examination of rats taken from zones free from the disease.

Surra beyond question is transferred from rat to rat, so that these

animals soon become important factors in its perpetuation in certain zones. In Manila the annual destruction of thousands of rats with the purpose of preventing the spread of plague will also have a beneficial effect in limiting one agent in the transmission and perpetuation of surra.

VI. GENERAL PATHOLOGIC ANATOMY.

Generally speaking, writers have been very brief in their description of the anatomical lesions of the different forms of Trypanosomiasis, the majority agreeing that they are not constant or pathognomic. Some, however, have held different views and have given excellent descriptions of their post-mortem findings, particularly Voges and Sivori and Lecler.

Laveran and Mesnil say that "nagana is certainly one of the diseases in which, at the autopsies of animals dead from the disease, there are slight lesions. Nearly all authors agree in giving as a constant lesion hypertrophy of the spleen. At the autopsy of one horse lesions of the internal organs were insignificant."

Voges states that in mal de caderas post-mortem examinations show edema and roughened hair, just as they are present during life. The skin is removed with difficulty, and when taken off a very dry flesh similar to that seen in cholera is observed. Cloudy serous fluids are usually found in the serous cavities, especially of the chest, which may contain several liters. There are fibrous layers on the pleura and other serous surfaces, especially marked on the abdominal organs. The subpleural lymphatic glands are often enlarged. The spleen is enormously enlarged, sometimes hard and firm and in other cases soft and friable. The follicles are often increased in size until they resemble grains of sago. The liver is enlarged. The kidneys are pale and sometimes enlarged, the lymphatics are slightly so. Fluids are often found in the larger socket joints.

Schilling, writing of surra in Africa, says that post-mortem examinations show marked general anemia, and numerous discrete, dark-red subpleural spots, enlarged soft spleen, enlarged follicles, and slight swelling and softness of the lymphatics of the neck, which contains a small amount of yellowish, opaque fluid. No special changes are observed in the liver and kidneys.

Sivori and Lecler, writing of "surra americain," state that the adipose tissue is replaced by a gelatinous mass. The muscles have a rose tinge, but are pale and in paretic cases may atrophy. Citron-colored fluid is present in the peritoneal cavity. The liver shows some increase in consistency and is darker in color. The spleen is enlarged and the glomerules are prominent and red; in the paraplegic form it is greatly increased in size and the lesions intensified, sometimes producing acute splenic tumor. There is enlargement of the malpighian corpuscles, which are often so increased in volume as to stand out in relief on the

surface. The bladder contains pale urine, which may show traces of albumen or without blood or biliary pigments. The pleural cavity sometimes shows a small amount of exudate. The lungs may be normal or edematous and in places congested. The pericardial cavity contains a yellowish serous fluid. The myocardium is pale and friable. The cardiac fat shows the same gelatinous changes as those of the subcutaneous tissues, and may show ecchymoses. The endocardium, particularly the left, has subserous punctate hemorrhages. The brain shows only an increased amount of subarachnoid fluid. Sections of the spinal cord usually show no lesions, but there may be small hemorrhages in the gray matter. These authors do not consider all the lesions attributable to *Trypanosoma*, some of them being due to secondary infection. They do not believe *Trypanosoma* destroy the red blood cells mechanically, but think they are destroyed by mononuclear macrophages. The mode of production of edema they say is unknown.

Bruce mentions as the anatomic lesions in nagana a gelatinous atrophy of the subcutaneous tissues, subserous and subcutaneous ecchymoses and enlargement of the spleen.

Weber and Nocard, writing of dourine, say that the section shows cachexia and hemorrhagic softening of the spinal marrow. The parasites found in these areas and in the serous effusions resemble those of surra, nagana, etc.

Kanthuck, Durham, and Blandford give as marked lesions enlarged lymph glands, especially around the inoculated wound, hypertrophy of the spleen and liver, and often fatty degeneration of the latter. Iron reaction is obtained with the liver, the spleen, and the kidneys.

Curry gives as the principal anatomic lesions marked pernicious and progressive anemia, general subserous edema, especially of the belly, sheath, and legs, moderate glandular enlargement, frequently bronchopneumonia and bronchitis, and often profuse muco-purulent nasal discharges, with marked glandular enlargment, particularly of the submaxillary glands.

In our experience necropsies have revealed anatomic pictures rarely as characteristic as in the chronic diseases peculiar to man. The ante-mortem lesions, provided the necropsy is made shortly after death, are still present. The body is emaciated, and the bands of edema so prominent during life may still be seen. A small amount of yellowish-tinged, gelatinous mucoid substance is found in the inner canthi of the eyes and even in the nostrils. The hair is roughened and often scant, leaving a scrawny, roughened epidermis. The mucous membranes are pale and dry looking and often show a yellowish tinge. The hide, as pointed out by Voges, is removed only with great difficulty, except in areas of subcutaneous infiltration, and when removed exposes the dry, hard, pale subcutaneous tissues. In the regions corresponding to the edema during life are found yellowish-tinged, gelatinous infiltrations, which are of a

similar consistency. A like condition is found throughout the body in the regions where adipose or areolar tissues are located, and especially is this true of the fat around the heart and the subperitoneal tissues. The muscles are pale, wasted, coarse, and granular looking. The serous membranes, particularly the peritoneum and the pleura, often show flakes of plastic fibrous material. These are particularly numerous over the surface of the liver and sometimes the spleen. All the tissues and organs have a peculiar dry, pale appearance, which has been so aptly

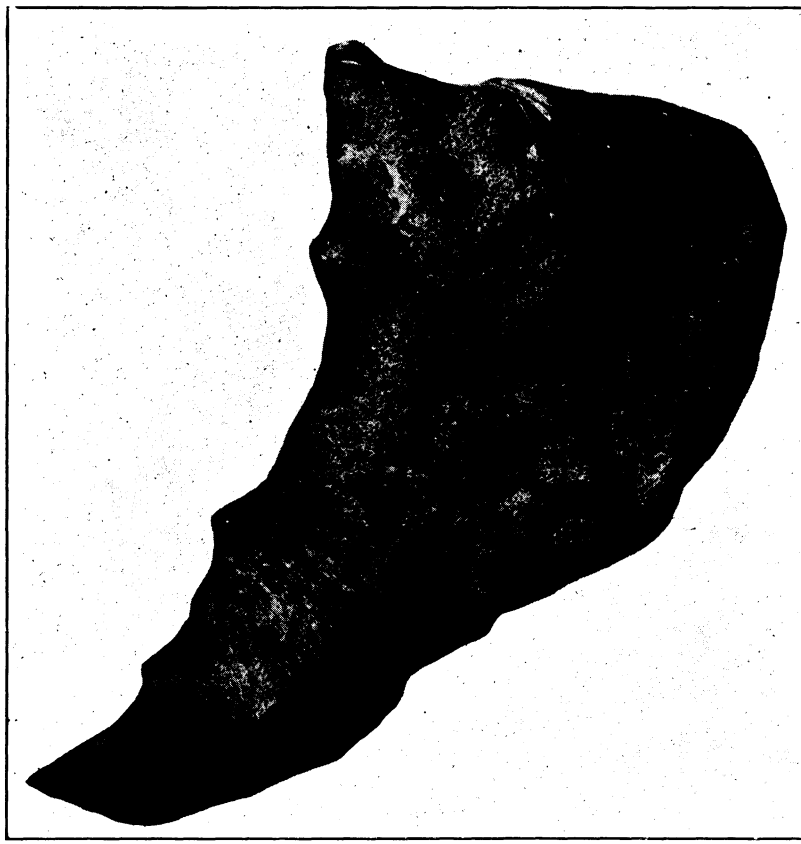


FIG. 106.—Spleen of a horse dead of surra, showing enlarged follicles and hemorrhages.

compared by Voges to their condition in cholera. There are numerous subserous hemorrhages, particularly on the right side of the heart and over the lower portions of the lungs. The lymphatics are in general somewhat enlarged, and often markedly so; and in a certain percentage of cases areas of broncho-pneumonia are present. The heart muscle shows parenchymatous changes, depending somewhat on the duration of the disease. Its chambers usually contain chicken-fat clots, which often

extend for a foot or more into the aorta. The appearance of the spleen varies somewhat, but in the majority of cases it is considerably enlarged, friable, and somewhat soft. The surface is uneven, due to the enormously swollen corpuscles, which stand out prominently. On section a typical "sago" spleen is often seen, while in other cases a typical acute splenic tumor such as is present in infectious diseases of man. In a few cases the spleen is but slightly swollen, but the dotted appearance, due to the swelling of the corpuscles, is a constant lesion and gives to this organ, regardless of its size, a most characteristic picture.

The liver is usually somewhat enlarged, pale, and cloudy. The intestine shows lesions due to anemia with now and then small ulcerations in the upper portion and sometimes in the cecum. The aqueous humor is often cloudy and contains *Trypanosoma*. The urticarial eruption observed during life is no longer evident. In some of the lower animals the scrotum and even the testicle in the male and the vulva in the female are greatly swollen, and in the male rabbit the tension may be so great as to rupture the scrotum. Small prepucial or labial ulcers are not uncommon.

VII. GENERAL REMARKS ON SYMPTOMATOLOGY.

Before proceeding to the study of Trypanosomiasis in the various animals, it might be well to make a few remarks on the symptomatology of the disease.

There is considerable variation in the clinical picture of surra in the same class of animals, even when the infecting parasites are known to be the same, and it is therefore not surprising that variations should exist in different species. In reviewing the literature relating to dourine, nagana, surra, and mal de caderas, one is struck with the great similarity in the descriptions of the so-called different diseases. A comparison of the descriptions of any one of them as given by different writers shows as great a divergence as may be found with those of the diseases acknowledged to be different. In all of them, however, there are a number of practically constant characteristic symptoms in the well-established infection such as to make, when taken together, a clinical picture easy to determine accurately even without the aid of the microscope.

After an incubation period, which varies in the same class of animals and in those of different species as well as with the conditions of infection, and during which the animal remains perfectly well, the first symptom to be noticed is a rise of temperature, and for some days a remittent or intermittent fever may be the only evidence of illness. Later on the animal becomes somewhat stupid; watery, catarrhal discharges from the nose and eyes appear; the hair becomes somewhat roughened and falls out in places. Finally the catarrhal

discharges become more profuse and the secretion more tenacious and even purulent; marked emaciation develops; edema of the genitals and dependent parts appears; a staggering gait, particularly of the hind parts, comes on, and is followed by death.

Voges divides the symptoms of mal de caderas into two stages, as follows: On the fourth or fifth day after inoculation the temperature rises rapidly, sometimes to 40° or 41° C., and then suddenly falls to normal or nearly so, usually on the second day. Within five days there is another rapid rise, reaching 40° C., followed by another sudden fall. These reactions may be repeated from two to eight times during the course of the disease. This is called by Voges the first stage. During this period the appetite is good and there is no emaciation. The thirst is increased. The feces are normal, but in rare instances may show a little clotted blood. Transient hemoglobinuria. The reflexes are normal. The coat is smooth, and the hearing and sight normal. Toward the end of this stage weakness becomes noticeable.

In the second stage the fever becomes less intermittent, and exacerbations to 40° C. or over are exceptional. The remissions are also less marked. The animal becomes inactive and sluggish and allows the head to drop carelessly. Progressive emaciation takes place; great thirst; progressive weakening. Edema, particularly of the hind legs, belly, and scrotum. The hair loses its gloss. Decreased sensibilities; digestion and respiration remain good. The gait becomes staggering and finally causes the animal to fall over. Some animals die suddenly during the later stages of the disease. Just before death the temperature variations usually become greater, vacillating between 34° and 39° C.; and death generally occurs when the temperature is low.

The fever is not continuous or characteristic in any of these diseases. It may be intermittent, remittent, or, according to some writers, relapsing in character, varying from 39° to 41.5° C. It is nearly always higher in the afternoons.

In describing the epidemic of surra which visited Java in 1900 Schat gives among the symptoms of the disease some which are remarkable in that they differ radically in many respects from those described by other observers. In reading his work one is struck by the fact that they form a very clear description of rinderpest in carabao. He found *Trypanosoma,* however, and it would appear to us that he was working with a combination of the two diseases.

A great deal of work has been done by various writers to demonstrate the relation of the temperature to the number of parasites in the circulating blood, some maintaining that these are numerous in proportion to the temperature, and others showing that no relation whatever can be determined. Kanthuck, Durham, and Blandford say that the parasites appear in the blood early in the disease and continue to increase

until death. The accounts vary and may reach 2,000,000 to 3,000,000 per cubic centimeter. The parasites appear to multiply first in the lymphatic glands around the point of inoculation and then to enter the blood, a fact which they believe explains the short latent period during which after inoculation they can not be found in the blood. Multiplication occurs also in the infected area.

During the incubation period parasites are not found in the blood by microscopic examination. This has been explained in various ways. Voges considers this to be because of their rarity, while others maintain that a stage of multiplication goes on in the lymphatics. A few conclusive experiments by animal inoculation, however, have shown that the circulating blood is infectious for one, two, or even several days before parasites are found by microscopic examination to be present, which would seem to indicate, as has been suggested, that they exist in the blood in small numbers during at least a portion of the time.

The periodical disappearance of the parasites from the circulating blood for varying lengths of time during the course of the disease has not been satisfactorily explained. All kinds of conjectures have been offered with but little evidence to support them. Voges's idea regarding this seems to us to be the most plausible. He states that the parasites are numerous during the first few days after the rise in temperature, following which they mysteriously disappear; and this appearance and disappearance may take place a number of times during the course of the disease. He considers it due to a certain amount of immunity, which is acquired by all animals in the early stages and which may be repeated a number of times before the animal becomes too weakened. This view is advanced in preference to the opinion that the temperature plays any part in this phenomenon. In the later stages of the disease parasites may be found in the blood in larger numbers and with a higher temperature than at any time previously.

Another symptom in this disease difficult of explanation is the anemia, which is progressive from the first. It has been explained that the parasites mechanically destroy the red blood cells and interfere with their manufacture in the bone marrow, and finally that on account of certain changes produced in the blood by the parasites the red blood cells are taken up by the large mononuclear macrophages. A number of less important explanations have been given. According to Voges, anemia is a constant, prominent symptom; and 10,000,000, the normal number of red blood cells in the horse, may be reduced to 4,000,000, 3,000,000, and even 800,000 in some cases before death. The sedimentation ring of leucocytes is increased and may be larger than that of the red blood cells. The hemoglobin is decreased in proportion to the diminution in the number of red blood cells; from the normal of 13.1 per cent it may fall to 3 or 4 per cent.

Several observers have spoken of the mechanical destruction of red blood cells by the parasites. Voges saw *Trypanosoma* hold erythrocytes against the body by their fixed ends until the cells disappeared. Crookshank, on the other hand, was unable to satisfy himself that they attack the red blood cells.

Laveran and Mesnil do not consider anemia sufficient to account for the death of animals. They say that the manner in which the parasites act is still unknown.

There is certainly something very curious about the presence of anemia in this disease and in the action of the parasites in producing it as well as bringing about death. The mechanical destruction of the red blood cells is not of the importance many writers attach to it. It seems to us that there is some factor in addition to mechanical action, which causes such profound changes, and strong evidence in favor of this is found in the peculiarity of the gelatinous deposits. The parasites appear in some manner to produce, or cause some part of the animal economy to liberate, this peculiar substance, which is not a simple infiltration of fatty tissue but is of different character. The deposit undoubtedly is formed gradually, as is inferred from the slow change in the secretions. The discharges from the nose and eyes, at first watery, gradually take on the same character, and before death become very tenacious and solidified in the nose and corners of the eyes.

Referring to the action of *Typanosoma* in the animal economy, Laveran and Mesnil state:

> Evidently in the presence of an infection so intense as that which is shown at the moment of death of rats, mice, and other animals, the mechanical action of such a number of parasites is to be considered. This alone, however, in our opinion, does not suffice to explain the cause of death. Rats infected with *Tr. lewisii* may have a great number of parasites and yet feel no inconvenience. In certain attempts at treatment, of which we shall speak later, a rat has had for more than fifteen days as many parasites in the blood as red cells.
>
> One is led to think of a toxic action of the parasites and of the intervention of the soluble products excreted by them. The observations of the course of the disease in rabbits, guinea pigs, and cows, in which the parasites are not so large as in other animals, even at the time of death, and the profound dejection of certain animals when infected, as the ass, plainly corroborate this view.

Strong thought that it was perhaps chiefly through its mechanical destruction of the red blood corpuscles that the Trypanosoma caused harm. Experiments were performed to show whether the parasite elaborated any toxic substance which acted injuriously upon its host.

> Large amounts of blood taken from monkeys suffering with experimentally produced Trypanosomiasis of severe type were passed through a Berkefeld filter and the filtrate injected into other monkeys. No symptoms of Trypanosomiasis were produced. Large celloidin capsules containing blood with many parasites were placed in the abdominal cavities of sheep, but the results were also negative.

All attempts to isolate a toxin have proved futile. It does not seem

to us that a toxin can enter into consideration; but, as has already been said, the character of the action which results in the formation of the peculiar gelatinous deposits will probably lead to a solution of the problem.

Voges believes that in mal de caderas death usually results from a gradually progressive heart failure, and in some cases occurs suddenly from the same cause. He says that death usually comes on with a fall of the temperature, rarely at its height.

This statement is true, but does not go far enough; an explanation of the cause of heart failure is what is desired. The condition described above may offer some solution, in that the gelatinous deposits are often abundant around the heart; and a microscopic examination of the tissues shows that a similar condition is present in the myocardium.

The incubation period of the disease in different animals has an important bearing upon the application of methods for the control of epidemics. It will be discussed in detail as the study of the disease in different animals is taken up. The evidence of previous workers and our own observations show that it varies with the manner of inoculation as well as with other conditions.

In all the forms of Trypanosomiasis the infection seems to involve particularly the genitalia, the skin, and the organs of special sense. The skin symptoms consist in a roughening of the hair, which also falls out in places; a thickening of the epidermis, often with exfoliation, and in some stages of the disease various skin eruptions. These may be simple erythema, and more rarely they may assume the severer forms, as urticaria, or in extreme cases a distinct localized ulceration may occur. The scrotum and penis in the male and the vulva in the female are often swollen, and ulcerations of the penis or vulva are frequent symptoms, especially in dourine.

VIII. TRYPANOSOMIASIS OF VARIOUS SPECIES.

TRYPANOSOMIASIS OF HORSES.

We shall begin the discussion of trypanosomiasis in the different species of animals with that of the horse, which from an economic standpoint is the most important animal naturally susceptible to the disease in the Philippine Islands.

Most of the writings relating to Trypanosomiasis deal particularly with the infection in equides, and as a consequence literature is rich in descriptions which in many points can not be improved upon. It is our intention briefly to review the most important writings on surra, nagana, dourine, and mal de caderas in each species of animal, following this with our own observations, and finally, when through with the species discussed, to devote a chapter to the discussion of the individuality of these diseases.

Surra, according to Lingard, manifests itself, after a period of incubation, in fever, a stumbling gait, and general or localized eruptions with the presence of *Trypanosoma* in the blood. A period of apyrexia may here supervene lasting for a day or so, during which the animal appears better. These apyrexial periods may occur a number of times during the course of the disease.

In every instance, however, they are followed by a fever usually from 38.7° to 40° C., thirst, slight loss of appetite, ecchymoses of the conjunctivæ, with increased lachrymation and mucous discharge from the nostrils. The submaxillary glands may be enlarged, and edema beginning on the legs or sheath may develop. Emaciation is rapid and progressive. With each exacerbation of fever the other symptoms become intensified, and the animal is made weaker. The edema spreads, the mucous surfaces become very pale and tinged with yellow, and the respiration is quickened. The appetite remains good. Toward the end paresis of the hind quarters becomes noticeable. Paralysis of the sphincter ani is frequent. Shortly before the end the heart's action in many cases becomes violent, and death may result suddenly from heart failure. When this does not occur, the animal finally falls to the ground and dies from exhaustion.

Nagana is carefully described by Bruce, who gives as the principal symptoms: Fever of a remittent or intermittent type; catarrhal secretions from the nose and eyes; staring of the coat; and edema of the abdominal region, the prepuce and the posterior extremities. The animal becomes markedly emaciated and has a dejected apearance, the head hangs, the hair becomes very rough and in places falls out, the mucous membranes of the eyes and genitals become very pale, and there is generally a slight opacity of the cornea. Just before death the animal falls to the ground and dies apparently without suffering.

Kanthuck, Durham, and Blandford inoculated two horses, one of which, a well-fed Russian cart horse, lived seven weeks, and the other eight days; wasting was very conspicuous. The period of incubation was followed by a smart rise in temperature and by the appearance of parasites in the circulating blood. A sudden rise of temperature immediately followed each increase in the number of parasites in the blood. At the time of death there was marked fever.

Laveran and Mesnil report two cases as follows: The first symptoms were the appearance of parasites in the blood and fever. One of the horses, which was not in a good condition at the time of inoculation, died in sixteen days; the other in forty-three days. With one or two exceptions parasites were always found in the blood by microscopic examination. The red blood cells gradually diminished and at death were reduced to half their original number, or even less. Parasites appeared in the blood in less than four days after subcutaneous inoculation, and their appearance was coincident with the first rise in temperature, which in a few days reached 41.4°. This was followed by a drop to 38° C. and a

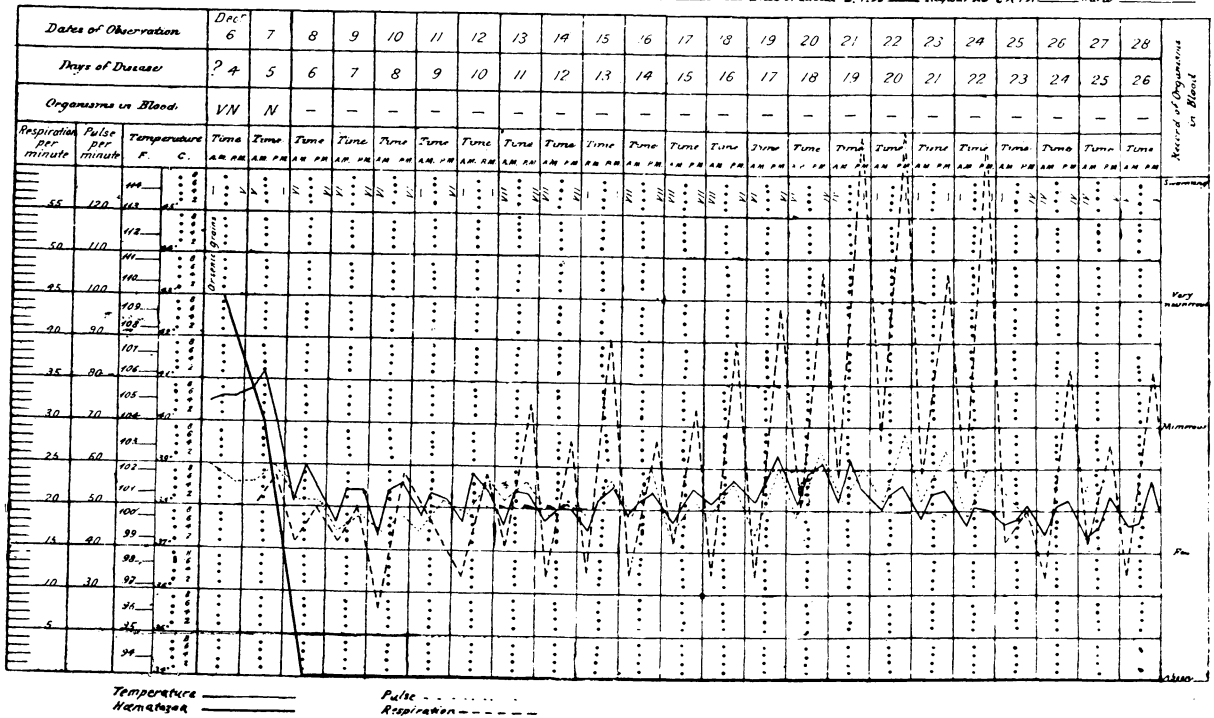


FIG. 107.—Temperature record of surra in a horse. (After Lingard.)

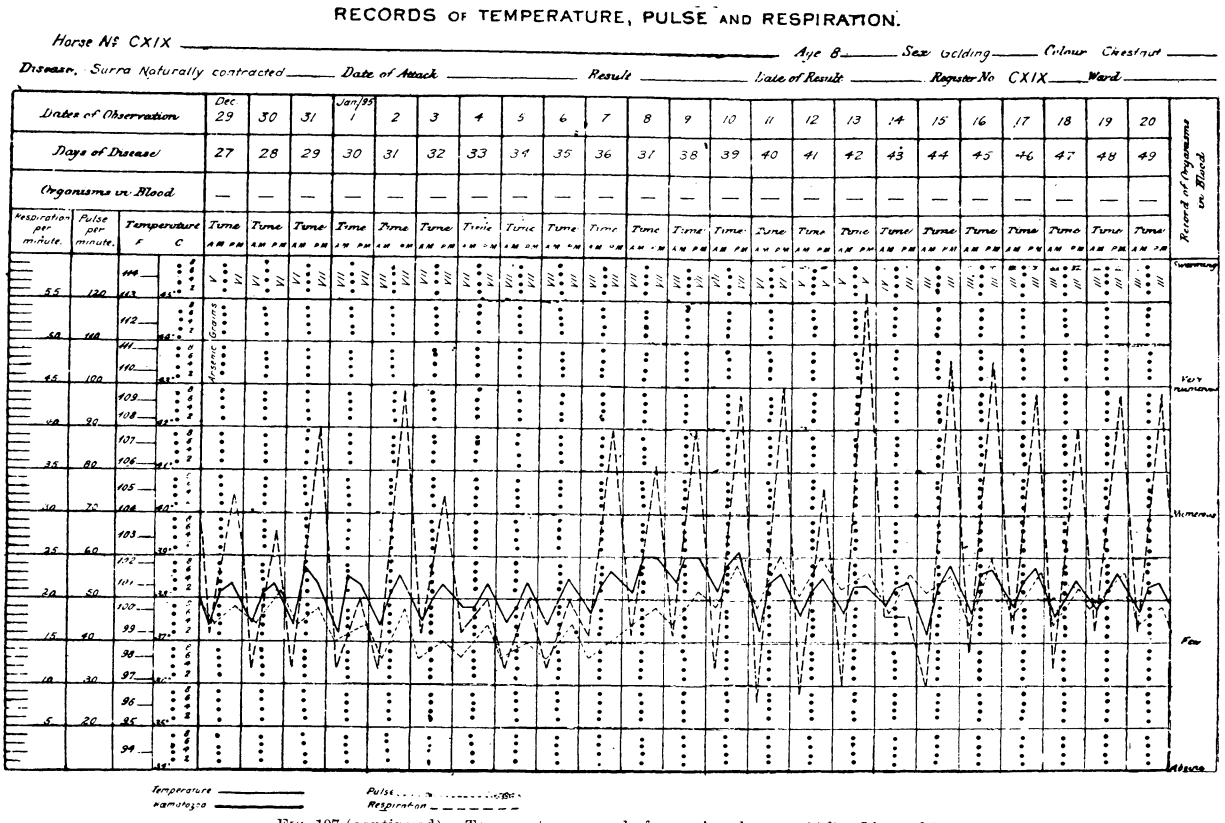


FIG. 107 (continued) —Temperature record of surra in a horse. (After Lingard.)

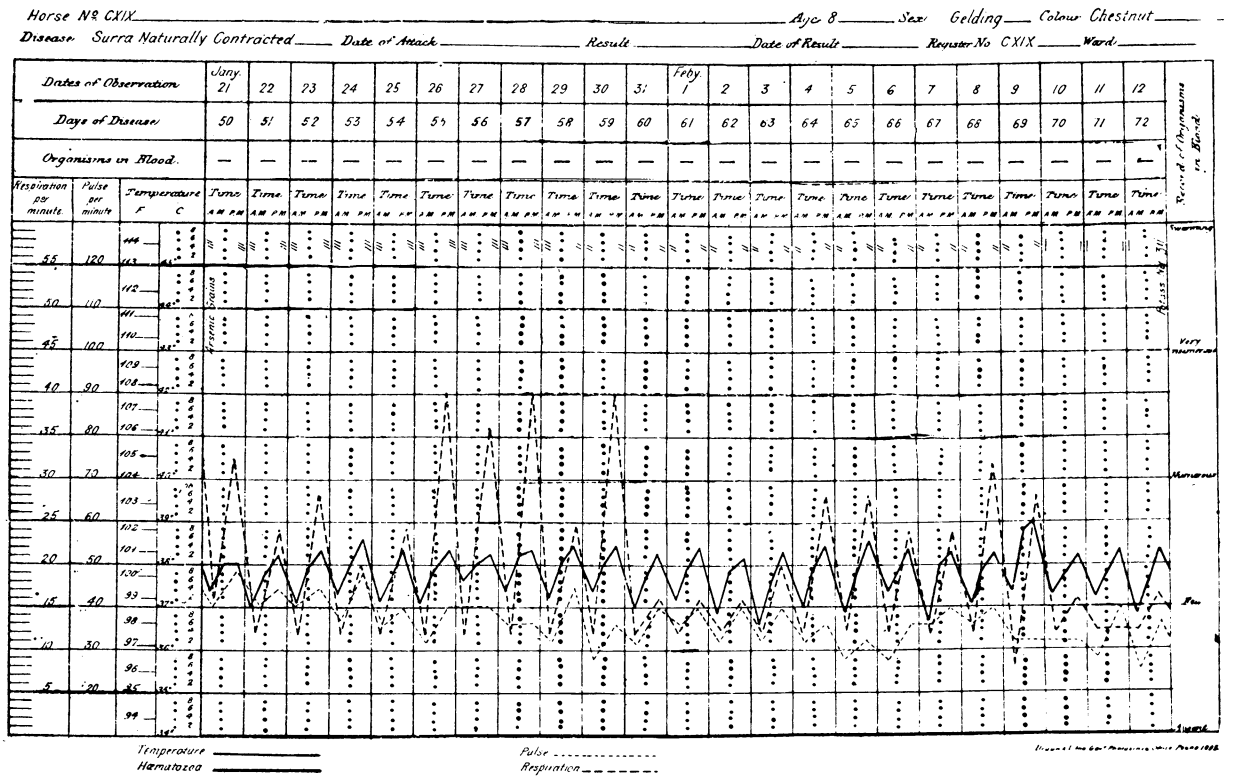


FIG. 107 (continued).—Temperature record of surra in a horse. (After Lingard.)

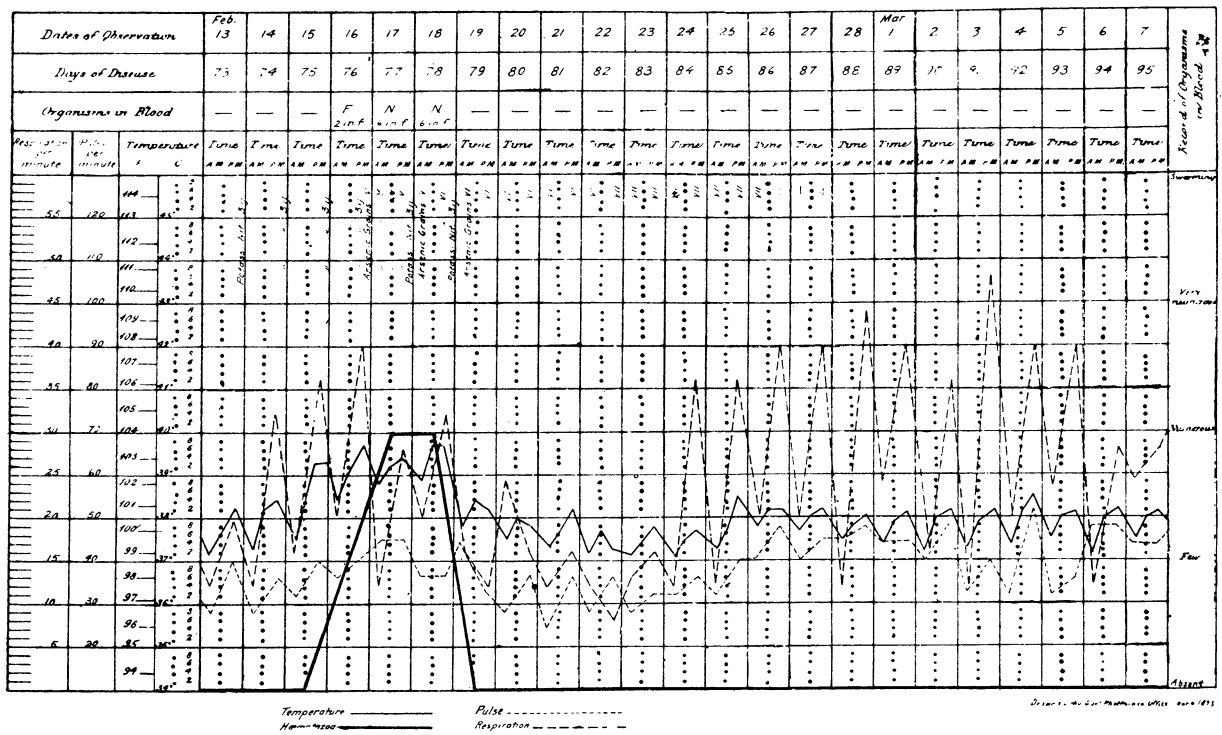


FIG. 107 (continued).—Temperature record of surra in a horse. (After Lingard.)

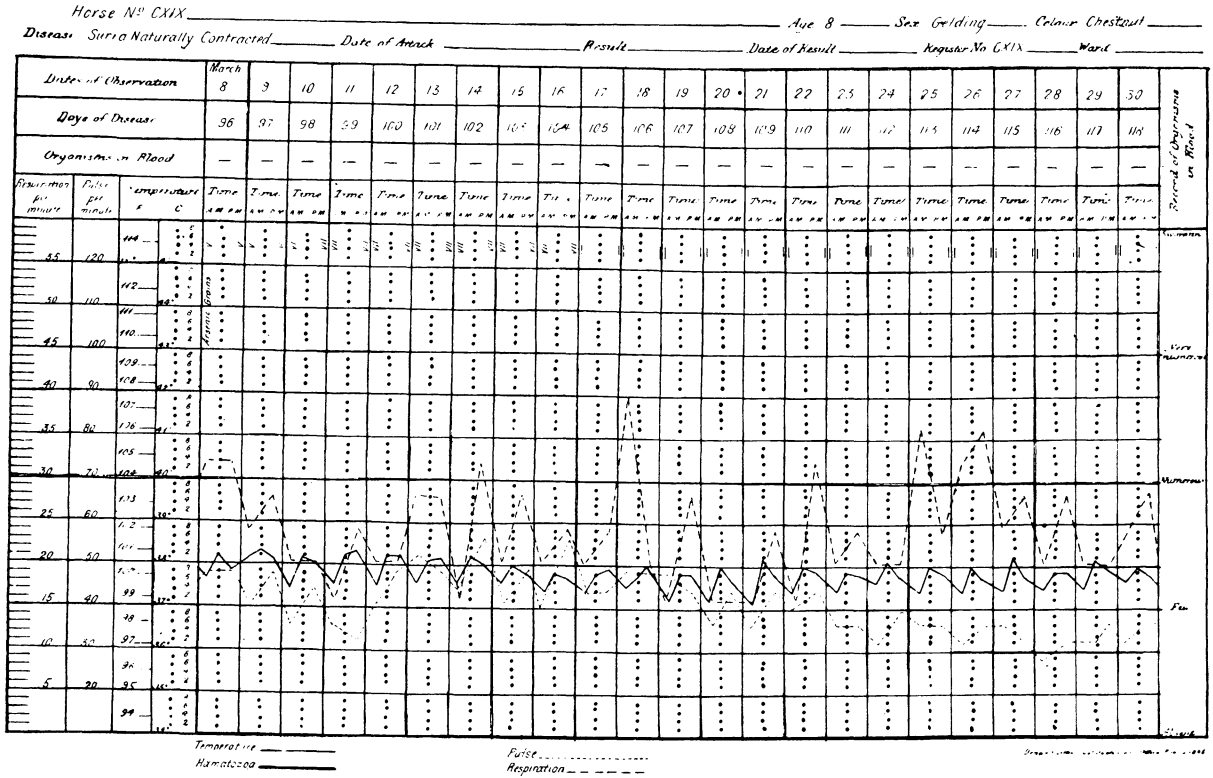


FIG. 107 (continued).—Temperature record of surra in a horse. (After Lingard.)

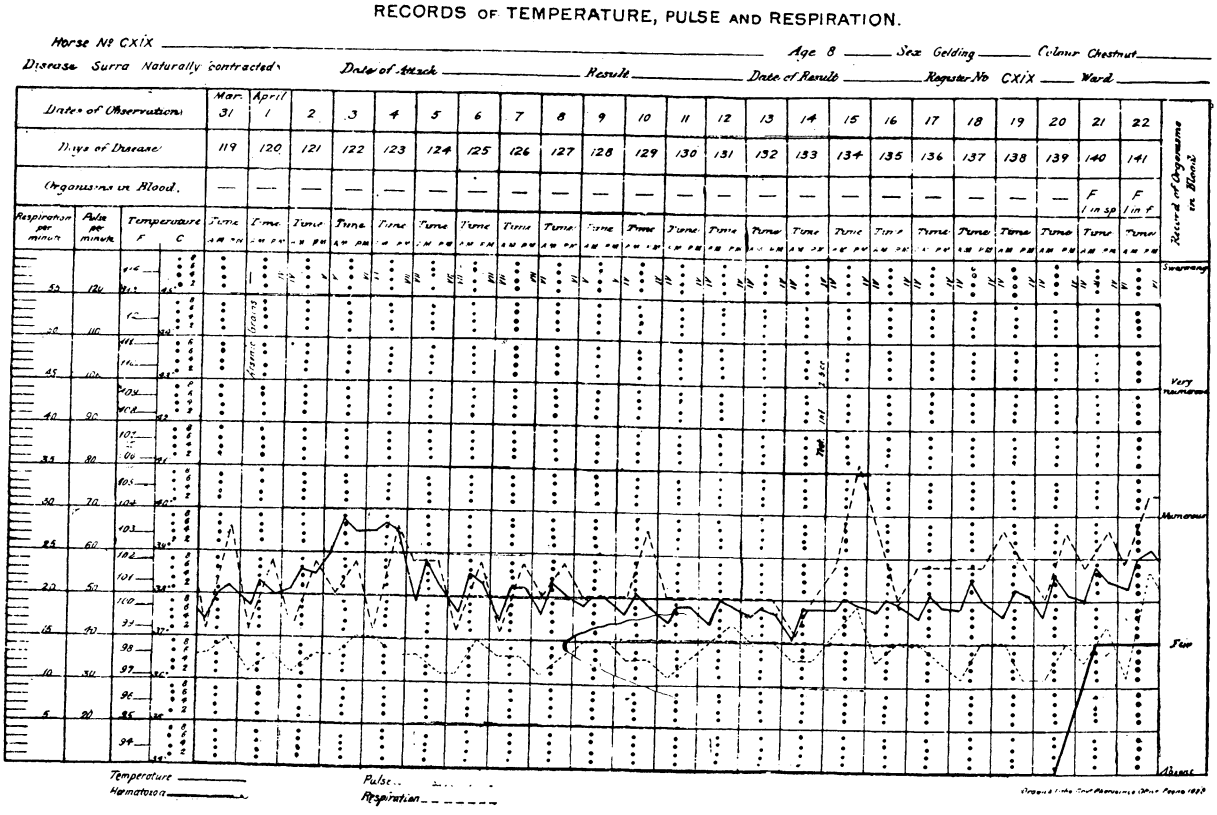


FIG. 107 (continued).—Temperature record of surra in a horse. (After Lingard.)

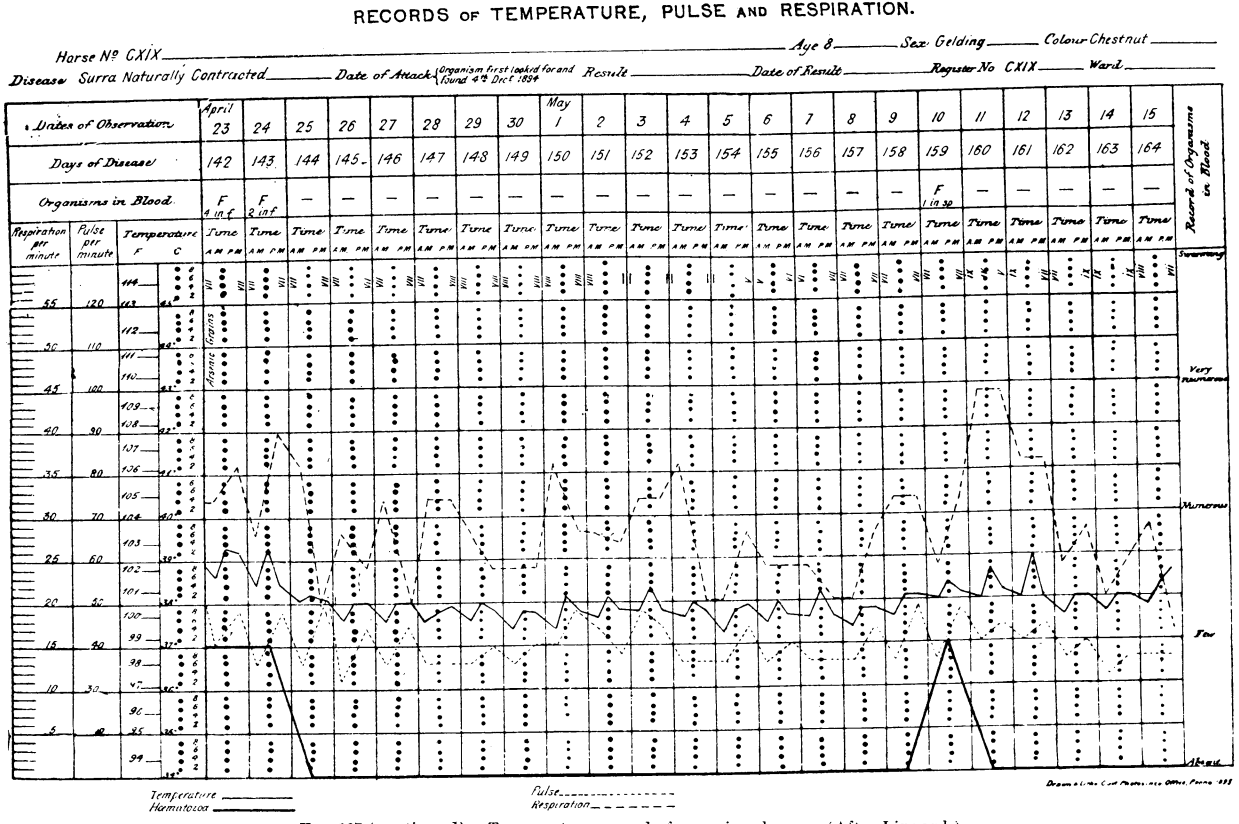


FIG. 107 (continued).—Temperature record of surra in a horse. (After Lingard.)

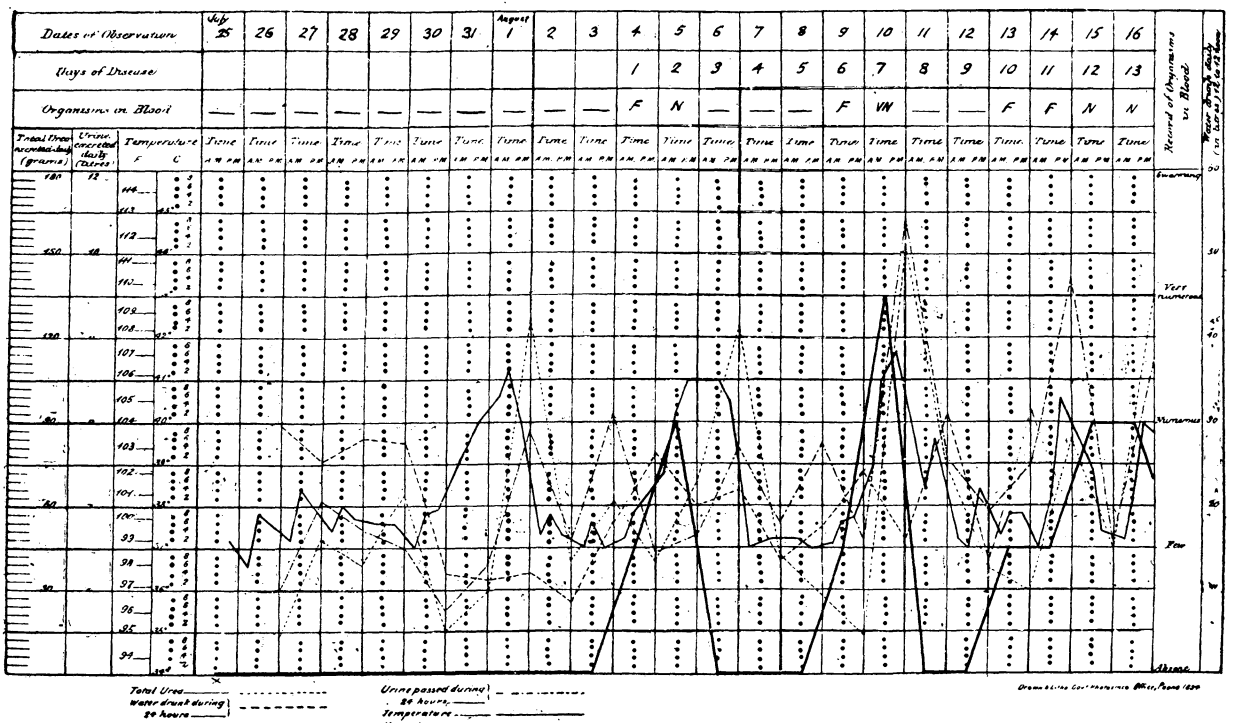


FIG. 108.—Temperature record of surra in a horse. (After Lingard.)

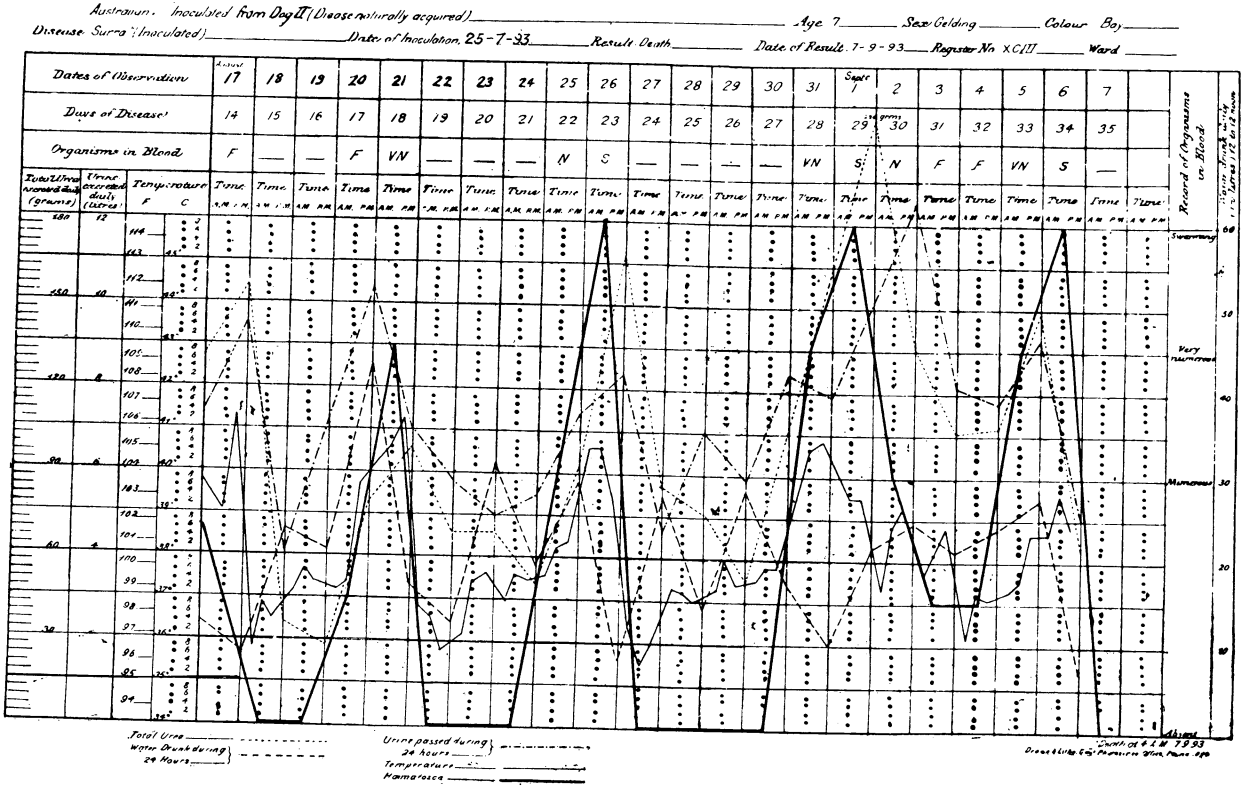


FIG. 108 (continued).—Temperature record of surra in a horse. (After Lingard.)

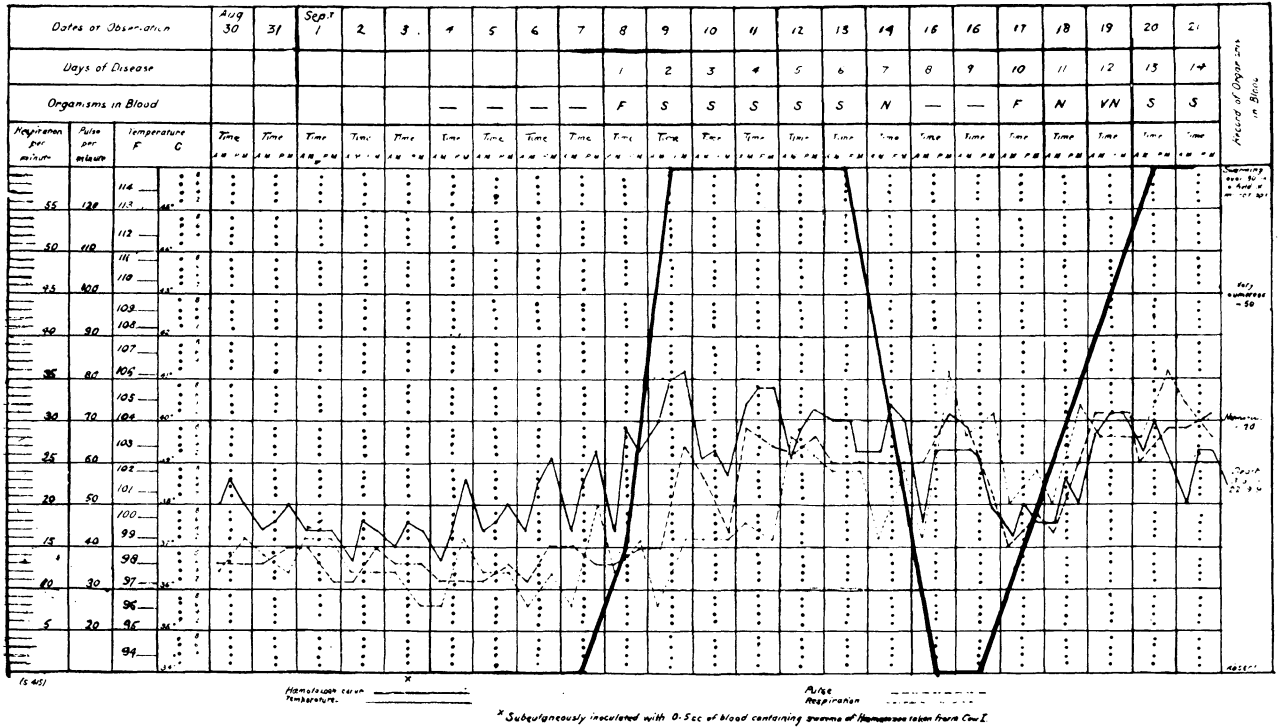


FIG. 109.—Temperature record of surra in a horse. (After Lingard.)

corresponding reduction of the number of parasites in the circulation. With the second rise of temperature to 40° C., where it remained oscillating between 30° and 40° until the day of death, the parasites again became numerous and remained so throughout the disease. Beginning about the fifteenth day after inoculation, there was edema of the penis, gradually involving the belly but not the posterior extremities. Lesions of the nose and eyes were not noticed. The appetite, except at the height of the fever, was good. There was no apparent emaciation and no serious loss of weight.

During the incubation period of mal de caderas, according to Voges, no symptoms are noticed; but as the disease progresses, the animal becomes inactive and heedless of what is going on about it. It allows the head to drop carelessly and the whole body loses its firmness and becomes more and more sluggish. On being ordered it responds very lazily, and "even the wildest and meanest horses no longer balk and bite." At this period of the disease the animal may fall to the ground and die suddenly. On the other hand, if assisted to rise, it may live for as much as two weeks.

Following the incubation period, which varies in duration, the temperature rises rapidly, often to 40° and 41° C., and on the following day falls to normal or nearly so. It then goes up again, and within five days reaches 40° C. or more. The period of apyrexia between these elevations is of uncertain length. This Voges calls the first stage of the disease, the important symptoms being the intermittent fever.

In the second stage the fever is prominent, but the intermissions become less marked as the disease advances, the temperature varying from 38.5° to 39.8° C.

Before death great variations, sometimes from 34° to 39° C. from morning until evening, may occur, the curve being as irregular as a septic one.

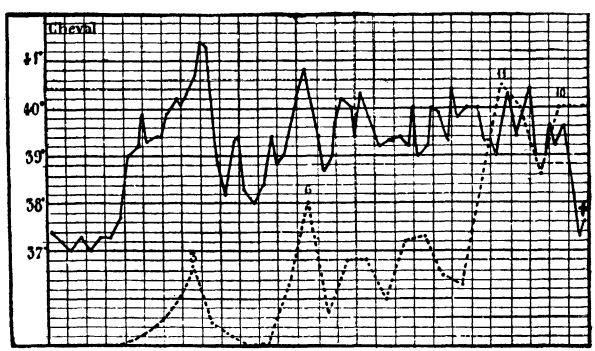


FIG. 110.—Nagana in a horse. (——) temperature. (-----) *Trypanosoma*. (After Laveran and Mesnil, 1902, fig. 4.)

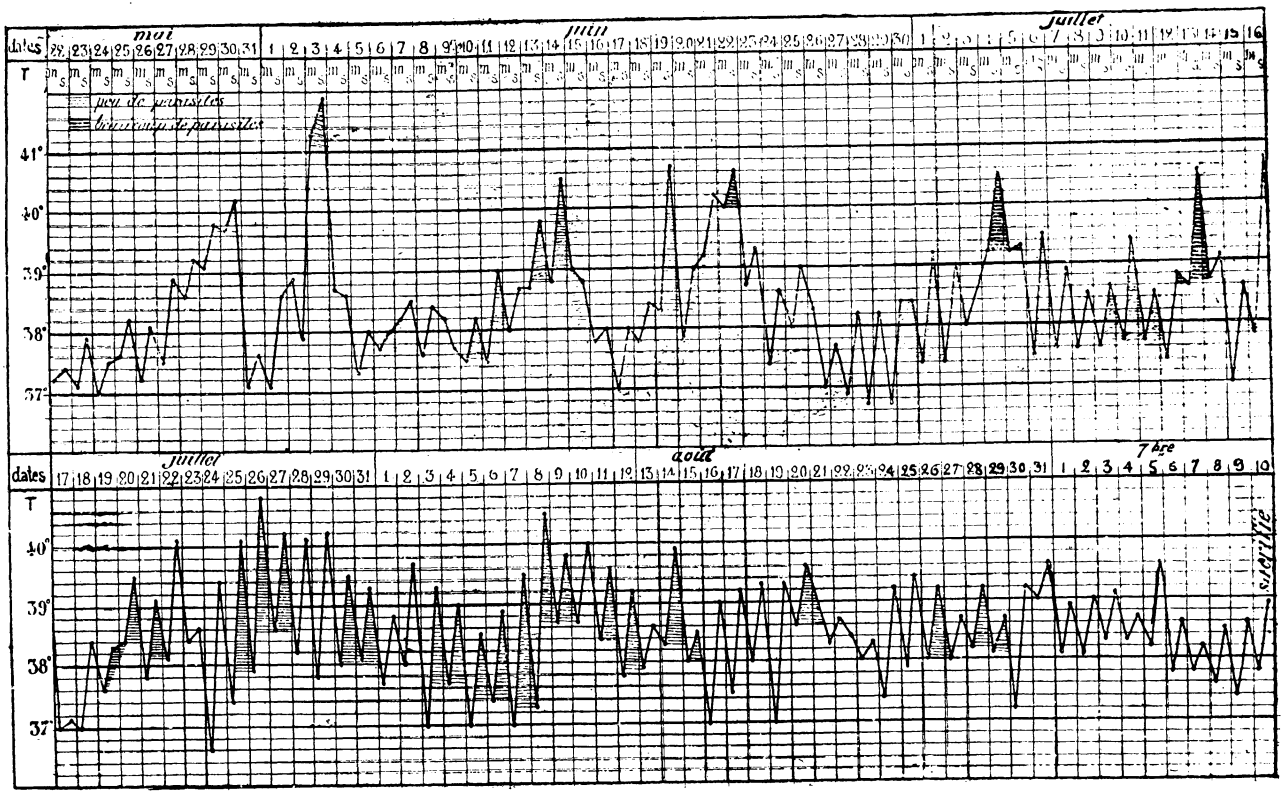
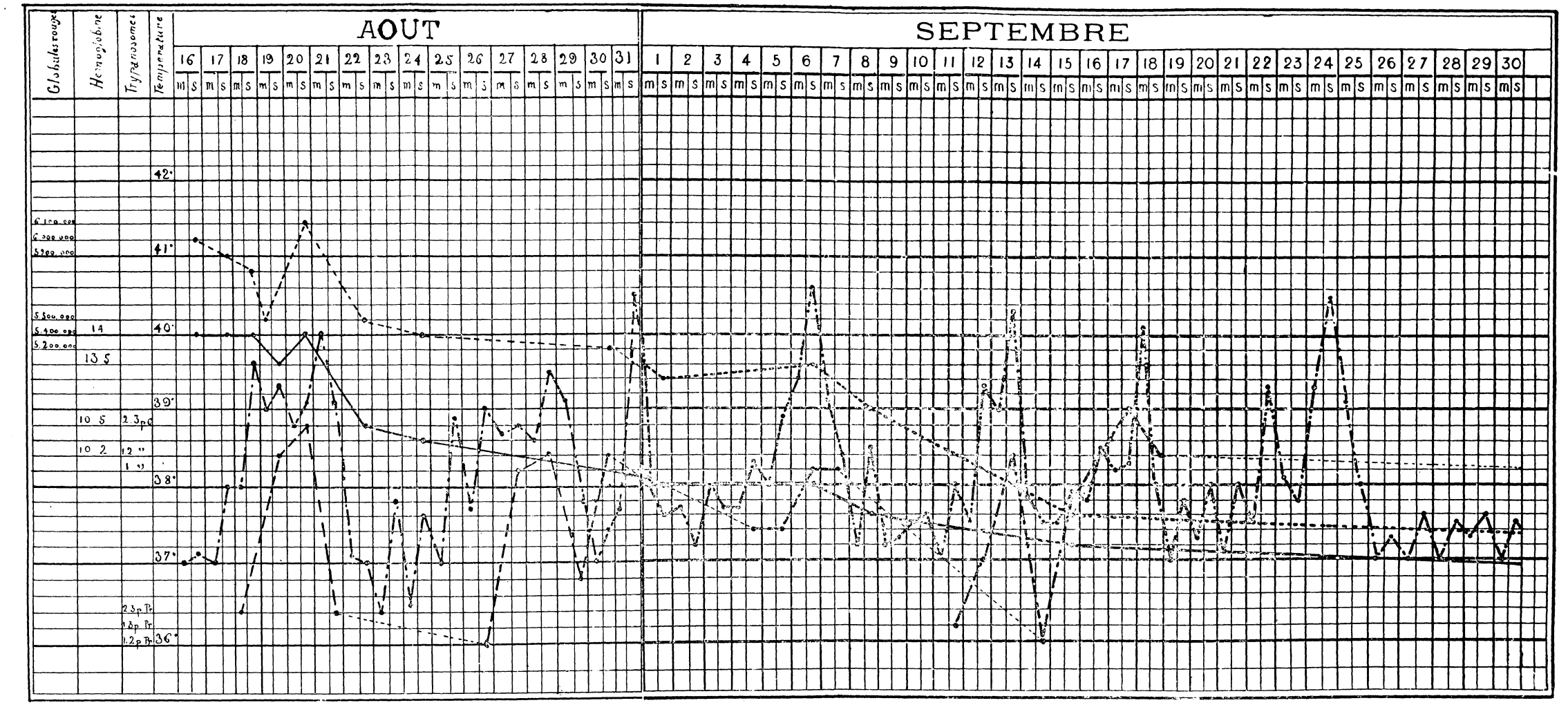
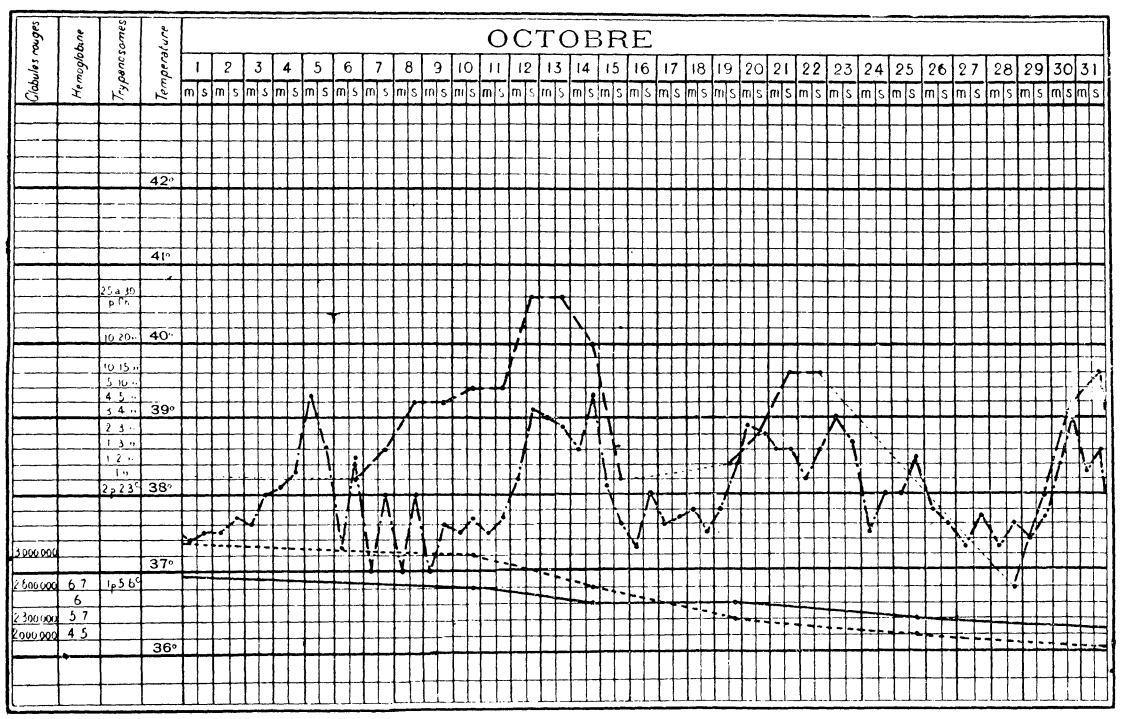


FIG. 111.—Temperature and its relation to the number of parasites in the peripheral circulation in "surra americain." (After Lignieres, 1903, fig. 10.)





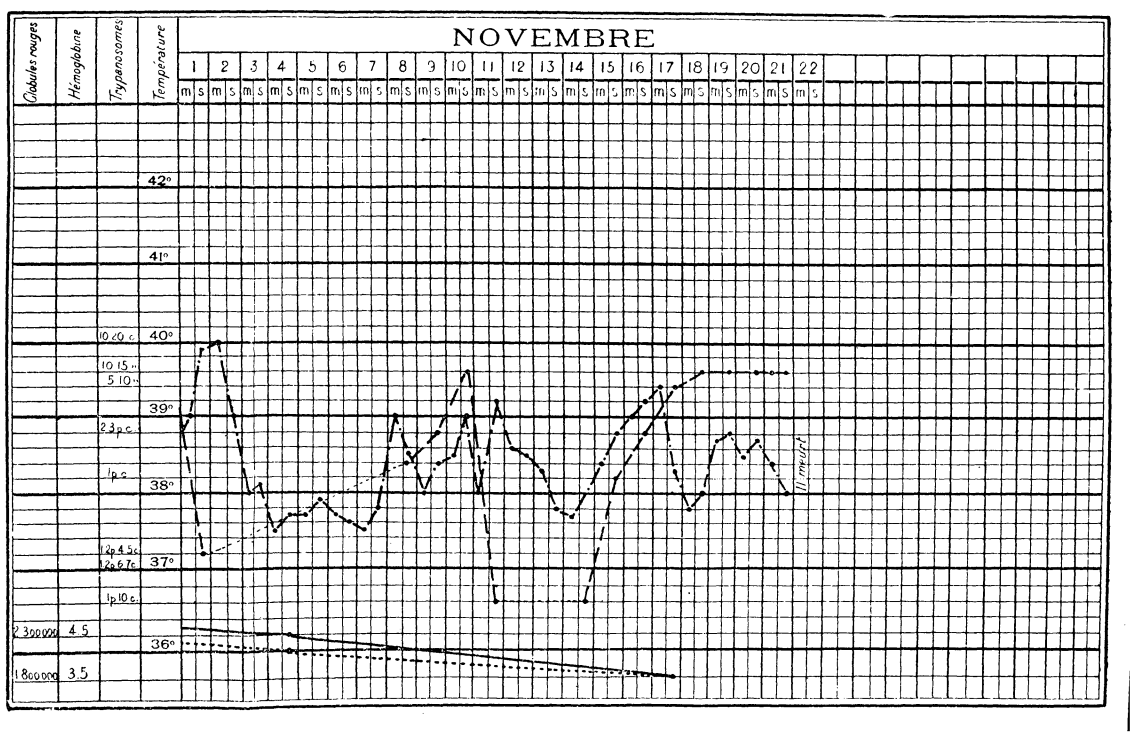


FIG. 114.—"Surra americain" in a horse. (After Sivori and Leeler, 1902.)

Hemoglobinuria may occur temporarily in the first stage of the disease. Red blood cells are usually present in the stools, which as a rule are normal in consistency and number, but in rare instances may be covered with a mixture of coagulated blood. Thirst increases and becomes marked as the disease progresses. The pulse is at first normal, but the heart grows weaker with the course of the illness, finally allowing the edema which is seen in later stages. Sudden death from heart failure sometimes occurs.

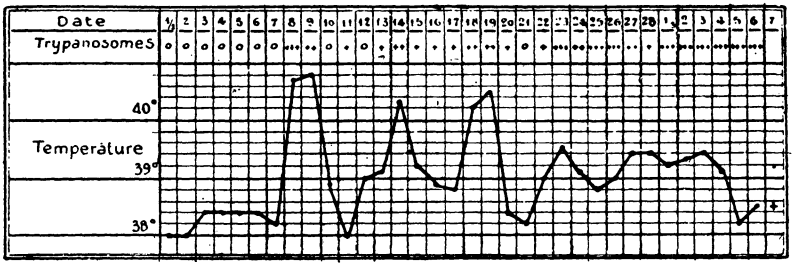


FIG. 112.—Temperature chart of a horse following intravenous injection of 20 c. c. of blood obtained from a horse which showed no parasites in the blood. Dead in thirty-four days. (After Lignieres, in Recueil d. Med. Vet. vol. 10, No. 4, Feb. 28, 1903, p. 117.)

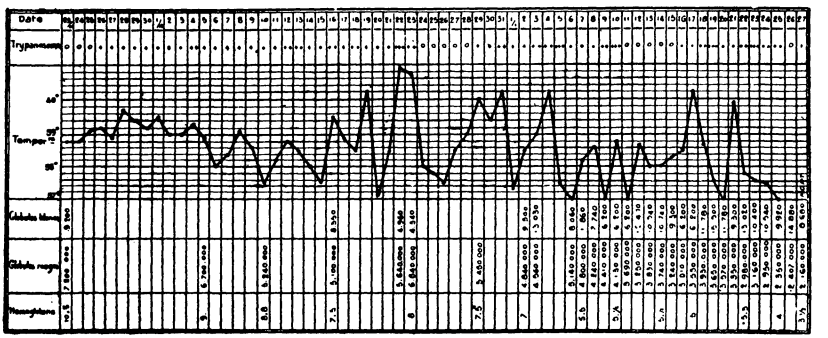


FIG. 113.—Temperature record of a horse inoculated intracerebrally with Trypanosoma from a dead rat. (After Lignieres, 1903.)

Animals with mal de caderas show no evidence of pain. During the first stage the reflexes are normal, but even as early as this there may be a diminished sensibility, which later on becomes marked, so much so that animals pay no attention to swarms of flies. Incoördination affecting particularly the hind parts becomes so severe that the animal reels as if drunken.

The hair remains smooth and glossy during the first stage, and shedding, if present, is normal. In the second stage it loses its gloss and lies

less smooth. Emaciation is not noticeable during the early part of the disease, and with good food animals often gain in weight, but during the later periods this symptom is marked and the loss may reach 100 kilos or more before death. The appetite as a rule is not disturbed, but continues good to the end, and in some cases it is noticeably increased.

Dourine is a recognized form of Trypanosomiasis in horses, but clinical descriptions are not so complete as for the other types. It is usually referred to as resembling one of the other forms. The emphasized symptoms, in addition to the ones already given, consist in phlegmonous ulcers of the genitalia and to a less extent of the various parts of the skin. The temperature as a rule does not run so high in this form of the disease as in the others, and parasites are much less numerous in the peripheral circulation. On the whole the course is considered more chronic than that of surra and the variety of susceptible animals is smaller.

As to the general description of the symptomatology of the disease as observed in the Philippines, we have nothing to add to the classical ones of the various writers in India, South America, and Africa.

With the ultimate object of discovering methods of prevention and cure, toward which all of our work is directed, one of the most important questions to decide and one which so far has not been definitely determined is the incubation period in naturally contracted cases. Authors writing of the disease under the same and different names give for it various lengths of time, and not a few say that it is unknown.

Evans fed two horses 20 ounces each of surra-infected blood, obtaining positive results and an incubation period of six days. He did not prove his animals free from infection at the time of feeding, does not state that biting insects were excluded, and of course can not say that there were no lesions in the mouth.

Lingard fed a horse frequently with small quantities of infected blood well diluted in water, with an incubation period of one hundred and thirty days or less, depending upon which feeding produced the infection. To another horse he fed 200 minims of infected blood at one dose, the incubation period being, according to the author, seventy-five days. These experiments are open to the same criticism as those of Evans.

Subcutaneous injection.—In twelve horses inoculated subcutaneously by Lingard, the average incubation period was five and two-thirds days, the longest being eight days following the injection of 1 c. c. of blood containing but few *Trypanosoma,* and the shortest four days, which occurred in four of the horses after the inoculation of 1 to 3 c. c. of blood containing *Trypanosoma* in large numbers. In three horses injected subcutaneously with blood taken during the intermissions of the disease and microscopically free from parasites, the average incubation period was six and two-thirds days, the longest being ten days and the shortest four.

In twelve horses inoculated subcutaneously with blood taken one and one-half to sixteen hours post-mortem, the average incubation period was nine and one-half days, the longest being thirteen days following the injection of 2 c. c. taken one and one-half hours post-mortem, and the shortest six days in a case of inoculation with 6 c. c. of blood taken one and one-half hours post-mortem.

In two cases of subcutaneous injection of 1 and 2 c. c. of serum taken forty-five minutes and two hours, respectively, post-mortem from a horse dead of the disease, the incubation periods were eight and nine days. A

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ANIMAL RECORD.

Horse *No* 147.
January 7 *190*3

Weight 700 lbs. *Age* 8 yrs. *Sex* Male *Color* Bay *Inoculation* Received with surra.
History

Bay native pony in good condition.

TREATMENT.	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										Jan. 7	Tryp. pos.
										8	Tryp. pos.
										9	
										10	Tryp. pos.
										11	
										12	Tryp. neg.
										13	Tryp. neg.
										14	
										15	Tryp. pos.
										16	Tryp. pos
										17	
										18	
										19	
										20	Tryp. pos.
										21	Dead.

FIG. 115.—Temperature record of surra in a horse.

horse injected subcutaneously with 1 c. c. of blood from the tunica vaginalis of a goat suffering from the disease, developed an incubation period of five days, and a horse inoculated with 1 c. c. of the blood of the same goat had one of thirteen days.

There are numerous observations to show that the incubation period in naturally contracted cases does not vary more than in experimental cases.

It is usually from four to seven days, although in exceptional cases it may be more. In one of our animals, in which the evidence was complete, it was eleven days.

The incubation period in horses artificially infected by us varied somewhat with the condition of the animal, the place of inoculation, the character of the infecting material, and perhaps with other causes; but from

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ANIMAL RECORD.

Horse *No* 50.....
September 16, , *190* 8

Weight 450 lbs. *Age* 3 yrs. *Sex* Male *Color* *Inoculation* Received with surra.

History. Native pony, emaciated, hair ruffled, enormous edematous distention of penis, from which lymph is exuding. Numerous parasites in the blood.

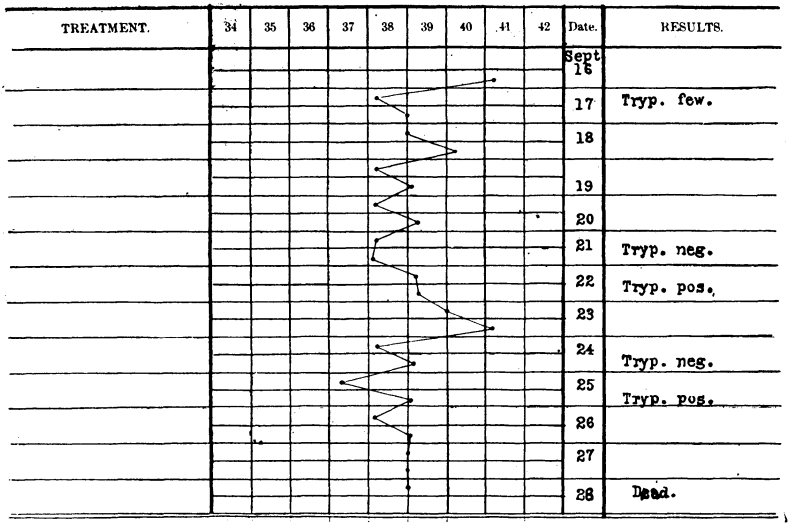

FIG. 116.—Temperature record of surra in a horse.

observation we are certain that variations in naturally contracted cases are not greater and that they occur within comparatively small limits, in mosts cases from four to seven days. One of our horses had an incubation period of eleven days, and another, which was suffering with a malignant growth and a temperature of 39.5 ° to 41° C., had one of eighteen days following a subcutaneous injection. As already stated, we are convinced that the naturally contracted disease does not differ from that produced by inoculation in the length of its incubation period, its symptoms, or any other respect.

Fever is one of the most important symptoms and is the first clinical evidence of infection. It can usually be determined during the incuba-

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ANIMAL RECORD.

Horse *No* 240
April 9, , *190* 3
Weight *Age* *Sex* *Color* *Inoculation* Surra
History Large bay American horse condemned on account of lymphangitis.

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
100 c.c. virulent rinderpest blood subcutaneously.										Apr 9	
										10	
										11	
										12	Serum reaction with surra blood negative
										13	
										14	Tryp. neg.
										15	Tryp. neg.
2 c.c. surra blood subcutaneously.										16	
										17	
										18	
										19	
										20	Tryp. neg.
										21	Tryp. neg.
										22	
										23	
										24	
										25	
										26	Tryp. surra pos.
										27	
										28	
										29	Tryp. pos.
										30	
										May 1	Tryp. pos.
										2	
										3	
										4	Tryp. pos.
										5	
										6	
										7	
										8	
										9	
										10	Tryp. neg.
										11	
										12	
										13	Tryp. neg.
										14	
										15	
										16	Few tryp.
										17	
										18	
										19	Few tryp.
										20	
										21	
										22	
										23	
										24	
										25	
										26	Reaction with human blood negative.
										27	
										28	
										29	
										30	
										31	
										June 1	
										2	Reaction with equal parts of blood surra animal, neg.
										3	do.
										4	do.
										5	do.
										6	
										7	
										8	Very sick. No great enlargement of sheath
										9	
										10	Numerous tryp.
										11	

FIG. 118.—Temperature record of surra in an American horse.

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ANIMAL RECORD.

Horse *No* 110
December 17, *190* 2

Weight *Age* *Sex* *Color* *Inoculation* Received with surra.
istory

Native pony early in disease.

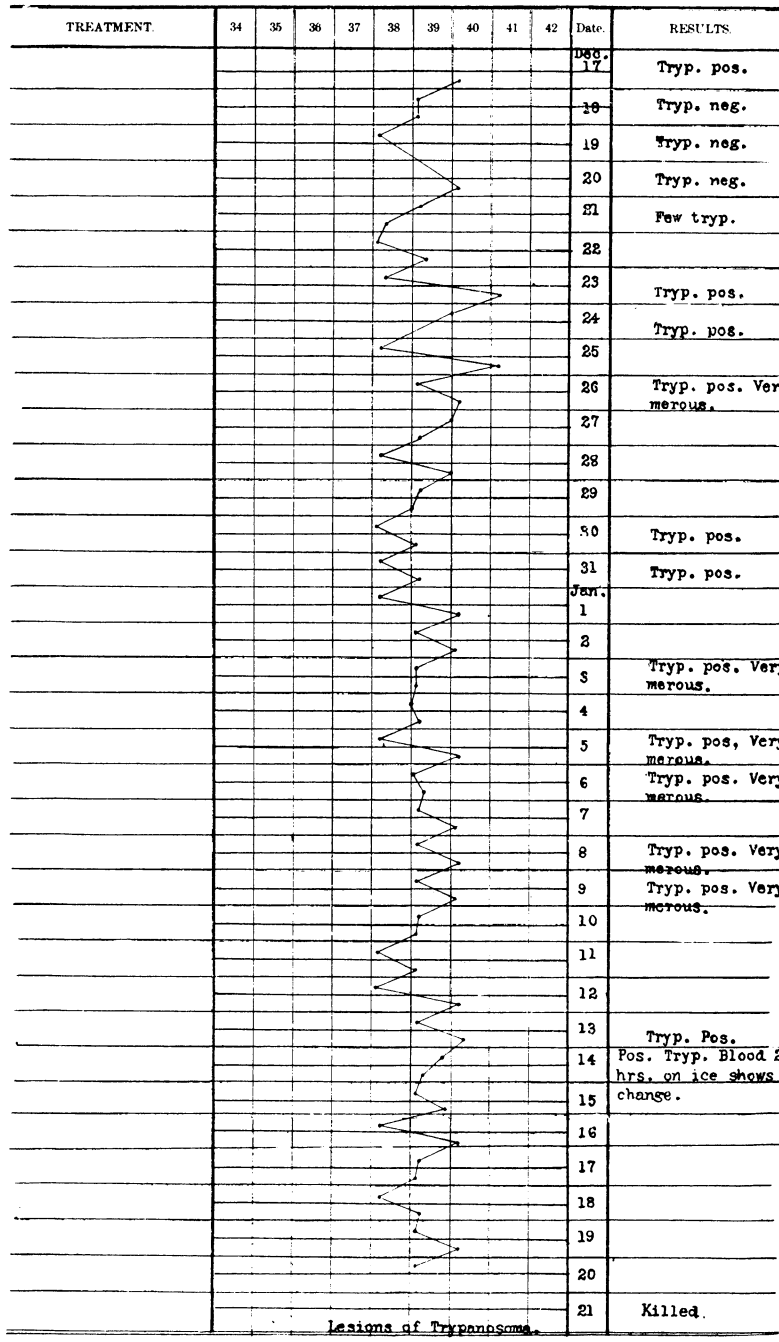

FIG. 119.—Temperature record of surra in a native pony.

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ANIMAL RECORD.

Horse *No* 94
December 7, *190* 2

Weight 600 lbs. *Age* 6 yrs *Sex* Male *Color* Gray *Inoculation* Received with trypanosomiasis

History Gray native pony showing symptoms of surra.

TREATMENT.	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										~~Dec.~~ 7	
										8	Tryp. pos.
										9	Tryp. pos.
										10	Tryp. pos.
										11	Tryp. pos.
										12	Tryp. pos.
										13	
										14	
										15	Tryp. pos.
										16	Tryp. neg.
										17	Tryp. pos.
										18	Tryp. pos.
										19	Tryp. pos.
										20	Tryp. neg.
										21	Tryp. neg.
										22	Tryp. neg.
										23	Tryp. pos.
										24	Tryp. pos.
										25	
										26	Tryp. pos.
										27	
										28	
										29	
										30	
										31	Tryp. neg.
										Jan. 1	
											Dead

FIG. 117.—Temperature record of surra in a horse.

FIG. 120.—Showing urticarial eruption and œdema.

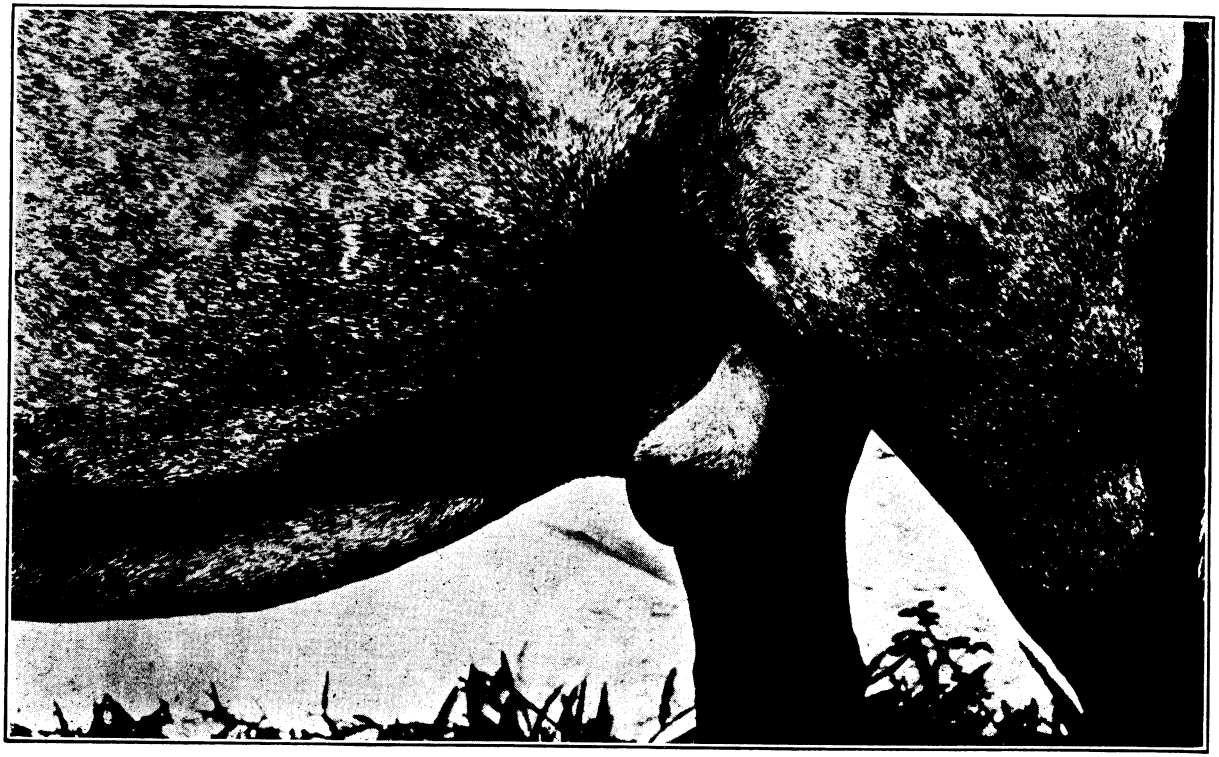

FIG. 121.—Showing edema of scrotum, penis, and belly.

tion period in exposed animals. The temperature as a rule rises very rapidly and during the first few days may reach 40° to 41° C., after which it becomes irregularly intermittent, remittent, or, in rare instances, relapsing in type, always being higher in the afternoon.

The especial value of the temperature in diagnosis is its mere presence in connection with other symptoms. There is at any time very little in its variations which is characteristic enough to be very significant; but taken over a long period, its course, while not constant, makes a suggestive picture.

The illustrations (see figs. 115–118) give an idea of the course of the fever in horses in Manila.

Simple observations of a horse suffering with this disease do not afford sufficiently exact data during the very early stages, but as the disease progresses they become of the greatest diagnostic value.

The hair, at first normal, soon becomes rough and shows a tendency to fall out in places, especially the long hair around the nose and eyes, though this never progresses to the same extent as it is seen to do in some of the smaller animals. The skin becomes dry and scrawny and sometimes shows eruptions in places, which may be erythematous, macular, or urticarial. We have occasionally noted in well-advanced cases bunches of macules, somewhat concentric in form, which became pustular and finally covered with a scaly uxudate caused by the drying of the purulent-looking discharge from the pustules.

Catarrhal symptoms, of the eyes particularly and less noticeably also of the nose, manifest themselves rather early in the disease, although they may come on late and in some cases are almost wholly absent throughout its course. At first the discharge is small in amount and watery, but as the disease progresses becomes more abundant and mucus-like, and finally takes on a yellowish tinge, becomes tenacious and often coagulates in the inner canthi of the eyes.

Subcutaneous edema, more or less marked, is a constant symptom, but varies greatly in the time of its appearance. In some cases it is seen early in the disease, becoming a very prominent symptom, while in others it comes on late and is very insignificant. Its intensity does not appear to bear any relation to the duration of the disease. In nearly every instance it is first noticed around the genitalia (fig. 120), which remain in the majority of cases the most severely involved part; from the sheath it spreads forward along the belly on both sides of the linea alba in two well-defined bands (fig. 121), which may extend between the forelegs, where they then unite and pass on to the chest as a large pod, as illustrated in fig. 122. When the swelling becomes marked, the two bands under the belly may unite. The edema extends also down the hind legs, being most marked below the hock; the forelegs may also be involved, but to a less extent. Other places which

FIG. 122.—Native pony with surra, showing edema and condition of hair.

occasionally show this swelling are the nose and the loose tissues around the eyes, the base of the jaw, the throat, and the base of the ears; but it is rare to see these parts involved to any considerable extent.

One of the earliest symptoms following a rise in temperature is the pallor of the mucous membranes, which first become pearly white and then take on a decided yellowish tinge. In a well-marked case this symptom alone is almost sufficient to make a diagnosis. The mucosa of the mouth, tongue, eyes, and nose assume a ghastly whiteness, which is out of all proportion to the pleural anemia. Before death these membranes become somewhat yellowish, a change which gives a jaundice-like appearance but is of the same character as that seen in some of the other tissues of the body and described as a gelatinous infiltration.

Symptoms of the organs of special sense are important. In many cases vision is impaired and total blindness may be brought about, usually by the clouding of the aqueous humor, which in such cases as a rule contains parasites. The sense of hearing is also involved, but generally to a much less extent.

Enlargement of the submaxillary and to a less degree of the other subcutaneous glands is a frequent symptom. In some instances the submaxillary glands may be greatly swollen and very sensitive to the touch; and again we have seen animals without any apparent enlargement or tenderness of these organs during the entire course of the disease. When Trypanosomiasis is once well established, respiration is usually quickened and in many instances more or less labored, as is evidenced by the bellows-like movement of the abdominal walls. These symptoms are intensified whenever broncho-pneumonia complicates the disease.

There are usually no gastrointestinal symptoms of importance, but in many cases a very severe diarrhea develops during the later stages, generally ten or twelve days before death.

The nervous symptoms vary considerably in the horse. In the larger number of cases the described incoördination of movement and the partial paralysis of the hind quarters are present to a certain extent, while cases are met with in which these symptoms do not at any time manifest themselves.

The morbid anatomy has already been considered in the chapter devoted to a general discussion of this subject.

TRYPANOSOMIASIS OF MULES.

Very little in regard to Trypanosomiasis of mules is found in literature excepting the bare statement that these animals are susceptible and have a long period of illness. Voges says that the duration of the disease may be a year or more but that often the parasites are not found by microscopic examination for days or weeks at a time, and that he would not be surprised at some future time to find an immune animal.

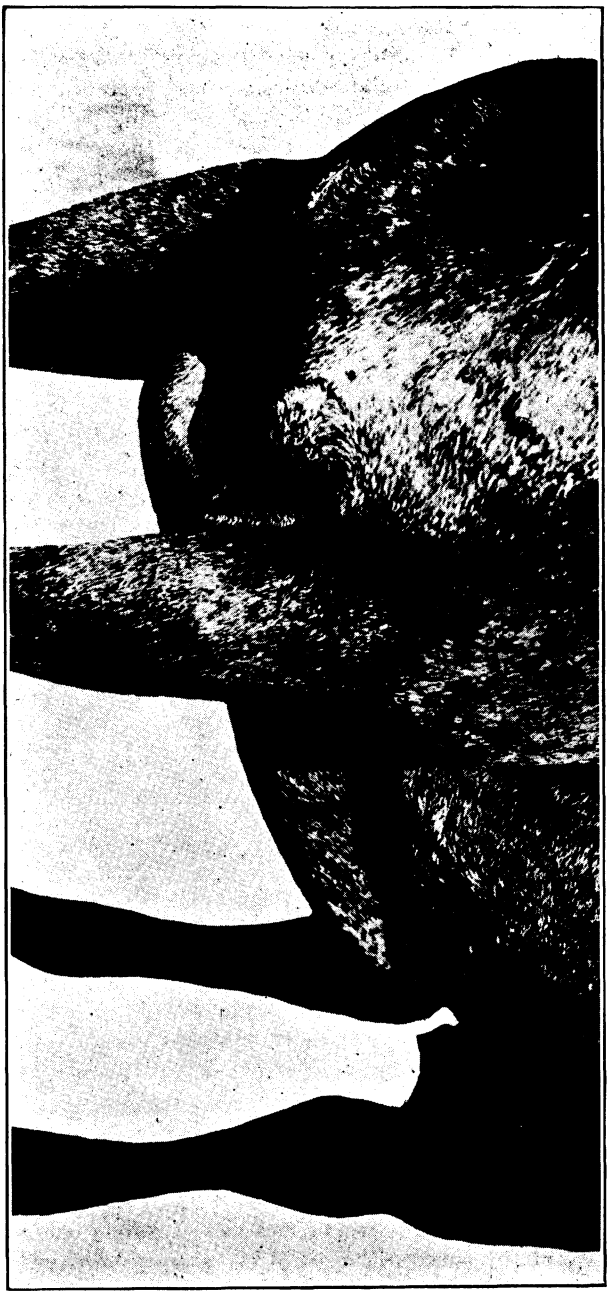

FIG. 123.—Showing œdema covering the abdomen and extending well up between the front legs; also a large pad on the right breast.

The disease in these animals in the Philippine Islands is of longer duration, just as is true in other infected zones. This fact might be taken advantage of in bettering conditions in countries where surra is prevalent and where means of eradication and prevention are not applicable, because these animals may be used for a long time without becoming useless through exhaustion incident to the disease. Mules are largely used as draft animals by the Military and Civil Governments of the Philippine Islands and are being introduced to an increasing extent in private enterprises.

By inoculation they are just as susceptible to Trypanosomatic infection as horses, but they appear to be less frequently attacked by natural infection; this is no doubt partly owing to the fact that flies disturb them less.

The symptoms in general are similar to those described for the horse, but there are certain slight differences. The temperature is less remittent and more rarely intermittent, and we have not seen a single case in which the fever was of a relapsing type. Edema, weakness, and anemia are

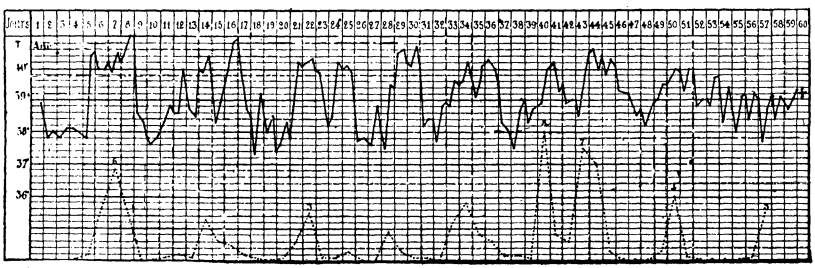

FIG. 124.—Nagana in the ass. (———) Temperature. (-----) Trypanosoma. (After Laveran and Mesnil, 1902, fig. 3.)

slower in their appearance, but when once well established show no suggestive differences. (See figures in preliminary report.)

The parasites, as determined by microscopic examination, as a rule are not so numerous in the peripheral circulation as they are in that of the horse, and the periods during which they are not found at all are more frequent and of longer duration. However, just as in horses, the blood is constantly infectious by inoculation throughout the course of the disease. The incubation period is the same as in the horse, the duration from four to twelve weeks or even longer, and the mortality 100 per cent.

As a general rule, skin lesions are more constant and decided than in the case of the horse, although of the same general character. The localization of symptons in the skin and genitals is more noticeable in animals showing some resistance to the infection than in others, so that in some of the lower animals, such as the rabbit, we have a very satisfactory picture of dourine.

The morbid anatomy in mules is very similar to that of the horse, which has already been discussed.

TRYPANOSOMIASIS OF ASSES.

According to Laveran and Mesnil, nagana shows the same general character of infection in these animals as it does in the horse. The course of the temperature is more irregular and the relation of the number of parasites in the peripheral circulation to the temperature is more constant. At a rule, they are less numerous in the blood and may be entirely absent for longer periods of time. The local symptons, particularly edema, are said to be scarcely noticeable in these animals. The average duration of the disease is given by these authors as fifteen days.

Voges states that asses are invariably susceptible to mal de caderas, and that the symptoms of the disease in them do not differ from those described for mules. Koch found the asses of Massai immune to the infection. He does not appear, however, to have demonstrated the immunity of these animals by inoculation; and as all other writers, referring to the susceptibility of the various species of asses, have always found them to be capable of contracting the disease, we can not but feel sceptical about Koch's conclusions. Lingard mentions particularly the chronic course of surra in the donkey. There are no asses in the Philippines, so that we have been unable to perform any work on these animals.

TRYPANOSOMIASIS OF OTHER EQUIDES.

Nearly all other equides, including hybrids, have been shown to be susceptible by various writers, although very little on the course of the disease in these animals is given in detail. As they are not of any economic importance in these Islands, no consideration will be given them here.

TRYPANOSOMIASIS OF CATTLE.

The great variations in results obtained in the study of this family of animals and their undoubted great importance in perpetuating epidemics, make it one of the most important to be considered. In nearly all countries where the infection is prevalent, cattle have been found to be susceptible.

With reference to the course of Trypanosomiasis in cattle and the mortality of these animals, there is wide difference of opinion in the same country as well as in different ones. So far as we know, Voges in South America is the only writer who states positively that some cattle are not susceptible. He is certain the cattle of that country do not contract the disease after being inoculated.

Certain writers in Africa maintain that cattle are very susceptible to nagana, with a high mortality. Others, as Schilling, have shown the infection not to be invariably virulent for these animals, the course of

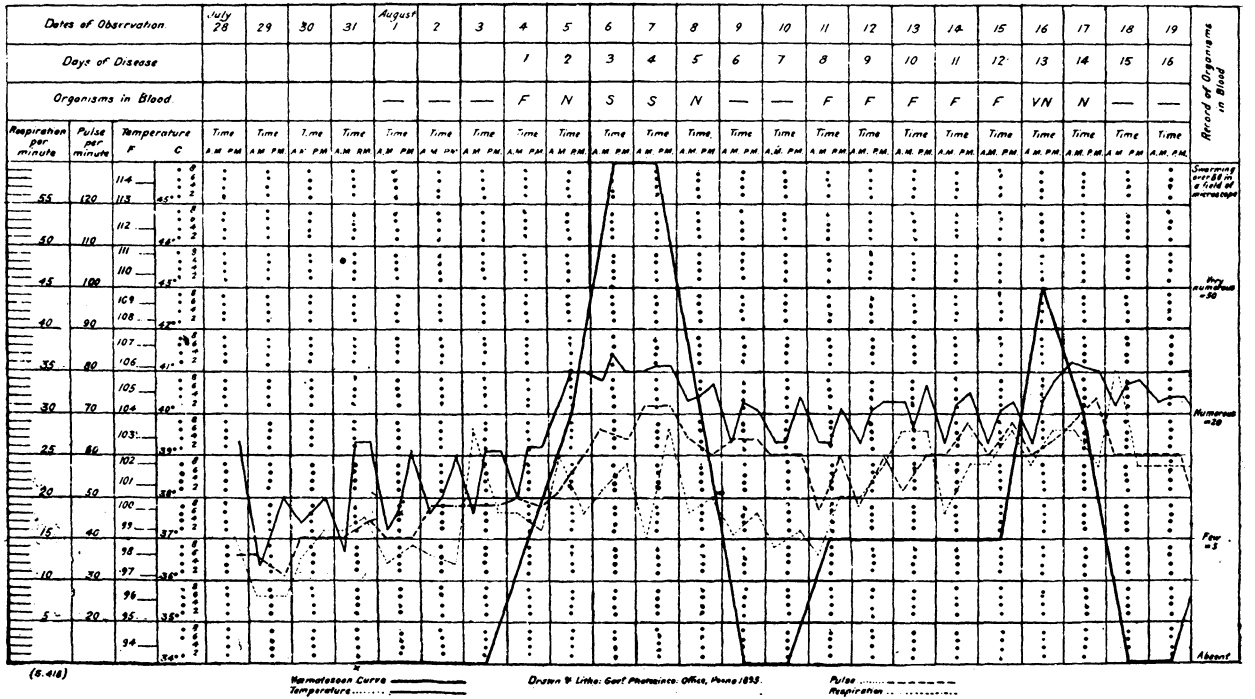

FIG. 125.—Temperature record of surra in a donkey. (After Lingard.)

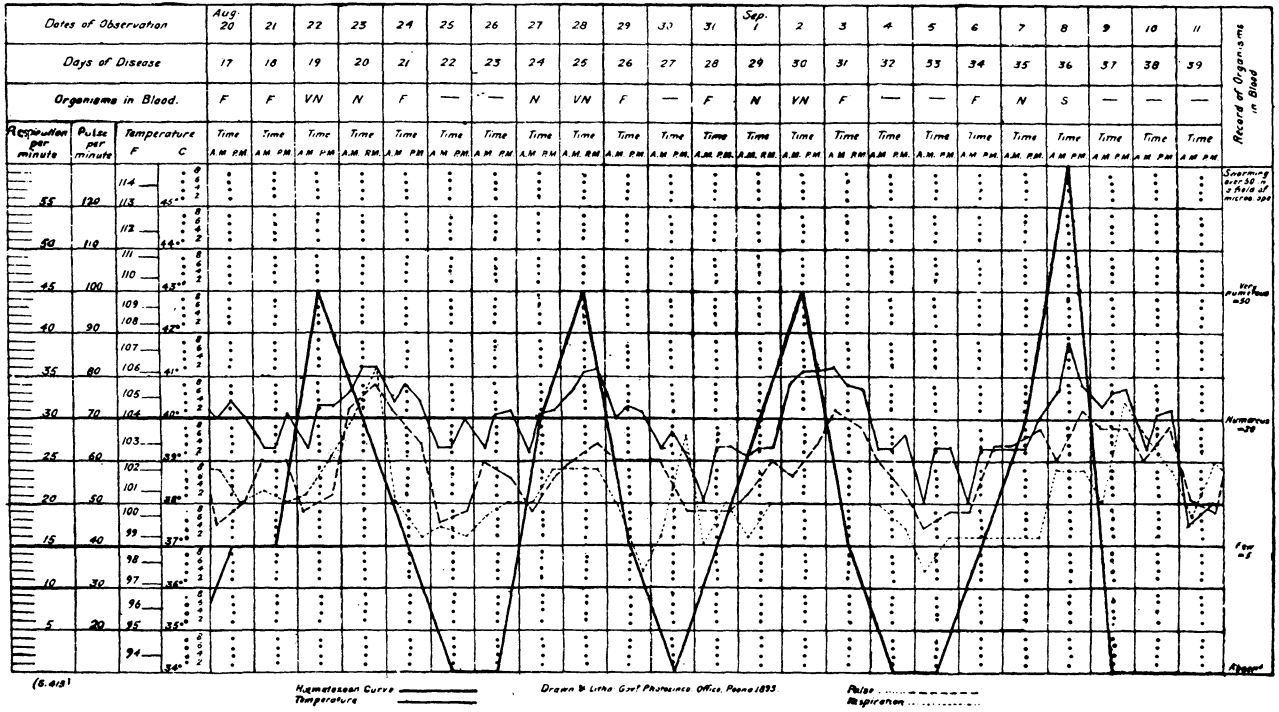

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

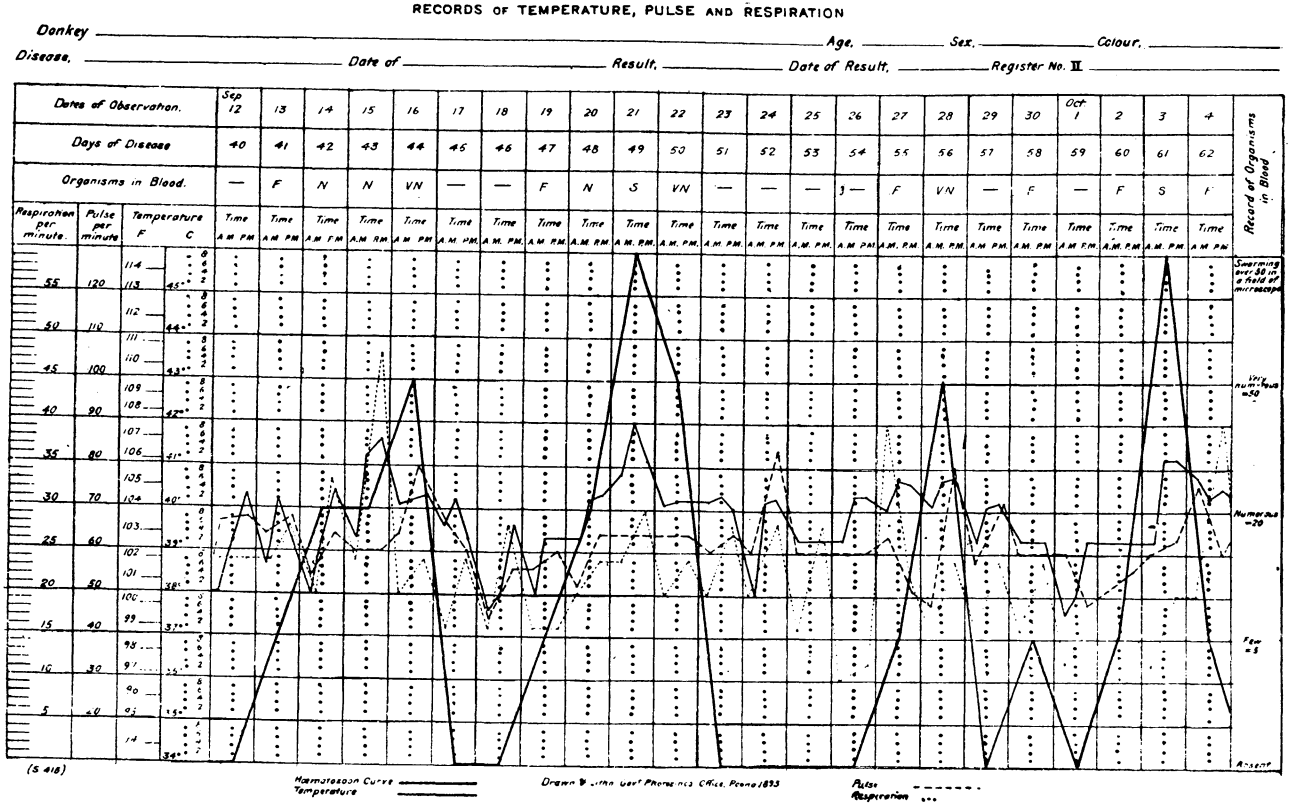

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

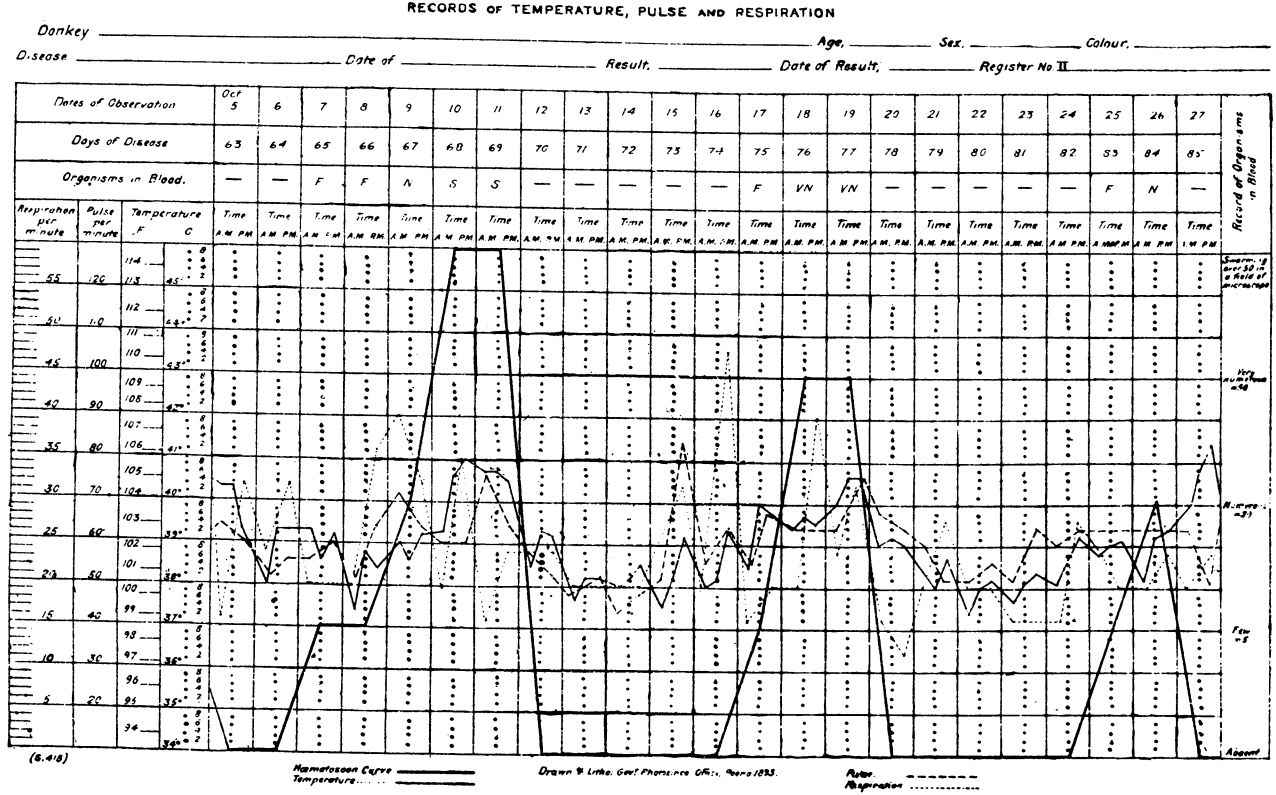

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

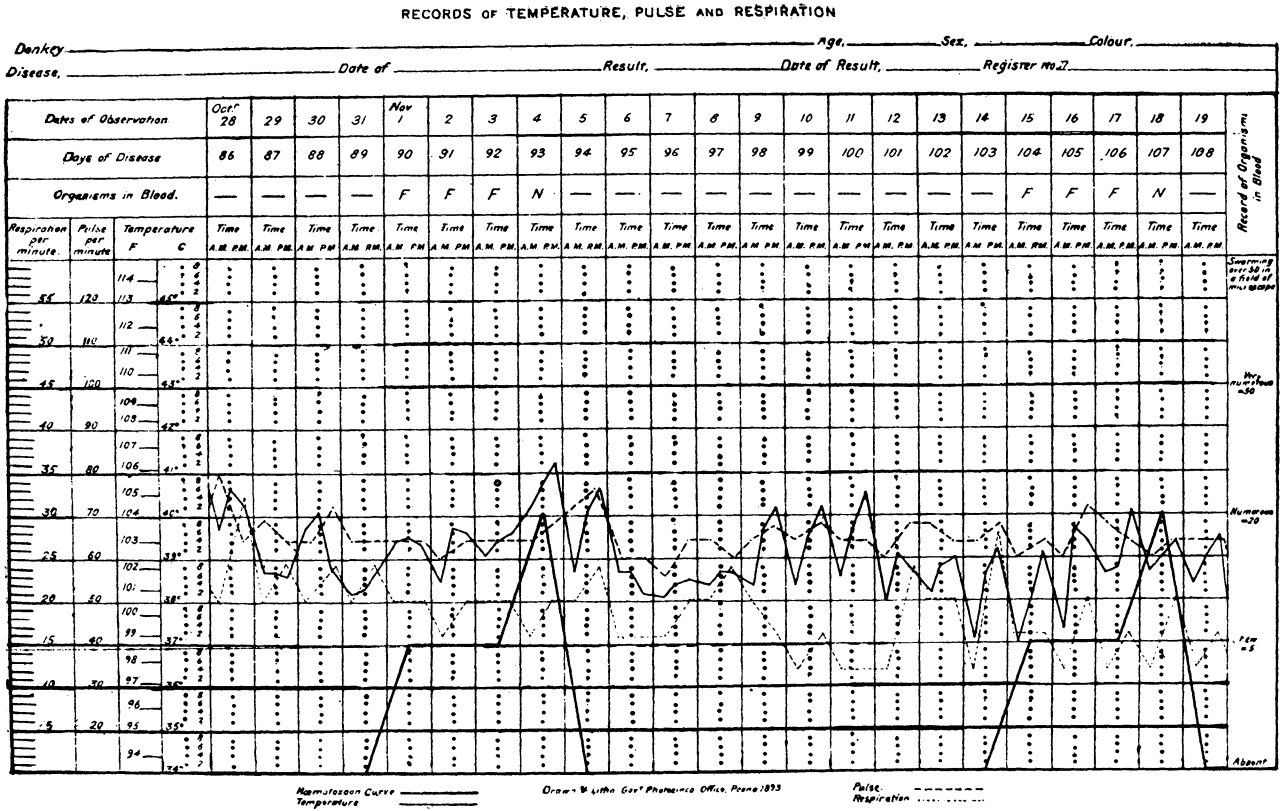

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

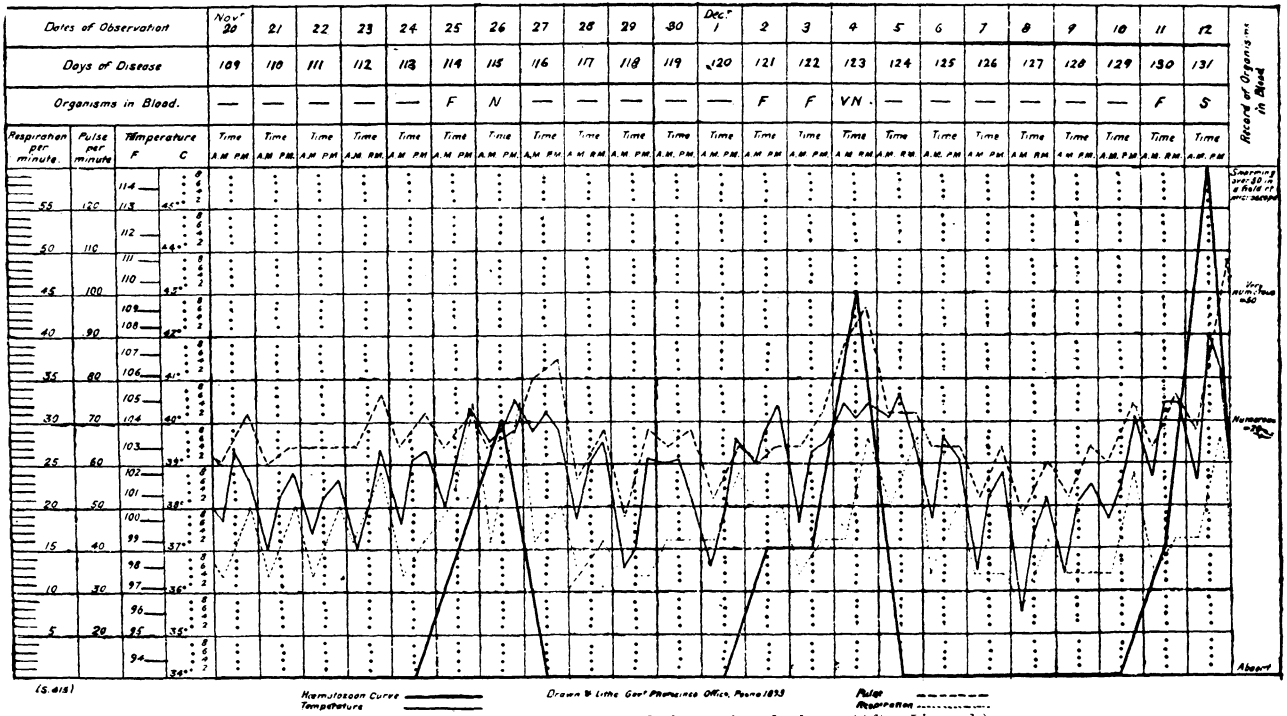

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

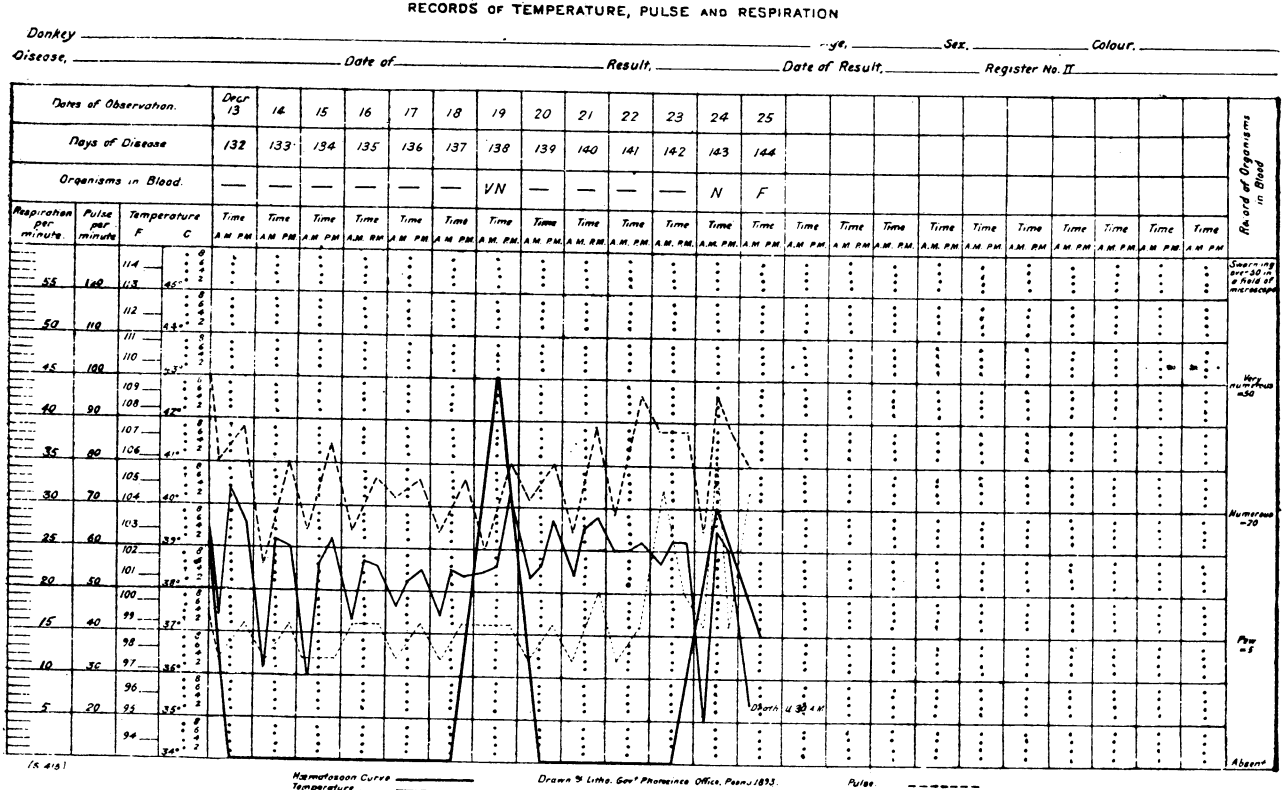

FIG. 125 (continued).—Temperature record of surra in a donkey. (After Lingard.)

the disease to be long and the mortality low, some cases of complete recovery being reported. Laveran and Mesnil working with *Trypanosoma* of nagana in France obtained a long course of the disease in infected animals, and the mortality was certainly much lower than the reports usually received from Africa would indicate for that country. Writers in India practically all agree that cattle are susceptible to the disease, but mention its long course, lower mortality, and some cases of complete recovery.

Bruce states that the duration of nagana varies from a week to six months or more. The symptoms are much less marked than in horses or dogs. Emaciation is rapid; the hair becomes rough and falls out; fluid runs from the nose and eyes; and there is a tendency to diarrhea. The dewlap becomes edematous, but the edema is not so prominent on the abdomen and posterior extremities as in the infection of the horse. Fever is constant, but not so high as in the case of horses, occasionally reaching 41° C. Parasites are rare in the blood.

Schat, working with the surra of Java, maintains that the disease is very virulent in that country for these animals, stating that the mortality is enormous, the infection sometimes being acute and of short duration and at others chronic with a longer course. However, as already stated, from Schat's description of the disease we can not but believe that there was some other element present to complicate many of his cases. He unquestionably worked with Trypanosomiasis, and *Trypanosoma* were no doubt present, but his description of the symptomatology and the morbid lesions greatly resembles that of rinderpest. It seems more than likely that he was working with a combination of these two diseases.

Theiler observed in the cattle of South Africa an acute pernicious anemia with only slight fever, which he considered due to a special *Trypanosoma* named by Laveran and Mesnil *Trypanosoma theilerii.*

Lingard speaks particularly of recurrent transient urticarial eruptions in cattle suffering from surra. Great variations were observed in the temperature, the remissions always being observed in the mornings.

Emaciation was usually marked. Parasites were few and intermittently present in the peripheral circulation. He gives the usual incubation period in inoculated cases as four to eleven days, and states that the course is chronic with no mortality in uncomplicated cases.

In the Philippines very little has been written about this disease in cattle, except that they are susceptible. In our work, which has now covered a period of nearly one year, we have examined the blood of hundreds of animals, and but few cases of natural infection have been found. It may be that during the wet season a large number of these animals suffer from Trypanosomiasis. By inoculation they are susceptible, and the course of the disease as well as its symptomatology corresponds to the descriptions given by the best authors in other countries.

The incubation period is about the same as in the horse, and the

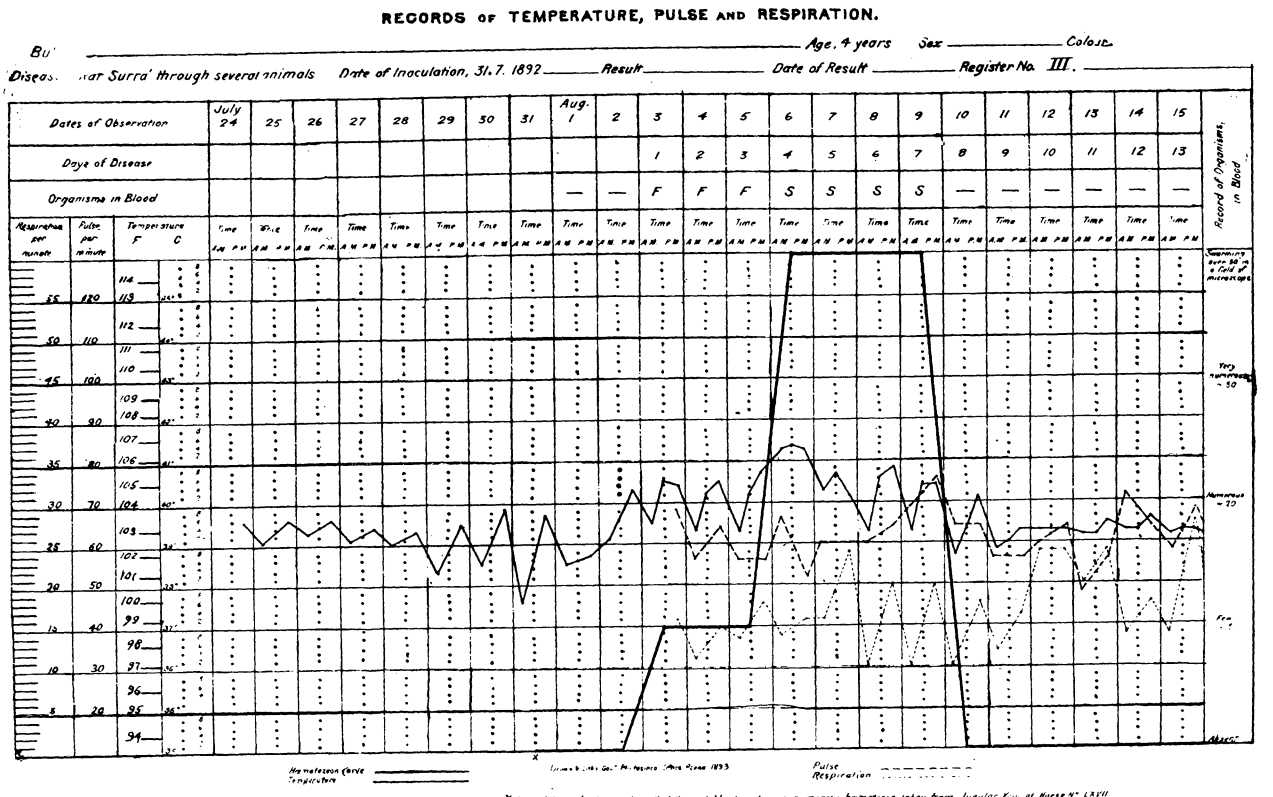

FIG. 126.—Temperature record of surra in a bull. (After Lingard.)

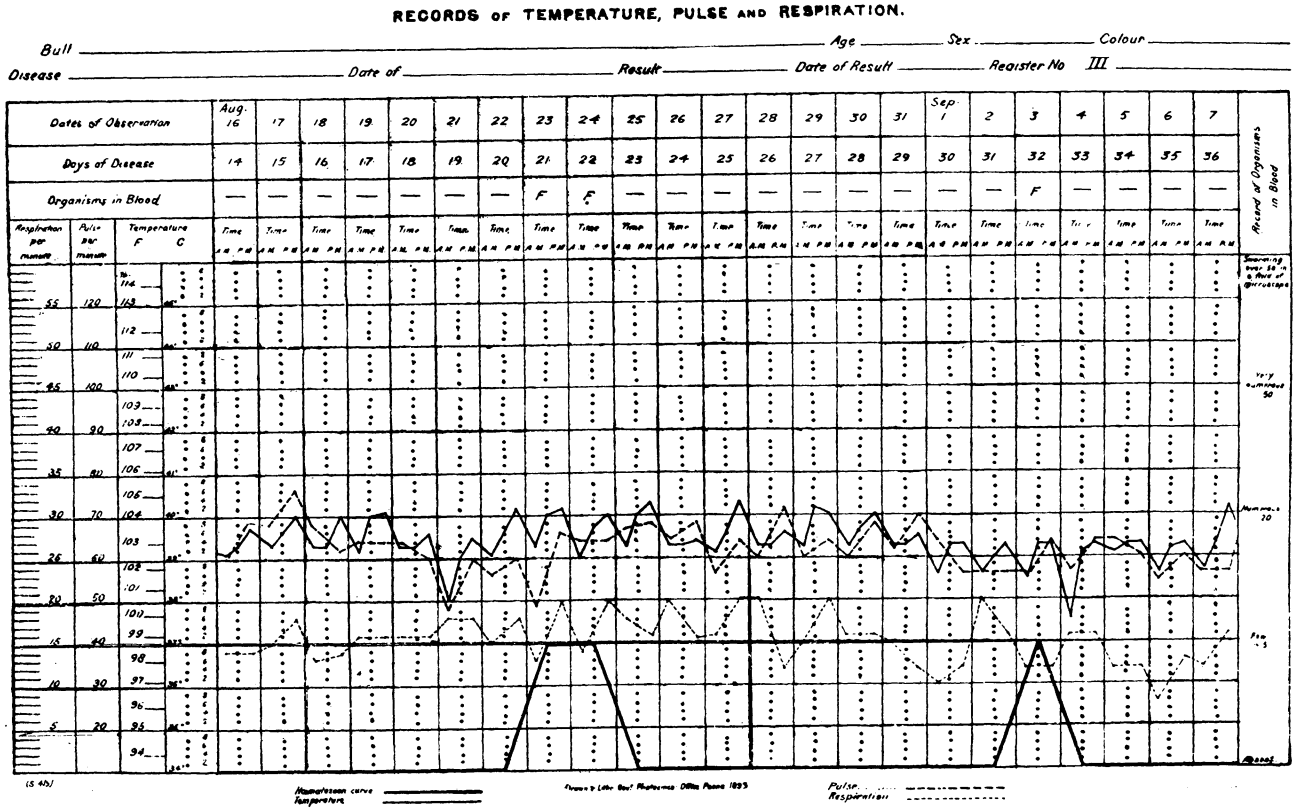

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

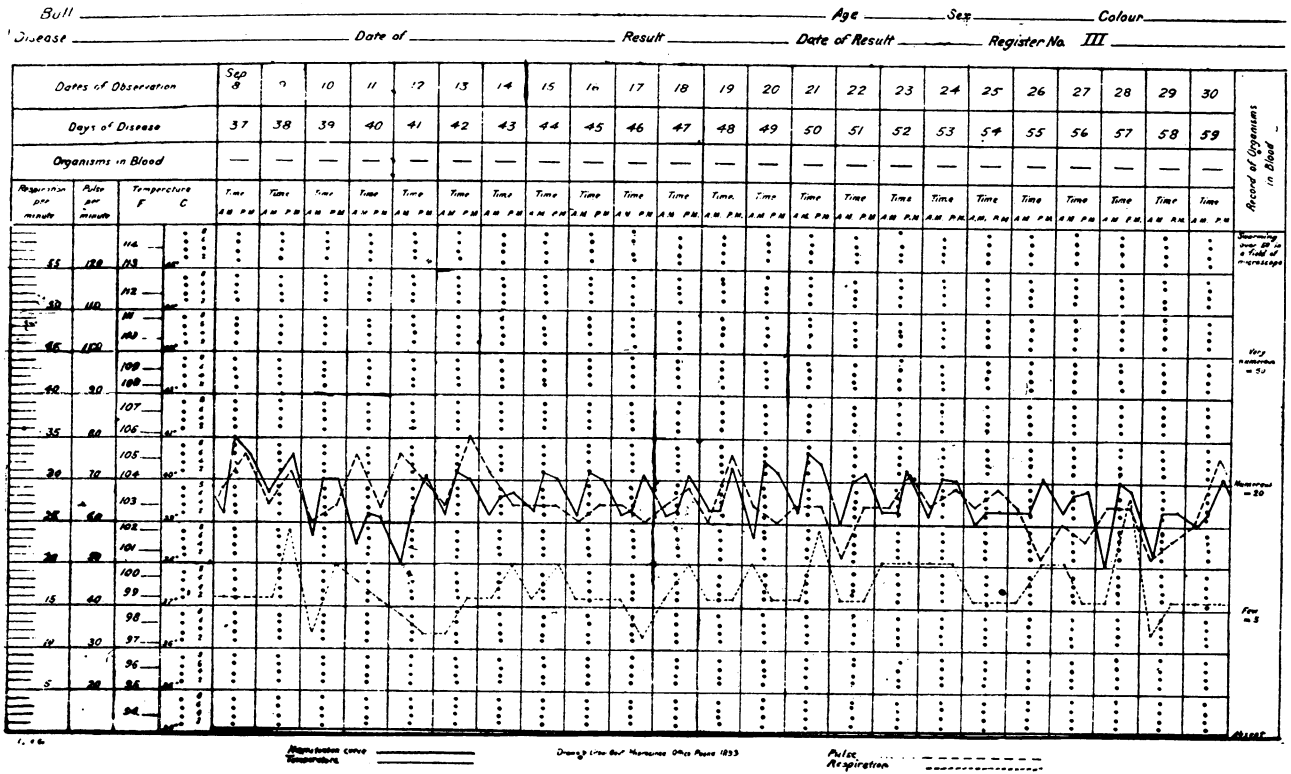

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

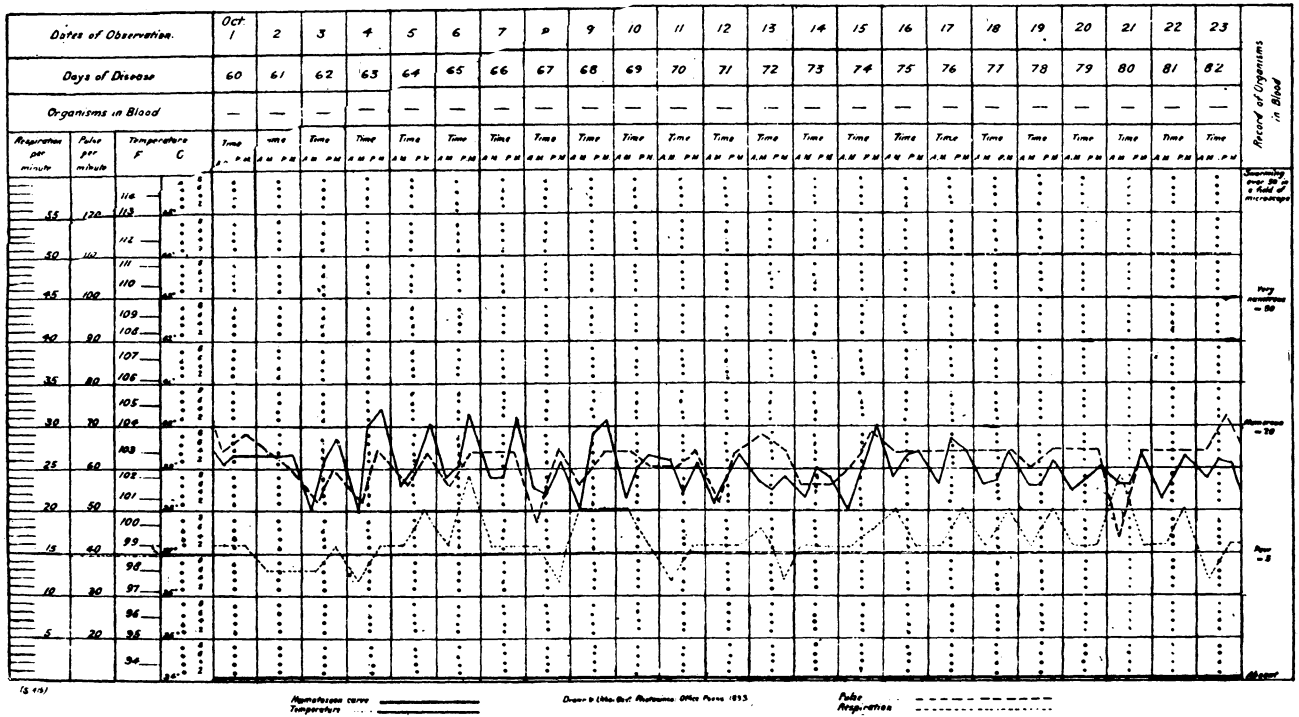

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

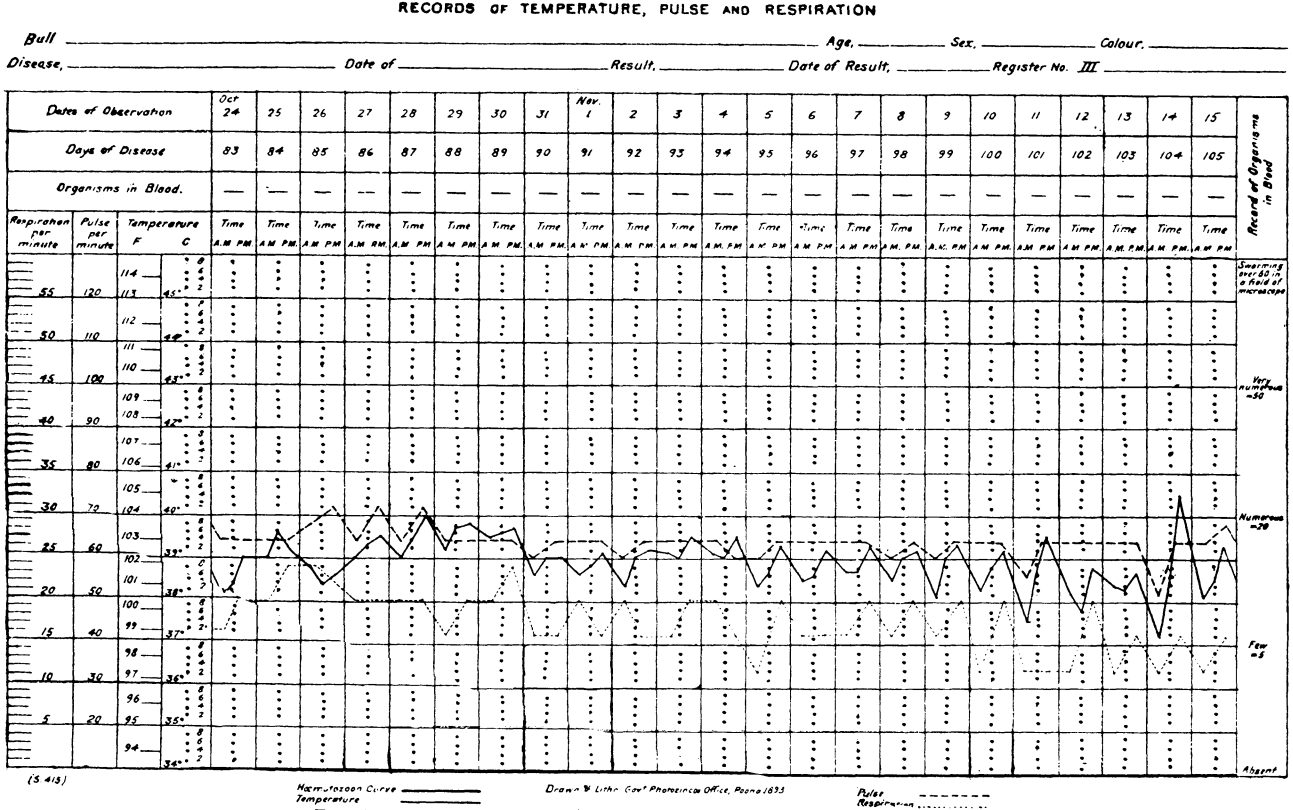

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

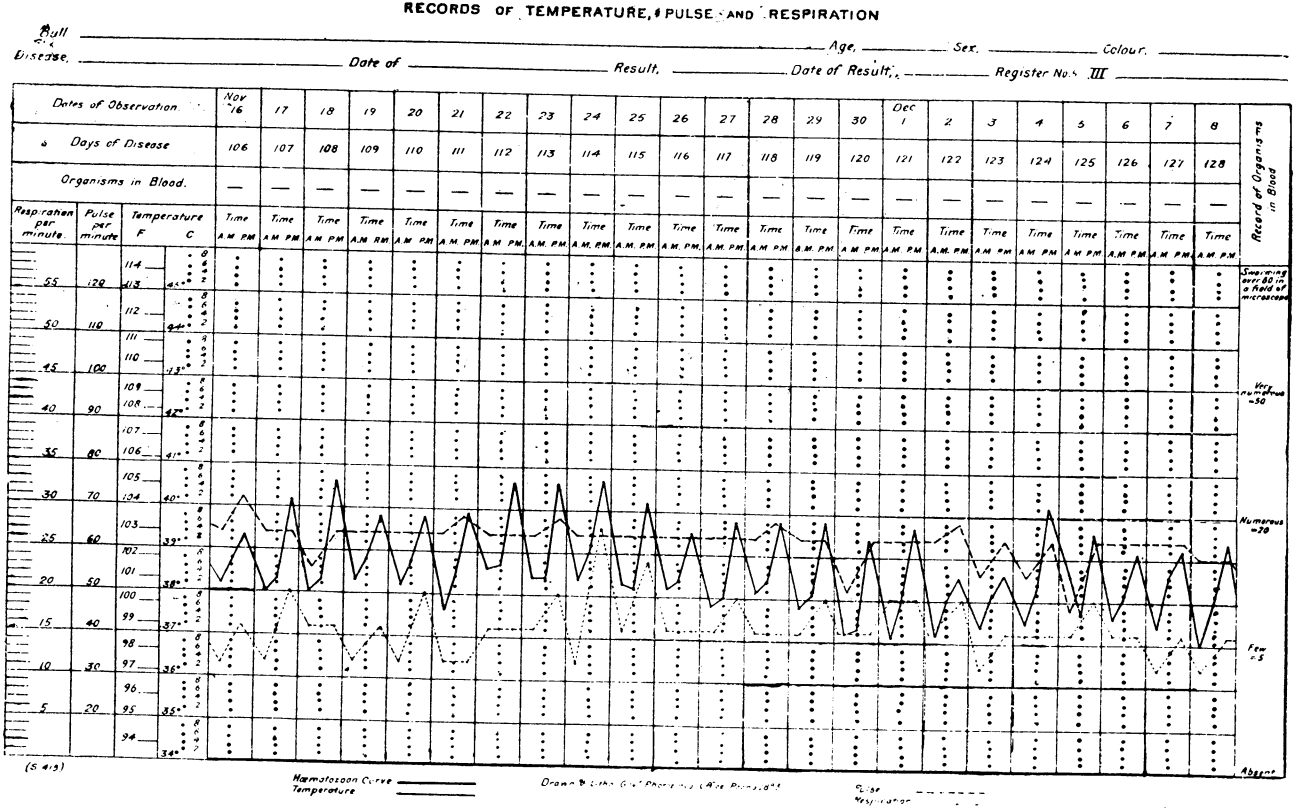

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

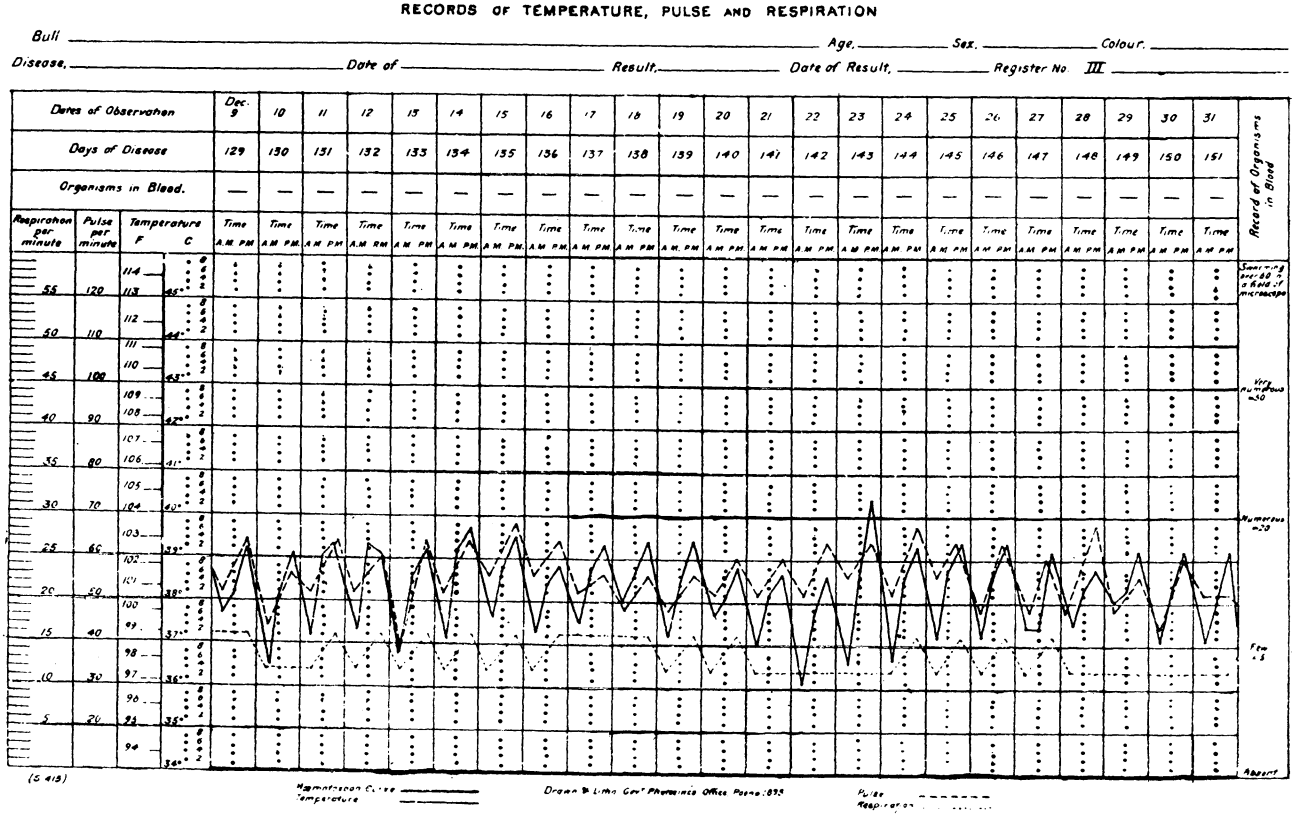

FIG. 126 (continued).—Temperature record of surra in a bull. (After Lingard.)

other symptoms begin in very much the same manner. The temperature (figs. 127, 128) as a rule is less intermittent than in the horse and does not run so high. No relation can be established between

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ANIMAL RECORD.

Cow *No* 280
June 1 , , *190*3.
Weight 500 lbs. *Age* 8 yrs. *Sex* Male *Color* Red *Inoculation* Surra.
History Rinderpest serum animal under observation for several months.

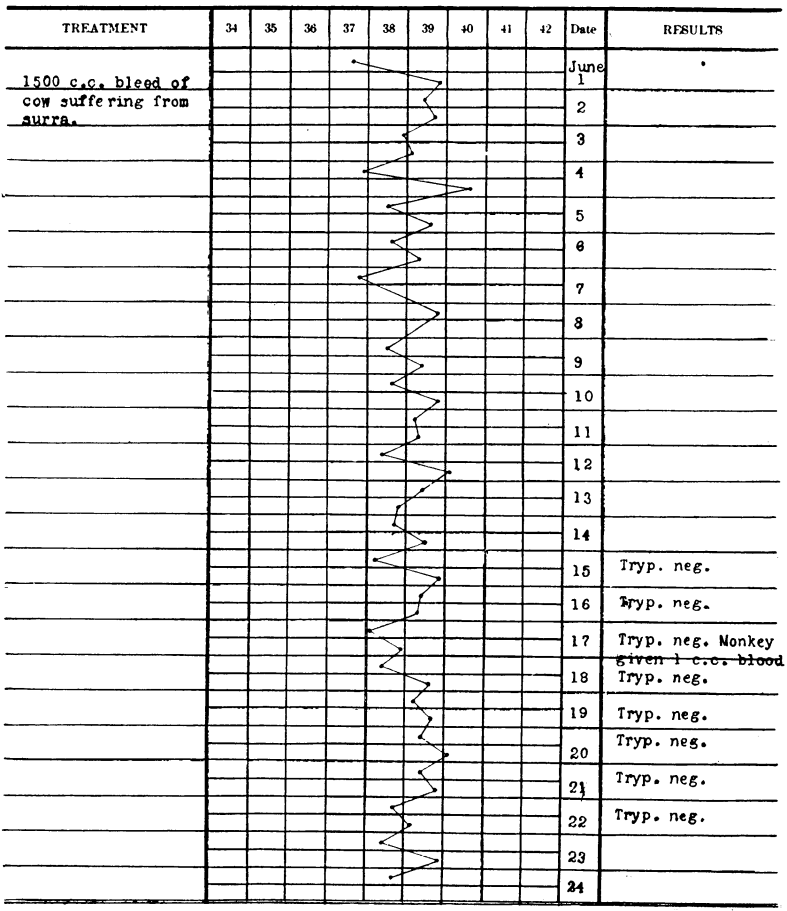

FIG. 127.—Surra in a cow with very rapid course.

the temperature and the number of parasites. *Trypanosoma* in sufficient numbers to be detected by the usual microscopic examination are intermittently present in the blood; but the latter, as in other animals, is constantly infectious by animal experiment. The appetite

usually remains good, but there are transient periods of anorexia in almost all cases and some animals refuse food for days at a time. The bowels remain normal or show a tendency to constipation.

Emaciation is rapid and as a rule begins earlier than in the horse. Anemia, as shown by the pallor of the mucous membrane, is probably less marked than in the horse. The catarrhal symptoms of the nose and eyes are slight in most animals, but in those cases which prove fatal may become a prominent symptom. Edema is decidedly less marked than in the horse and in some animals is scarcely perceptible, while in others it appears particularly in the dewlap and less so on the abdomen and hind legs. The hair becomes rough and in places falls out. Urticarial eruptions are quite frequent.

On the whole the picture is similar to that seen in other animals, and in well-advanced cases a diagnosis should be easy. Owing to the scarcity of parasites in the circulating blood and their apparent intermissions, the laboratory diagnosis of these animals should include animal experiment.

The course of the disease is usually chronic, and in animals observed here the mortality is low. In some cases the disease may be very acute; one of our inoculated animals, for example, lived only twenty-four days. (Fig. 127.) We have not been able to examine a sufficiently large number of cases, and for that reason do not desire to give definite figures as to the mortality.

Several varieties of cattle are found in the Philippine Islands in addition to the native ones, these including Australian, Chinese, American, Straits Settlement, and Javanese.

TRYPANOSOMIASIS OF CARABAO.

The Indian buffalo, of which the so-called carabao of the Philippine Islands is a species, has been proved susceptible to surra by Lingard.

The course of the disease in his animals very closely resembled that of the cow. The incubation period was about five days in inoculated animals; and the duration in two of his animals was forty-six and one hundred and twenty days, respectively, followed in each case by death. According to his description, there were very distinct exacerbations and remissions of temperature in both cases. The appetite remained good, but emaciation was marked and progressive. Nothing of especial interest was noted at post-mortem examination.

Curry mentions Trypanosomiasis of carabaos in the Philippine Islands, but does not give any data of importance.

TRYPANOSOMIASIS OF MONKEYS.

Monkeys, where available, are among the most valuable animals for the study of Trypanosomiasis. They are seldom naturally infected, but are very susceptible to inoculation and run a regular course.

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BIOLOGICAL LABORATORY

ANIMAL RECORD.

Bull *No* 362

Weight May 15, *Age* 1903 *Sex* *Color* *Inoculation* Tr. evansii

History

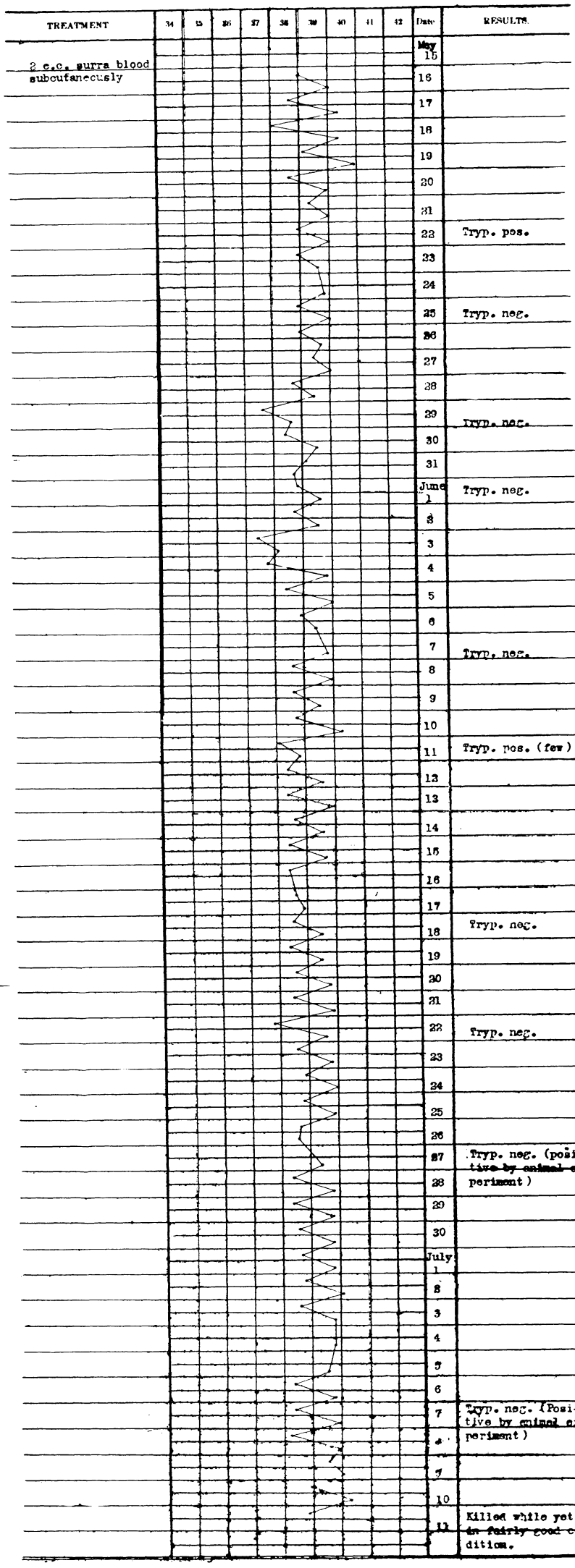

FIG. 128.—Surra in a bull.

Kanthuck, Durham, and Blandford inoculated a monkey with *Tr. brucei*. During the two weeks of its illness parasites were constantly present. The post-mortem examination showed advanced pulmonary tuberculosis.

Nocard subcutaneously inoculated an old monkey with several drops of blood from a nagana mouse. He gives the incubation period as four days and the duration of the disease as fifteen days. Parasites

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BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Monkey *No* 49

September 11, *190* 2

Weight *Age* *Sex* *Color* *Inoculation* Trypanosoma

History Medium-sized monkey in healthy condition.

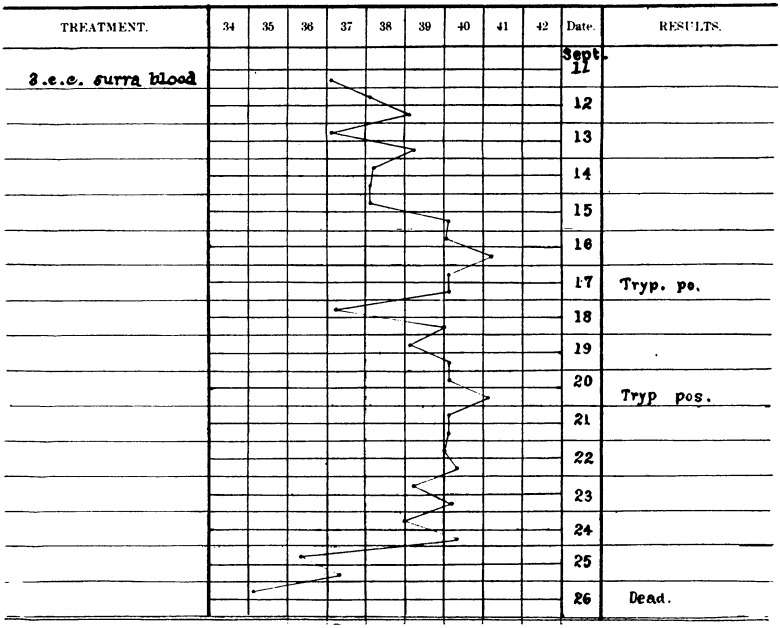

FIG. 129.—Temperature record of surra in a monkey.

were very numerous throughout its course and at the time of death exceeded the red blood cells in number. The principal symptoms were high temperature, edema of the eyelids and pockets, and dejection of spirit.

Sivori and Lecler give the incubation period in "surra americain" as three days, followed by death about the sixth day. The temperature is high at first, and just before death drops to 36° C. Anemia is rapid and

progressive. The appetite remains good. Toward the end there is some drowsiness, followed by death in coma. The post-mortem examination shows an enlarged spleen with dark-red pulp, edema of the lungs, and a small quantity of citrine liquid in the serous sacs.

Voges says that monkeys (*Nictipitechus felinus*) inoculated with *Tr. equinum* succumbed to the disease. Several observers in India have shown monkeys to be susceptible by inoculation to the surra of that country; they have also been proved capable of contracting dourine.

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ANIMAL RECORD.

Monkey *No* 66
October 21 . *1902*
Weight *Age* *Sex* *Color* *Inoculation* Trypanosoma
History

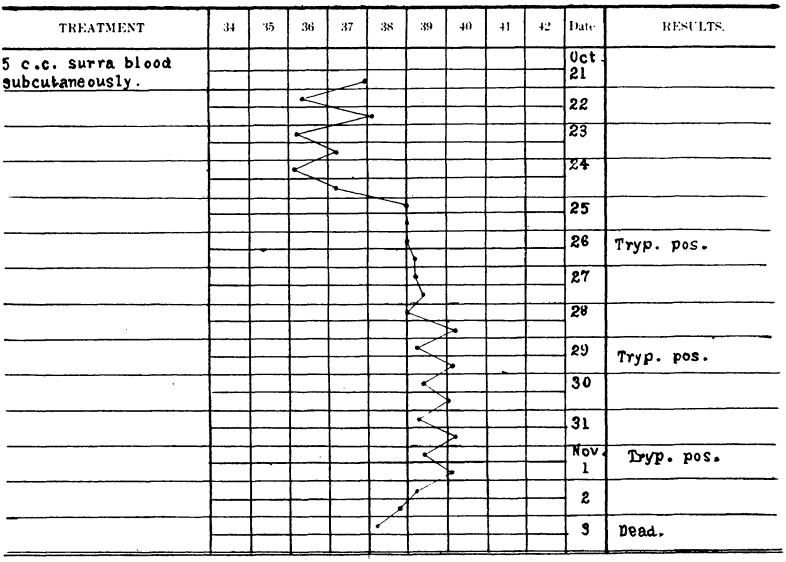

FIG. 130.—Temperature record of surra in a monkey.

Monkeys have been extensively used in our work, and the following statements are based upon the clinical and post-mortem study of a large number of these animals. In the course of this investigation the blood of hundreds of monkeys from all parts of the Islands, from infected areas and from those not infected, has been examined; and only once has a naturally infected animal been found, although they are very susceptible to the disease, which, when given by inoculation, invariably proves fatal.

The incubation period in these animals varies with the manner of inoculation, being on the average one to three days by subcutaneous or scratch inoculation, whether by syringe or insect, and somewhat shorter by inter-abdominal inoculation. The duration is from five to thirty-five days and the mortality 100 per cent.

Monkeys are the only animals that show undoubted evidence of having pain caused by the infection. The manner in which for hours at a time

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BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Monkey *No* 18
March 5, 1902
Weight *Age* *Sex* *Color* *Inoculation* Trypanosoma
History

TREATMENT.	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										Mar. 5	
1 c.c. surra blood										6	Tryp. pos.
										7	
										8	
										9	
										10	
										11	Tryp. pos.
										12	
										13	
										14	
										15	
										16	
										17	Tryp. pos
										18	
										19	Dead.

FIG. 131.—Temperature record of surra in a monkey.

they hold their heads between their hands leaves little doubt but that they suffer from headache.

The character of the fever varies considerably. (See figs. 129–132.) It is generally intermittent or markedly remittent, and always higher in the afternoons. In some cases it may be nearly continuous, especially in the later stages of the disease. Just before death there may be hyper-

pyrexia and the temperature may fall to subnormal, although death may occur without either of these changes.

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ANIMAL RECORD.

Monkey *No* 157
January 16, *190* 3
Weight Medium *Age* *Sex* Male *Color* *Inoculation* Tryp. from rat.
History Healthy animal under observation for one month

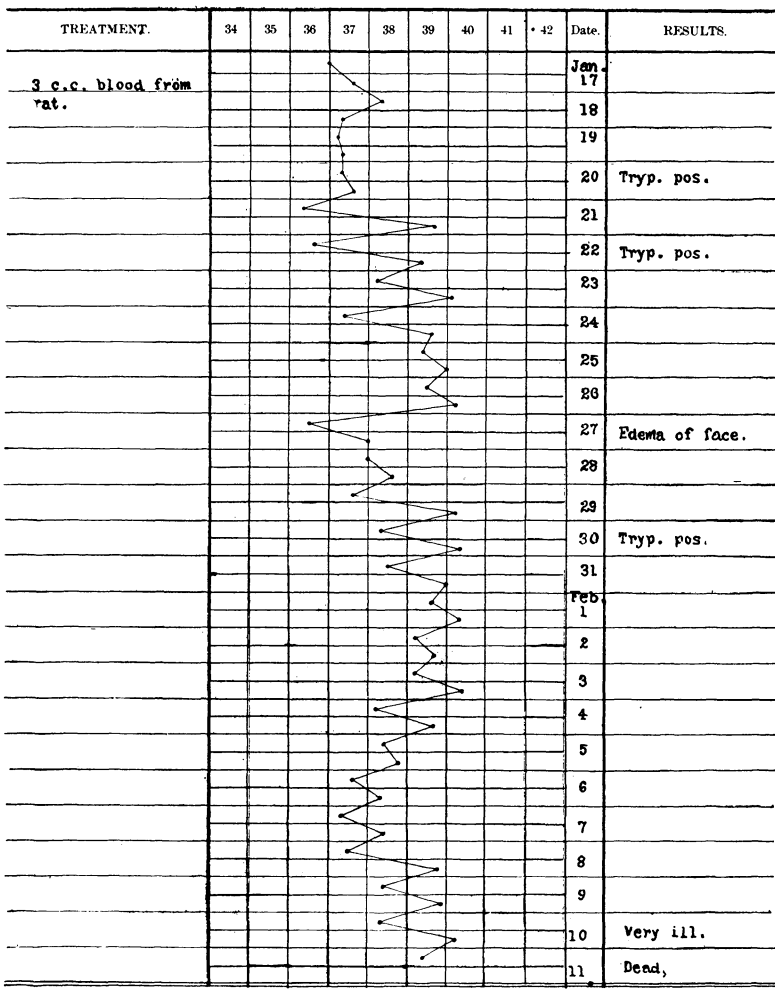

FIG. 132.—Temperature record of surra in a monkey.

Parasites may as a rule be found by microscopic examination throughout the course of the disease. In not a few cases, however, there are

intermissions of short duration; and in one case we found parasites only once in daily examinations for seven days, though the blood was infectious by animal experiment during this time.

Edema as a rule is not a prominent symptom, but is sometimes noticeable about the face and genitals. Anemia is rapid and severe, but the emaciation is not so great as that observed in other animals. Some interference with the gait is occasionally noticed, but it is neither constant nor very severe. Gastro-intestinal symptoms are absent in most cases, but diarrhea is sometimes noticed toward the end.

Necropsy shows the general lesions seen in other animals. In addition to the evidence of severe anemia, the most constant changes are an enlarged mottled spleen, enlarged lymphatics, fluid in the serous cavities, and flakes of fibrin over the surfaces of the organs.

TRYPANOSOMIASIS OF DOGS.

Dogs are susceptible to surra in India, and show the same general symptoms as those seen in other animals. The incubation period is short and the course rapid.

Lingard mentions as the principal symptoms: Paroxysmal fever, anorexia, later a swelling of the skin about the head and throat, injection of the conjunctiva, increased lachrymation, in some cases effusions into the joints, marked edema of the limbs and the belly, extravasation of the blood into the anterior chambers, opacity of the cornea and later total blindness. He gives as the principal anatomic lesions subpleural extravasations and sometimes localized consolidation of the lungs, enlarged spleen and kidneys with subcapsular petechiae.

Rouget proved dogs susceptible to dourine. The symptoms were edema, particularly marked in the genitals, paralysis of the hind quarters, and conjunctivitis, sometimes followed by keratitis.

Dogs, according to Voges, contract mal de caderas by eating the flesh of animals dead of the disease, not, however, through the sound mucosa, but through injuries, which are always found to be present on examination and are caused by fighting. The incubation period is short, and the duration of the illness varies from two to three months.

He describes the symptoms as follows:

> The animal becomes stupid, emaciates, no longer responds when called, sleeps, hides in dark corners, and its head becomes swollen (bulldog appearance) as a result of the edema, which affects particularly the eyelids. The conjunctiva are involved to a pitiful extent and secretions similar to those seen in the rabbit are observed. The hair about the eyes falls out. The vision is likewise impaired by the chronic conjunctivitis. There is marked edema of the scrotum, which is first revealed by the swelling of the testicles. * * * The penis is not involved. On section enlarged spleen and serous exudates are observed. * * * There are days when *Trypanosoma* are not found in the blood.

Nagana, according to Bruce, has a rapid course in these animals (eight to sixteen days) and is invariably fatal. He mentions as the principal

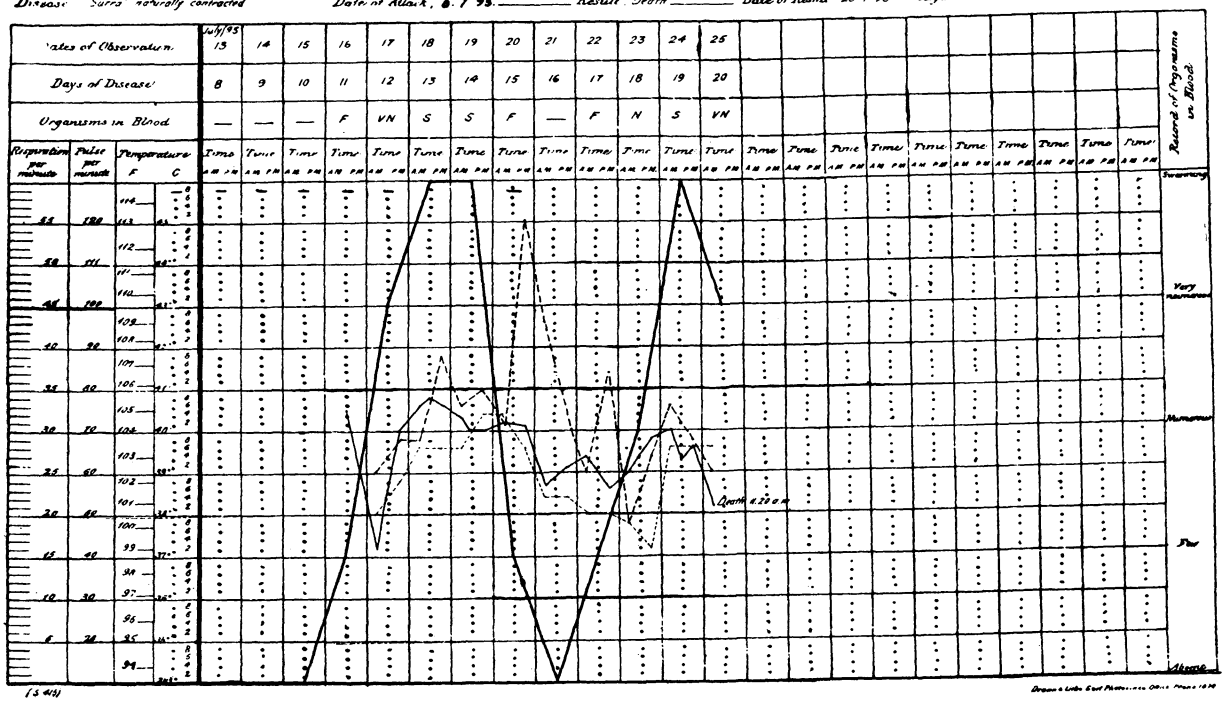

FIG. 133.—Temperature record of surra in a dog. (Lingard.)

symptoms continuous fever (rarely intermittent), with elevations to 40° and 41° C., extreme emaciation, pustular eruptions near the extremities, and a milky aspect of the cornea.

Kanthuck, Durham, and Blandford give the period of incubation as from four to six days, and the average duration of the disease as eight-

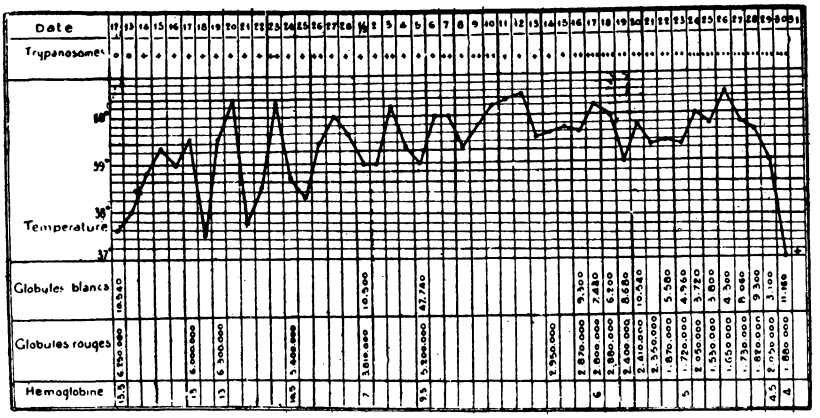

FIG. 134.—Temperature record of dog inoculated February 12, 1902, intravenously with ½ c. c. of rat's blood very rich in Trypanosoma. Dead in 48 days. (After Lignieres, in Recueil d. Med. Vet. Vol. 10, No. 4, Feb. 28, 1903, p. 131.)

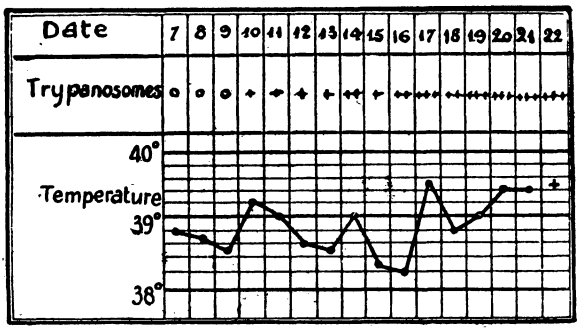

FIG. 135.—Temperature record of surra in a dog. Inoculated on January 6, 1902, subcutaneously with 1½ c. c. of blood from Dog No. 2, containing from 3 to 4 parasites in the microscopic field. Dead in 16 days. (After Lignieres, in Recueil d. Med. Vet. Vol. 10, No. 4, February 28, 1903, p. 130.)

een days. Fever is a constant symptom, the temperature becoming subnormal near death. Edema is common and more marked about the head, legs, belly, and genitalia. Turbidity of the aqueous humor, fibrinous plaques in the anterior chamber and corneal opacities are occasionally seen. Corneal ulcers and conjunctivitis are frequently associated with the edema of the eyelids and face. Parasites may be absent from the blood from four to six days, but continue to increase in number, and before death may reach 100,000 to 300,000 per cubic millimeter. Ter-

minal bacterial infections are apt to occur in these animals, thus accelerating death.

Anatomically, muscular wasting is well marked, but the fatty tissues are less affected, except at the base of the heart, where the fat may undergo edematous degeneration. Lymphatic hyperplasia is well marked, the glands being congested or hemorrhagic. The spleen is enlarged, granular, firm, and friable. Serous effusions and subserous hemorrhages are present.

Laveran and Mesnil state that the virus was frequently more active in their experience than in that of others. Their dogs lived from six and

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BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Dog No. 206
March 20, 1903

Weight *Age* *Sex* *Color* *Inoculation* Tr. Evansi

History

TREATMENT	34	35	36	37	38	39	40	41	42	Date	RESULTS
2 c.c. surra blood subcutaneously										Mar. 20	
										21	
										22	
										23	
										24	Tryp. pos.
										25	
										26	Numerous tryp.
										27	
										28	Dead.

FIG. 136.—Temperature record of surra in a dog.

one-half to twelve days. The incubation period from subcutaneous inoculation varied between two and four days. Parasites could always be demonstrated to be present in the blood by microscopic examination, and from the time of their first appearance until death they usually increased in number; but in the dogs which lived for twelve days there were remissions on the eighth and ninth days, followed by augmentation. Parasites were always numerous at the time of death.

The principal symptoms, according to these authors, are edema of the genital organs and hypertrophy of the inguinal lymphatics, although these symptoms may be absent. Less frequently edema of the head and slight and transient paresis of the posterior extremities may occur. Important lesions of the nose and eyes are found only occasionally. The

temperature rises on the third to the fifth day and usually remains above 40° C. until death. Considerable loss of weight is constantly observed.

In the Philippines dogs are very susceptible to surra by inoculation, and we have thus far observed two which contracted the disease naturally. Owing to their susceptibility and the ease with which an unlimited supply of the animals may be obtained for experimental work, they have been used in large numbers in the present investigation.

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BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Dog *No* 99
December 11, , *1903*

Weight *Age* *Sex.* M *Color* *Inoculation.* Trypanosoma.

History Dog under observation one week.

TREATMENT	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
										Dec. 11	
										12	
										13	
1 c.c. trypanosoma blood										14	
										15	
										16	Tryp. pos.
										17	Tryp. pos.
										18	Tryp. pos.
										19	Tryp. pos.
										20	
										21	
										22	
										23	Tryp. pos.
										24	
										25	Tryp. pos. Very numerous.
										26	Dead.

FIG. 137.—Temperature record of surra in a dog.

The incubation period is from four to seven days, the course is rapid, being from eight to twenty-four days in length, and the mortality is 100 per cent.

The temperature (figs. 136–138) varies considerably, but is usually remittent and rarely runs as high as in some other species of animals. Death may occur with hyperpyrexia, but more usually it is preceded by a drop of the temperature to normal or subnormal.

The animals rarely live long enough for anemia and emaciation to become extreme, but both are very noticeable from the beginning. In dogs the appetite as a rule is very poor, although there are exceptions

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BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Dog *No* 156
January 16, , 190 3

Weight Average *Age* *Sex*, Male *Color* *Inoculation* Rat tryp. from Monkey 113.

History

Under observation for ten days.

TREATMENT.	34	35	36	37	38	39	40	41	42	Date.	RESULTS.
3 drops tryp. blood from Monkey No. 113.										Jan 16	Tryp. neg.
										17	
										18	
										19	Tryp. neg.
										20	
										21	
										22	Tryp. pos.
										23	Tryp. pos.
										24	
										25	
										26	Tryp. pos.
										27	
										28	
										29	Tryp. pos.
										30	
										31	
										Feb. 1	
										2	Numerous tryp.
										3	
										4	
										5	Dead.

FIG. 138.—Temperature record of surra in a dog.

in which it is ravenous throughout the entire course of the disease. The bowels remain normal.

The "bulldog head," produced by the subcutaneous edema about the face, occurs to a varying degree, which depends somewhat upon the length of time the animal lives. Edema of the scrotum and belly

is also present, but sometimes where the course is very rapid it may scarcely be noticeable.

Urticarial eruptions on various parts of the body are hardly a prominent symptom; they do occur, however, and ocasionally are very marked. As in other animals, the hair becomes rough and falls out; this is especially true of the eyelashes and the long hairs about the nose.

Catarrhal symptoms accompanied by watery discharges from the nose and eyes are noticed early, and later become severe. The discharges become muco-purulent and acrid, excoriating the sides of the nose. Clouding of the fluid in the anterior chamber is of frequent occurrence and may lead to total blindness. Partial deafness also occurs. In many cases the partial paralysis of the hind-quarters seen in other animals is also observed. Parasites as a rule are constantly present

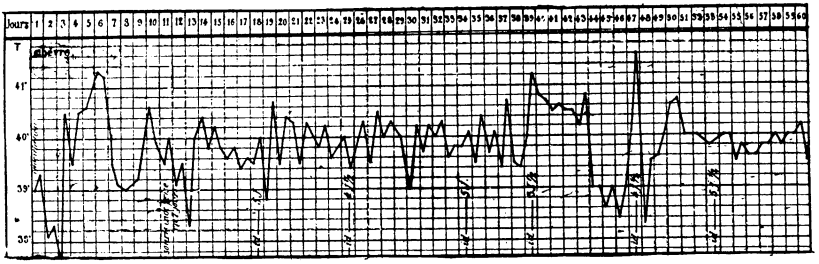

FIG. 139.—Nagana in a goat. (After Laveran and Mesnil, 1902, Fig. 5.)

in the blood from the time of their first appearance until death. Post-mortem examinations show lesions closely resembling the ones found in other animals.

TRYPANOSOMIASIS OF GOATS.

This species of animals is apparently not susceptible to natural infection, and on inoculation the disease runs so chronic a course that some authors consider them immune. The duration and the mortality do not appear to be well defined.

Rost says that goats inoculated with surra blood have fever, but soon recover, and subsequent doses do but very little harm. They are refractory to the disease and parasites are not generally found in the blood.

Voges considers them susceptible to mal de caderas by inoculation and says the disease lasts for several months. The animals at first show no symptoms, and often do not do so for months; but emaciation finally begins, and death is usually sudden. *Trypanosoma* are periodically absent from the blood.

Bruce considers goats susceptible to nagana by inoculation, but says that the disease runs a chronic course, often lasting for several months.

Laveran and Mesnil inoculated a goat with *Tr. brucei,* and it was still alive at the time of publication of their article three months later.

They say that the beginning of the disease in these animals is much the same as in horses, the incubation period being from three to eight days, followed by a rise of temperature to about 41° C. Parasites are only temporarily present and are not again found, but the blood continues to be infectious by inoculation.

In our experience goats have always proved susceptible by inoculation.

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Goat *No* 142
January 2, *190* 3
Weight *Age* *Sex* Male *Color* *Inoculation* Surra
History Healthy animal under observation a month.

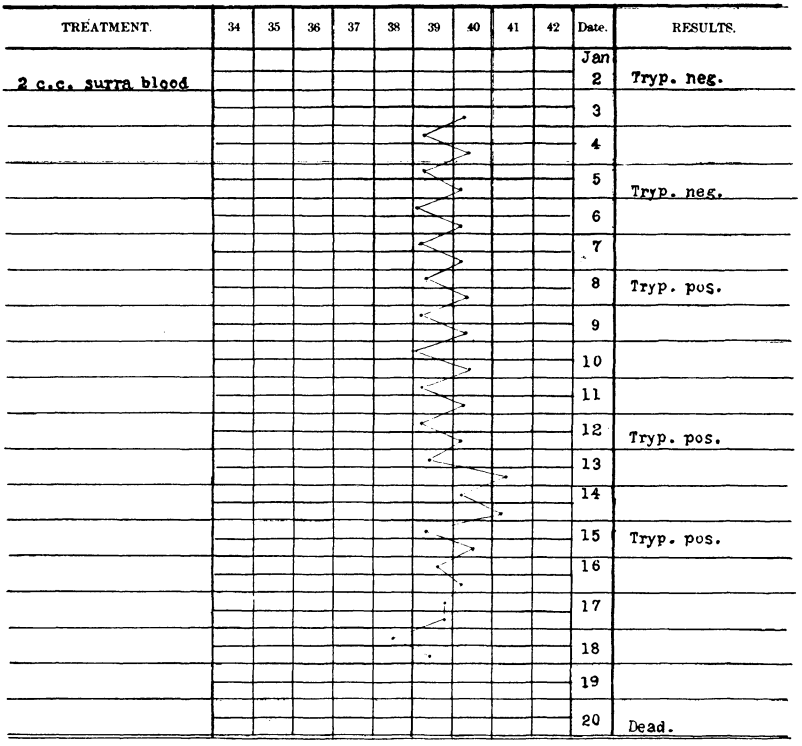

FIG. 140.—Temperature record of surra in a goat.

Parasites are usually scarce in the peripheral circulation, and indeed in some of our animals were not found at any time during the disease, but the blood was always infectious by inoculation and the disease invariably proved fatal.

The incubation period varies in length and is difficult to determine

accurately without daily animal experiment. The temperature curve is illustrated in figs. 140–142, and does not show anything characteristic, nor does it differ much from that of other species of animals. Neither emaciation nor anemia are marked. Edema is never prominent and may be entirely absent. Paresis of the hind parts was observed in only one of our animals.

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Goat *No* 143
January 2, *190*3

Weight *Age* *Sex* Male *Color* *Inoculation* Tr. Evansi

History Healthy animal under observation for 2 months.

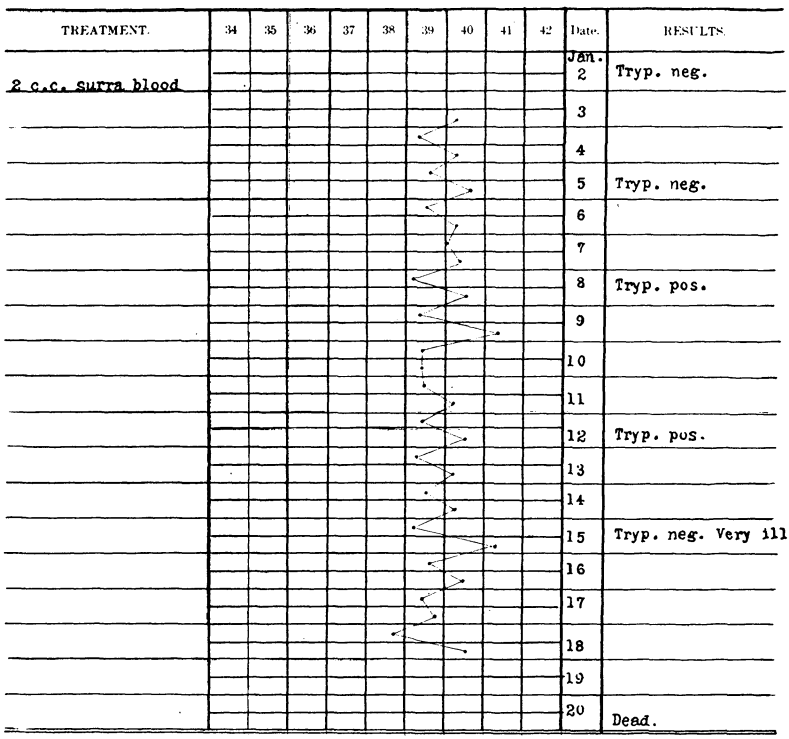

FIG. 141.—Temperature record of surra in a goat.

Goats manifest their illness by preferably lying in the shade and by the listlessness and sluggishness of their movements. They seem to suffer some pain, just as is the case with monkeys.

Post-mortem examination reveals nothing characteristic, the lesions closely resembling those observed in other animals.

Most authors, writing of surra, nagana, dourine, and mal de caderas, regard the nature of the disease in these animals as very similar to that in goats. The sheep of eastern Africa are considered by Bruce

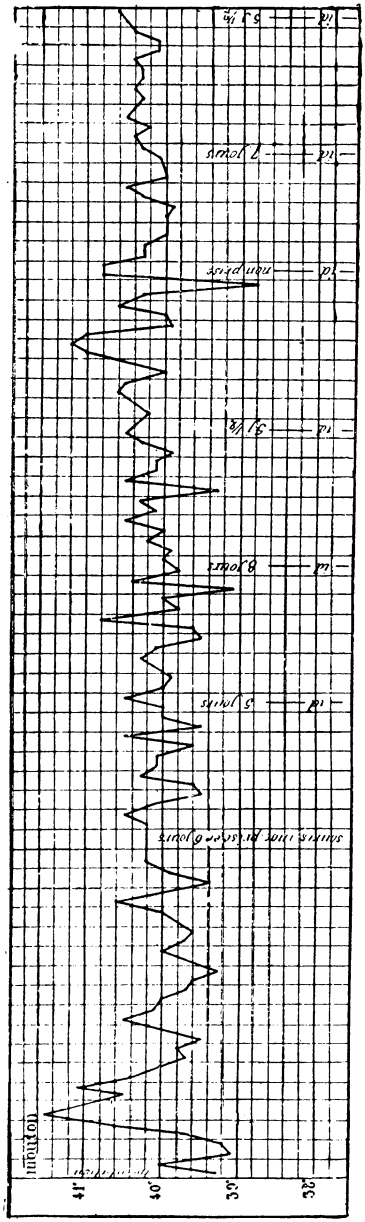

FIG. 143.—Surra in a sheep. (After Laveran and Mesnil, 1902, Fig. 6.)

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Goat *No* 131

December 31, *190* 2

Weight *Age* *Sex* *Color* *Inoculation* Surra

History Healthy native goat under observation for three months.

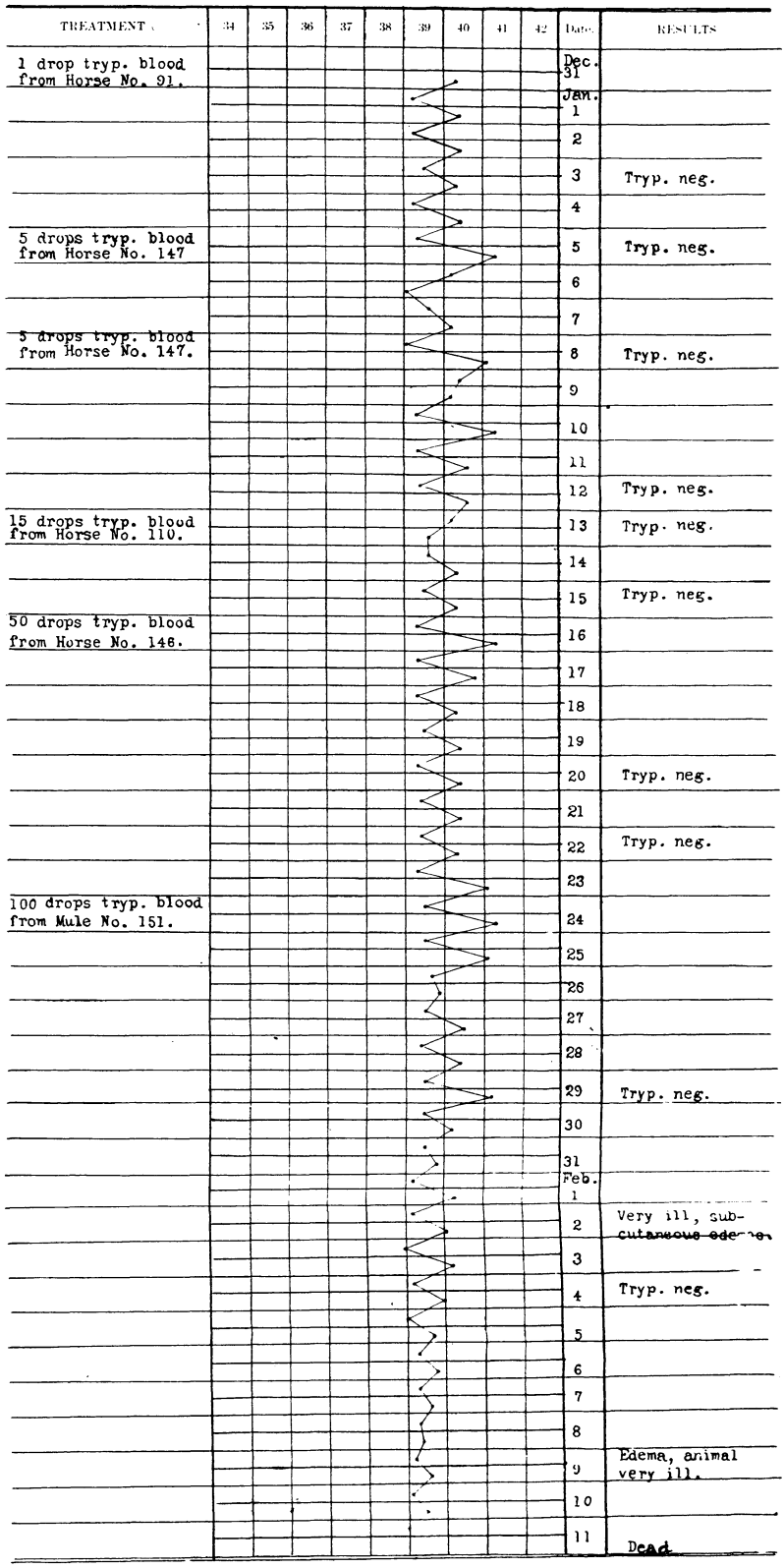

FIG. 142.—Temperature record of a goat repeatedly inoculated with *Tr. evansi;* parasites not found by microscopic examination.

to be somewhat refractory. The disease in these animals, he says, runs a very chronic course and some of them live for five months.

Laveran and Mesnil inoculated a sheep with *Tr. brucei,* and in an article published three months later stated that it was still living. They consider the beginning of the disease much the same as in horses. There is generally an incubation period of three days, followed by the appearance of parasites and an elevation of the temperature to 41° C. *Trypanosoma* then become so rare that they are not found in the blood by microscopic examination, although the blood is constantly infectious when injected into mice. The temperature remains near 40° C. with occasional intermissions, although it sometimes rises to 41° C.

Regarding one sheep, which lived exactly one hundred and ninety-seven days, they write as follows:

> On the sixth day after inoculation it showed a temperature of about 41° C., which shortly afterwards fell to between 39° and 40° C.; on the twenty-fourth day there was another rise to 41.5° C.; after which the temperature remained for a long time in the neighborhood of 41° C., taking thirty days to return to 40° C.; multiple edematous areas appeared in the face and eyes and then in the testicles. It was only during this period that *Trypanosoma* could be found by microscopic examination, and for eight days there were several in the field. The edema increased and extended to the neck and shoulders (end of the third month). Its disappearance was rapid; the animal (during the fourth and fifth months and the first half of the sixth) appeared well (the temperature being between 39° and 40° C.); but the blood was still virulent. During the last month the animal emaciated rapidly and died with profound lesions of cachexia and gelatinous exudates of the throat, the pericardium, and the lips.

As with some of the other animals, neither the study nor the description of the infection in sheep is as accurate as might be desired for purposes of comparison. In the Philippine Islands they do not appear to be naturally susceptible to the disease. We have kept a sheep in the same ground with surra animals for several months, but no infection has resulted.

The symptoms, the course, and the duration of the disease in these animals are so similar to those observed in the goat that a description of them is considered unnecessary.

TRYPANOSOMIASIS OF GUINEA PIGS.

There are on record a few instances in which guinea pigs have been found naturally infected with *Trypanosoma,* but literature affords little detailed study of any of the forms of the disease in these animals. It is admitted that they are susceptible by inoculation to *Tr. evansii, Tr. brucei,* and *Tr. elmassianii,* while some of them show a transient infection from *Tr. lewisii.*

Laveran and Mesnil noticed multiplication forms on the second and fifth days after inoculating one of these animals in the abdominal cavity

BUREAU OF GOVERNMENT LABORATORIES
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Sheep *No* 290

June 25, 1903

Weight *Age* *Sex* *Color* *Inoculation* 3 c.c. surra blood

History Large, healthy native sheep

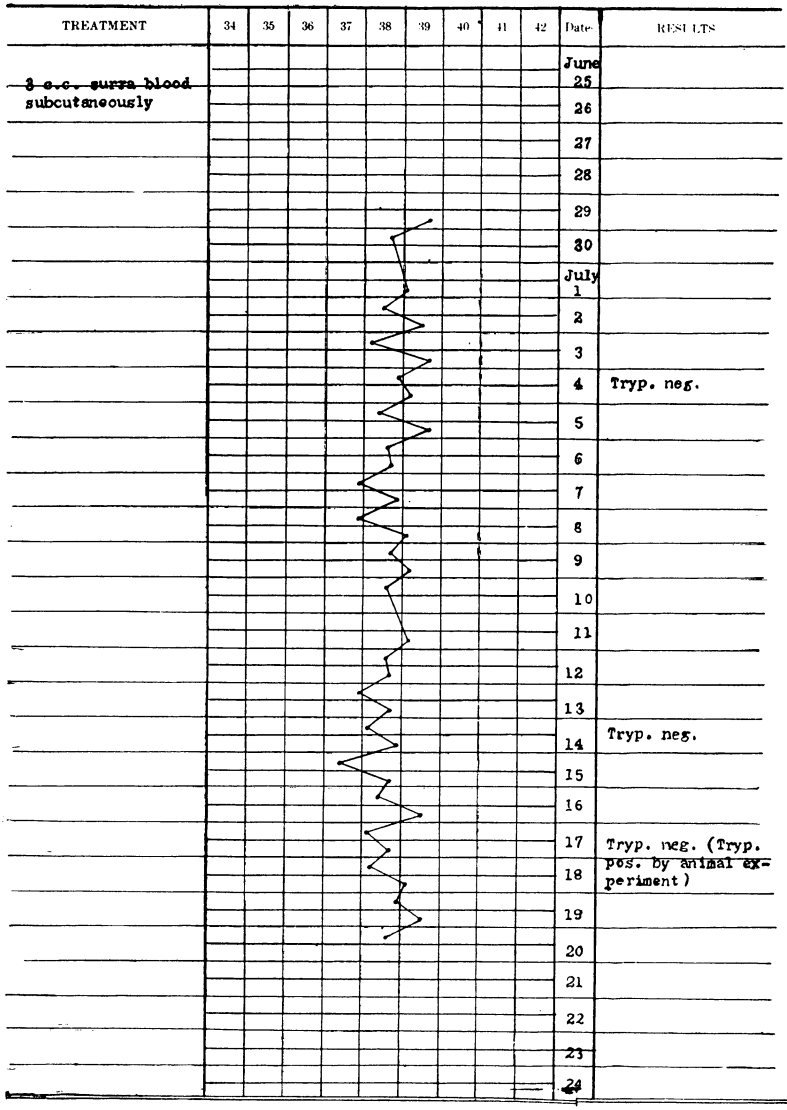

FIG. 144.—Temperature record of surra in a sheep.

with *Tr. lewisii*. Many of the parasites in the abdominal cavity were in various stages of digestion by the large mononuclear leucocytes. There were a few *Trypanosoma* in the blood on the fifth and seventh days.

Sivori and Lecler give sixty days as the average duration of *surra*

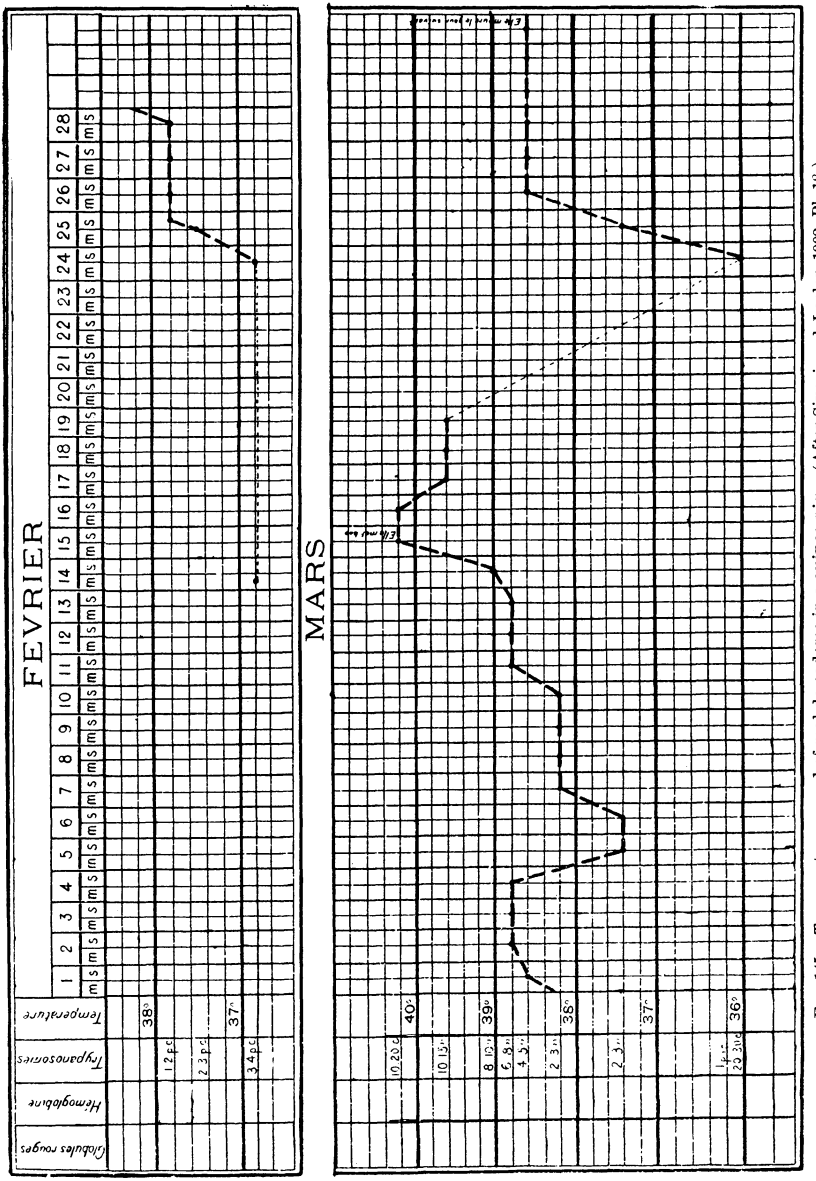

FIG. 145.—Temperature record of mal de caderas in a guinea pig. (After Sivori and Lecler, 1902, Pl. 18.)

americain in these animals, although it varies from twenty-five to one hundred sixty days. In pregnant females parasites are more numerous than in other cases, and almost constantly present.

Voges says that one-half to two-thirds of these animals when inoculated with mal de caderas die of the disease, the duration in those which finally succumb being from two to five months. He has some guinea pigs that have been alive for a year, have grown fat, and have had young. The generative power of the male suffers from the infection more than does that of the female.

We have succeeded, as did Laveran and Mesnil, in producing a slight infection with *Tr. lewisii,* but it is always transient and devoid of symptoms.

Guinea pigs do not naturally contract any form of Trypanosomiasis in this country, but when inoculated with the *Trypanosoma* of the present epidemic always show a long chronic infection.

As nearly as can be determined, the incubation period varies from two to eleven days. The duration of the disease is from one to four months, and but few animals recover from it.

The appearance of parasites in the circulating blood is very intermittent, not always in sufficient numbers for microscopic diagnosis, although the blood is constantly infectious by animal experiment. Sometimes parasites are not found by the usual microscopic technique for days and even weeks.

The temperature curve (see fig. 145) is very irregular, more so than in any other class of animal with which we have worked. The symptoms in general resemble those of the rabbit. Edema of the genitals is marked, but in the rest of the body is less prominent than in the case of other animals. Anemia and emaciation develop slowly, but reach an extreme degree before death. The hair falls out in places, and small ulcers may appear on the belly and prepuce or vulva. Partial paralysis of the hind parts occurs but is not constant, being absent in some cases while well marked in others.

Post-mortem examination reveals a condition similar to that observed in many other animals. There is as a rule less fluid than is ordinarily found in the serous cavities of other animals, and the changes in the spleen are often slight. The gelatinous infiltrations in the subserous and subcutaneous tissues closely resemble those seen in the horse.

TRYPANOSOMIASIS OF RABBITS.

Rabbits are susceptible by inoculation to all the important forms of Trypanosomiasis, but we have read of no reported cases of natural infection in these animals.

Rouget very irregularly found the parasites in the blood of rabbits suffering from dourine, but their presence in the peripheral circulation was intermittent and bore no relation to the temperature of the animals.

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY

ANIMAL RECORD.

Guinea pig *No* 248

April 16, 1903

Weight *Age* *Sex* *Color* *Inoculation* surra.

History Small healthy animal. Temperature record after 41st. day of the disease. Parasites were present in the peripheral circulation after 7th. day.

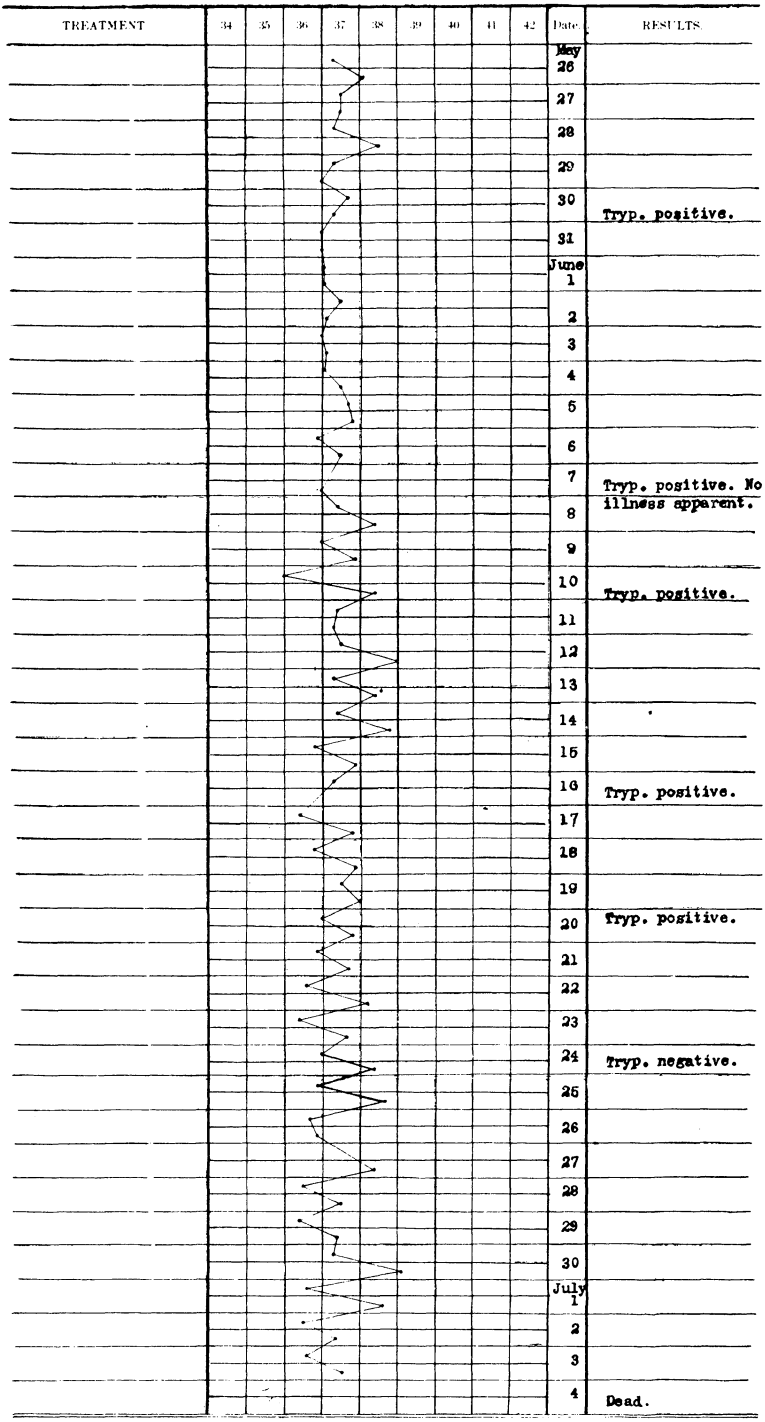

FIG. 146.—Temperature record of surra in a guinea pig.

As the principal symptoms he gives edema of the ears, falling out of the hair, paralysis of the hind parts, mucous conjunctivitis, which later becomes purulent, and edema of the genitals. The duration of the disease is from one to four months. The principal anatomic lesions are hyperemia of the abdominal layers, inflammation of the spleen and liver and of the lymphatics near the point of inoculation.

Mal de caderas, according to Voges, lasts for one to three months in these animals. Parasites may not be found in the blood for the first four weeks. The rabbits remain active for weeks, but toward the end emaciation is apparent. The fever is very irregular. Catarrhal conjunctivitis supervenes, becoming purulent and causing the lids to adhere to each other. The hairs of the eyelids always drop out, and sight finally becomes greatly impaired. Inflammation of the nose occurs, causing the hairs to stick and fall out. The testicles swell, but the penis is unaffected. *Trypanosoma* are found in the inflamed testicles and vulva, and necropsy, indeed, in all parts of the body, the spleen is enlarged, and serous exudates are always observed.

Sivori and Lecler, working with the "surra americain" of South America, say that parasites may be found in the blood eight hours following intraperitoneal inoculation, and that the duration of the disease is from sixteen to one hundred and sixteen days. The disease is characterized by emaciation, tumefaction of the eyelids, purulent blefero-conjunctivitis, and marked edema of the nose, penis, and vulva. The temperature is irregular and without relation to the number of parasites in the circulating blood.

Kanthuck, Durham, and Blandford regard the rabbit as relatively immune to nagana. They say that the incubation period is from five to seven days and the duration from twenty to one hundred and eighty-three days, the average being about fifty.

Laveran and Mesnil consider it to be a susceptible animal. The incubation period is from two to four days and the duration of the disease from fifteen to thirty, although death sometimes occurs in five to six days. Parasites appear in the peripheral circulation intermittently. When the disease lasts twenty days or more, conjunctivitis sets in and the hair about the eyelids falls out; edema of the vulva or prepuce and forelegs occurs, but the lesions are always slight. During the whole course of the disease the rabbit has a continuous temperature, with rare intermissions; it is generally above 40° C.

In this country rabbits have not been found naturally infected. They are susceptible by inoculation and afford most interesting subjects for the study of the disease. Fig. 146 illustrates the course of surra in these animals as given by Lingard.

The incubation period is difficult to determine accurately for the reason that, contrary to the results obtained, in many animals, it is not,

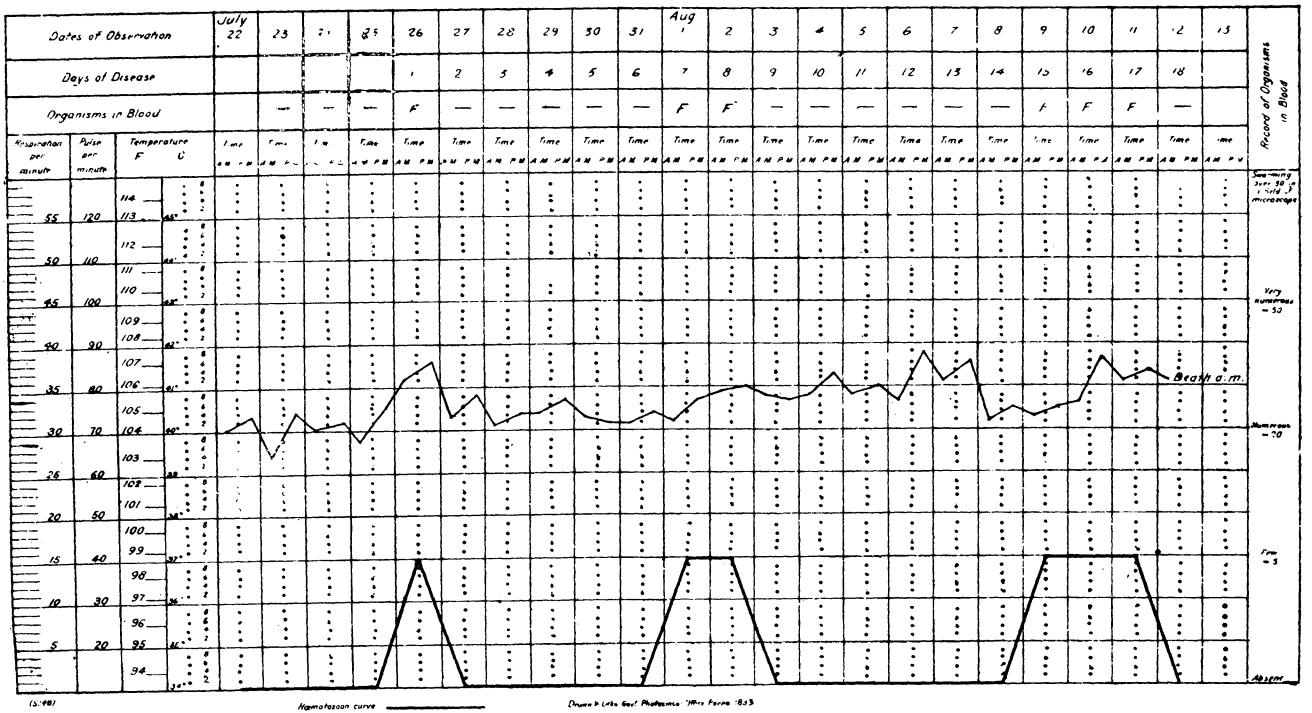

FIG. 147.—Temperature record of surra in a rabbit. (After Lingard.)

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Rabbit. *No* 169
January 26, , 1903

Weight *Age* *Sex* *Color* *Inoculation* Liver and blood of mule dead of surra.

History

Large healthy animal under observation for months.

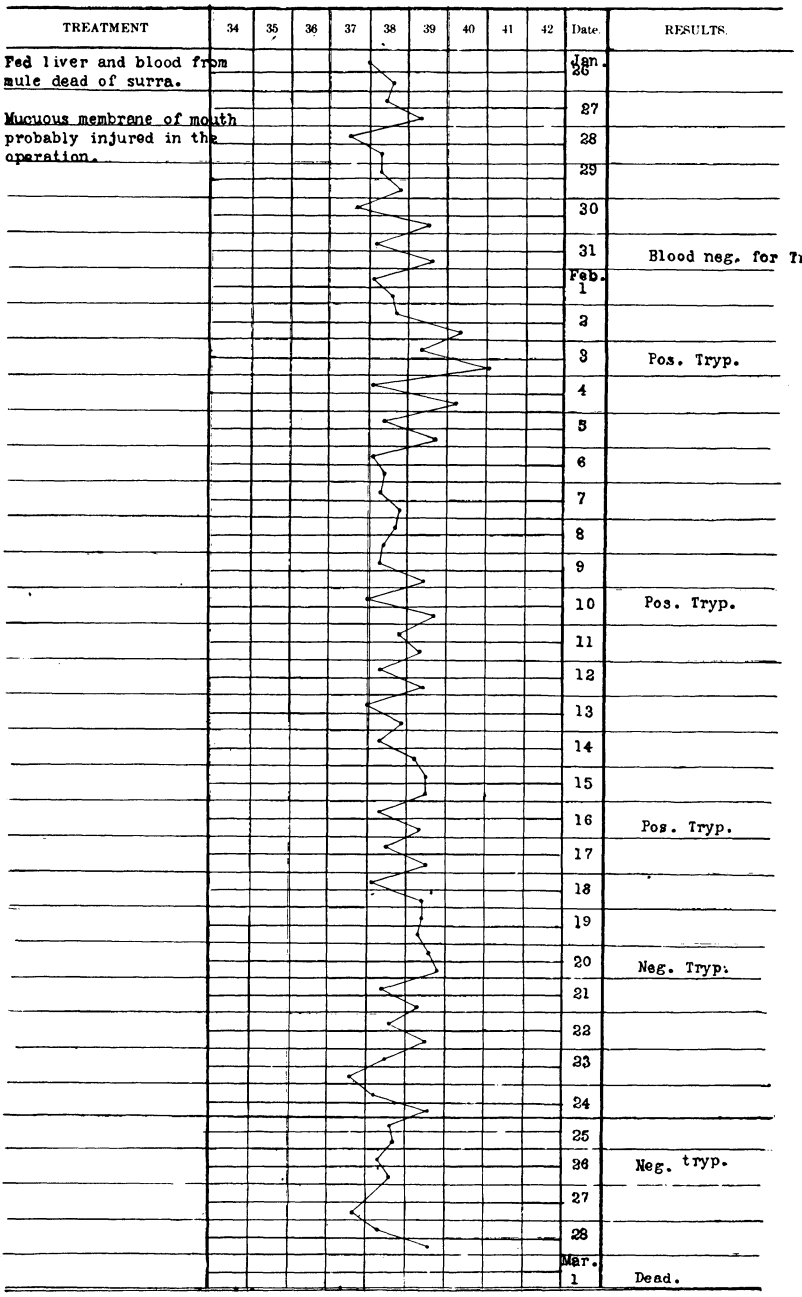

FIG. 148.—Temperature record of surra in a rabbit.

as a rule, followed by a sharp rise of temperature and the appearance of parasites in the blood, a fact which probably accounts for the great variations in length of time assigned to it. In fact, there does not appear to be a distinct incubation period in all cases, for in some cases animal experiment may prove the blood infectious as early as eight hours after inoculation, while in others it does not become so until the fourth or fifth day. The course of the disease is somewhat chronic, lasting from fifteen days to three months or more, with a mortality of 100 per cent.

It is seldom that parasites are numerous in the peripheral circulation; and determinations by simple microscopic examination show that inter-

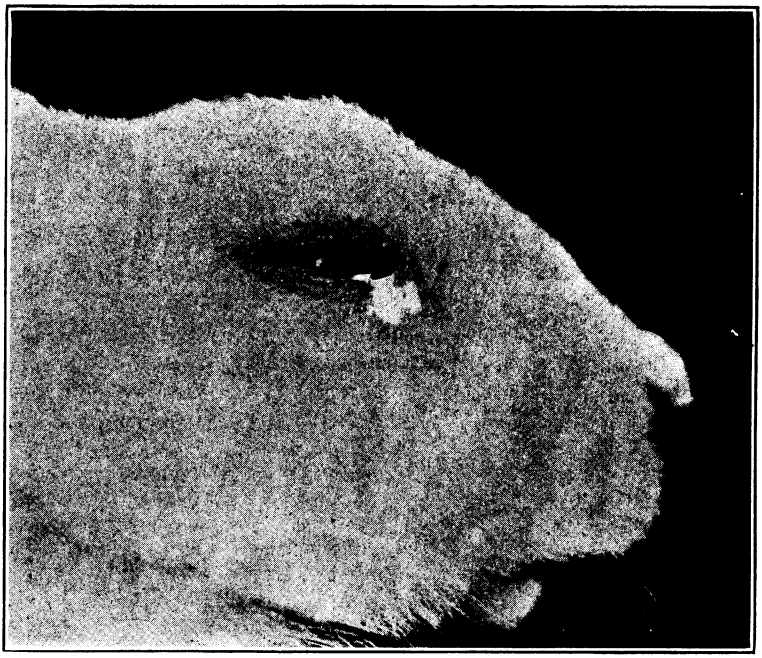

FIG. 150.—Showing muco-purulent discharge from eyes, falling of long hairs, blepharitis and conjunctivitis in rabbit.

missions are frequent, lasting from one or two days to several weeks, during which parasites are not found. As in other animals, however, the blood is continuously infectious by animal inoculation. The temperature (see figs. 148, 149) throughout the disease is less markedly remittent than is usual in most animals, while exacerbations and remissions are rare.

Anemia and emaciation come on rather slowly, but develop to an extreme degree before death. Watery discharges from the nose and eyes appear early, gradually becoming muco-purulent and tenacious, solidifying on the margins of the eyelids and nose, and encrusting and entan-

gling the long hairs, which fall out and leave excoriated surfaces. Edema occurs around the base of the ears, the nose, and the abdomen, involving especially the scrotum, which becomes enormously distended and may break open and suppurate. (See fig. 151.) There is a discharge from the prepuce similar to that from the eyes and nose. In the female the external genitals are scarcely less affected than in the male. Urticarial eruptions and falling out of the hair are common symptoms. Lameness of the hind parts occurs in most cases, and may reach to such a degree that the posterior extremities become useless. The subcutaneous lymphatics are often palpable, and in some instances swelling of the joints occurs.

FIG. 151.—Showing enormous swelling of genitals in rabbit.

Necropsy reveals lesions similar to those observed in other animals. The lymphatics, particularly of the inguinal and postperitoneal regions, are somewhat enlarged and red in color. The serous sacs contain fluid and often show fibrinous flakes over the surfaces and adjacent organs. The spleen is usually enlarged and friable, but a typical acute splenic tumor is often seen, while "sago spleen" occasionally occurs.

TRYPANOSOMIASIS OF CATS.

Cats are reported susceptible by inoculation to surra, nagana, dourine, and mal de caderas; but the course of the disease does not seem to have been carefully studied in them.

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Rabbit No 168
January 26, 1903

Weight *Age* *Sex* *Color* *Inoculation* Trypanosoma

History

Healthy animal under observation for months.

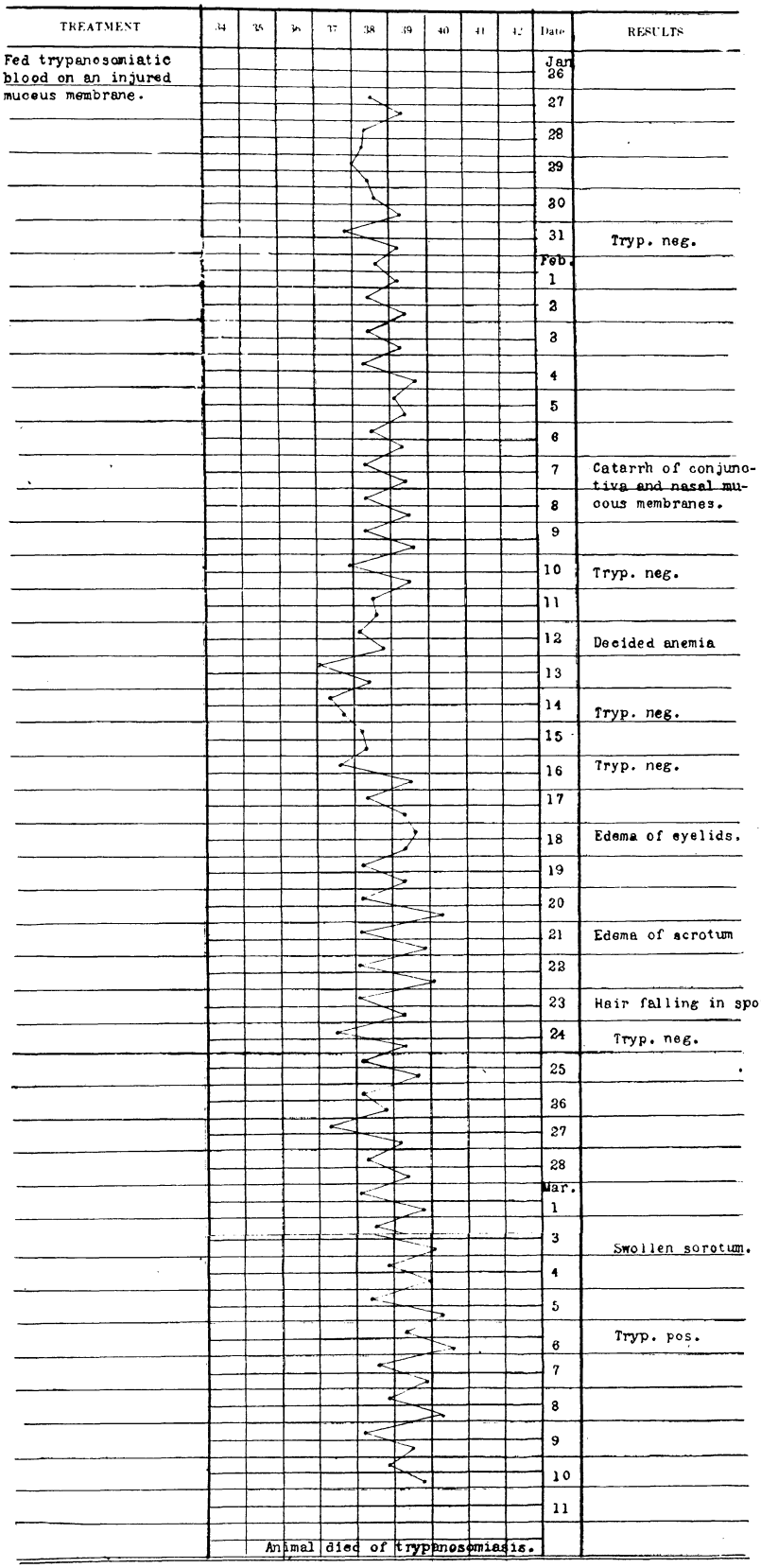

FIG. 149.—Temperature record of surra in a rabbit.

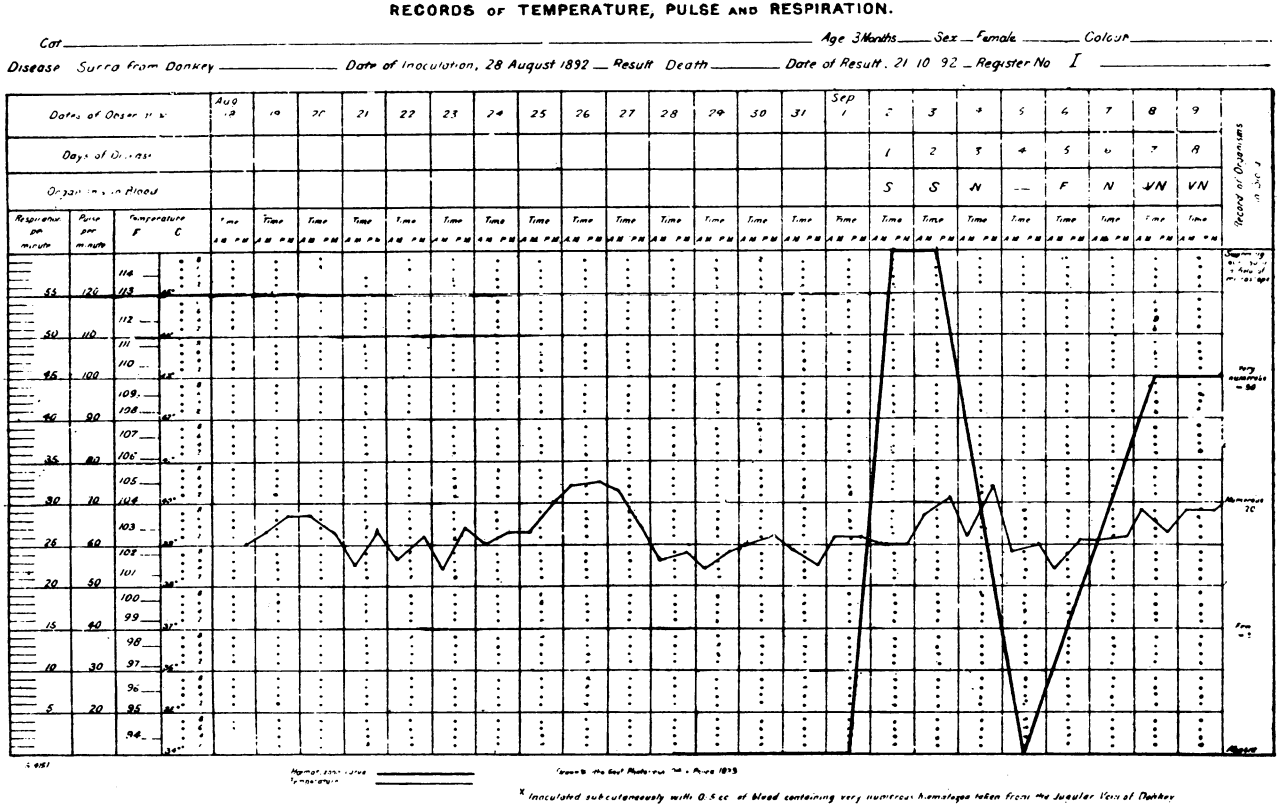

FIG. 152.—Temperature record of surra in a cat (After Lingard.)

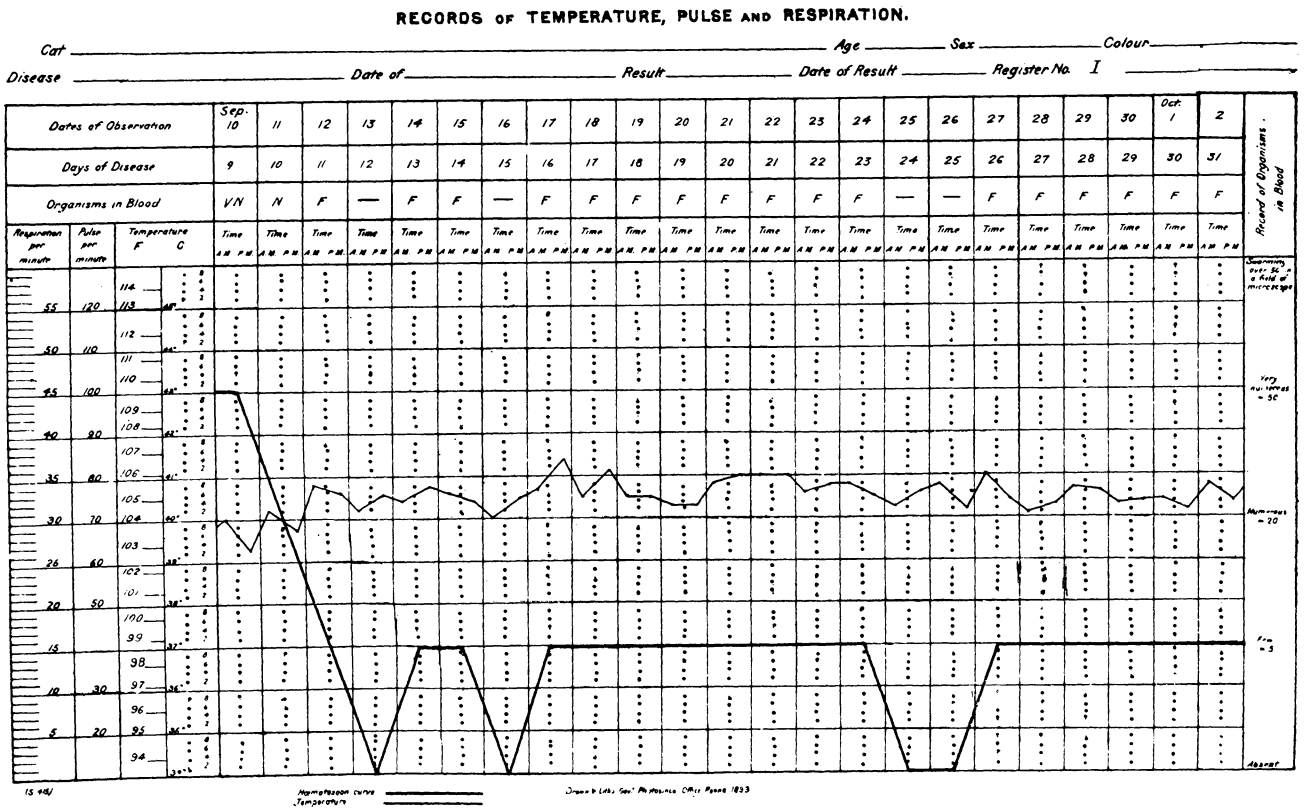

FIG. 152 (continued).—Temperature record of surra in a cat. (After Lingard.)

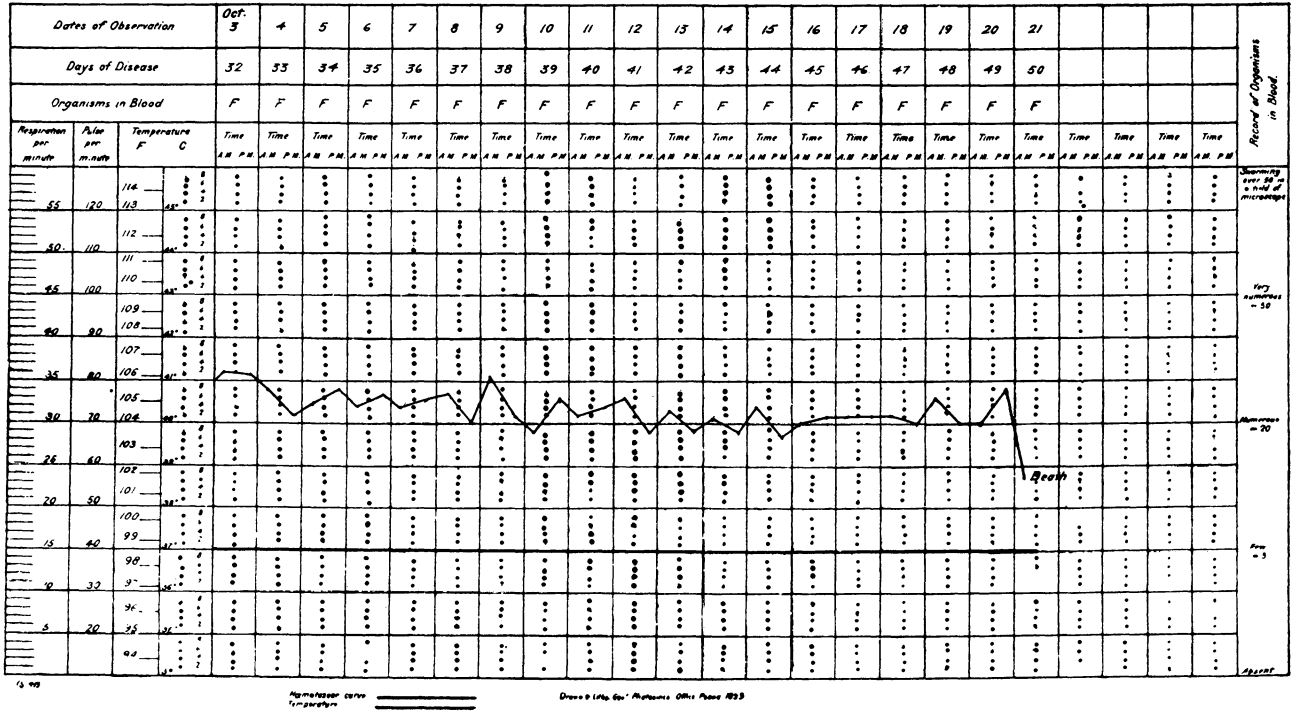

FIG. 152 (continued).—Temperature record of surra in a cat. (After Lingard.)

Fig. 150 illustrates the temperature record in surra as given by Lingard and fig. 151 that of "surra americain" as given by Sivori and Lecler.

In the Philippine Islands they are susceptible to the infection by any of the usual forms of inoculation. The incubation period is from two to five days, the course rapid, varying from three to fifteen days, and the mortality 100 per cent.

Parasites are constantly present in the blood, but vary considerably in numbers at different times. The temperature curve is illustrated in figs. 154 and 155.

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Cat *No* 865
May 28, , 1903
Weight *Age* *Sex* *Color* *Inoculation* Tr. Evansi
History Small white cat.

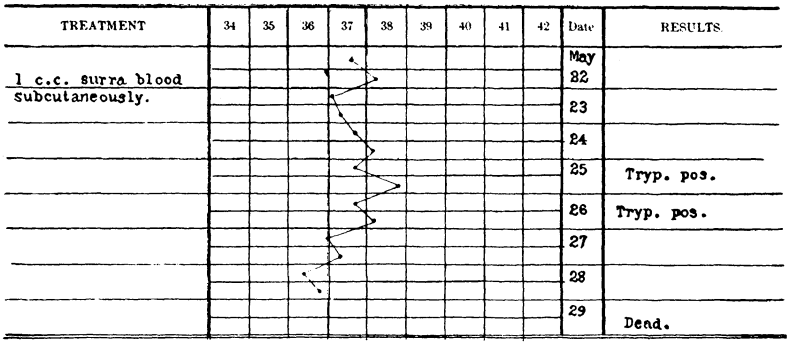

FIG. 154.—Temperature record of surra in a cat.

Skin lesions in these animals are very prominent and are similar to those described for dourine. Urticarial and macular eruptions are common, and not a few animals show phlegmanous ulcers, particularly on the abdomen and flanks. Edema is slight.

The hair, particularly about the nose and eyes, becomes rough and falls out. Profuse discharges from the nose and eyes, resembling those in the case of rabbits, are usual symptoms. Cloudiness of the fluid in the anterior chamber and opacity of the cornea may occur in one or both eyes. Anemia is profound and emaciation moderate. The appetite is usually poor, but the bowels remain normal. Tendency to paralysis in the hind quarters was noticed in only one animal.

Necropsy reveals the usual lesions, in addition to the changes already mentioned as present during life. The acuteness of the disease in these animals probably accounts for the fact that the lesions are less pro-

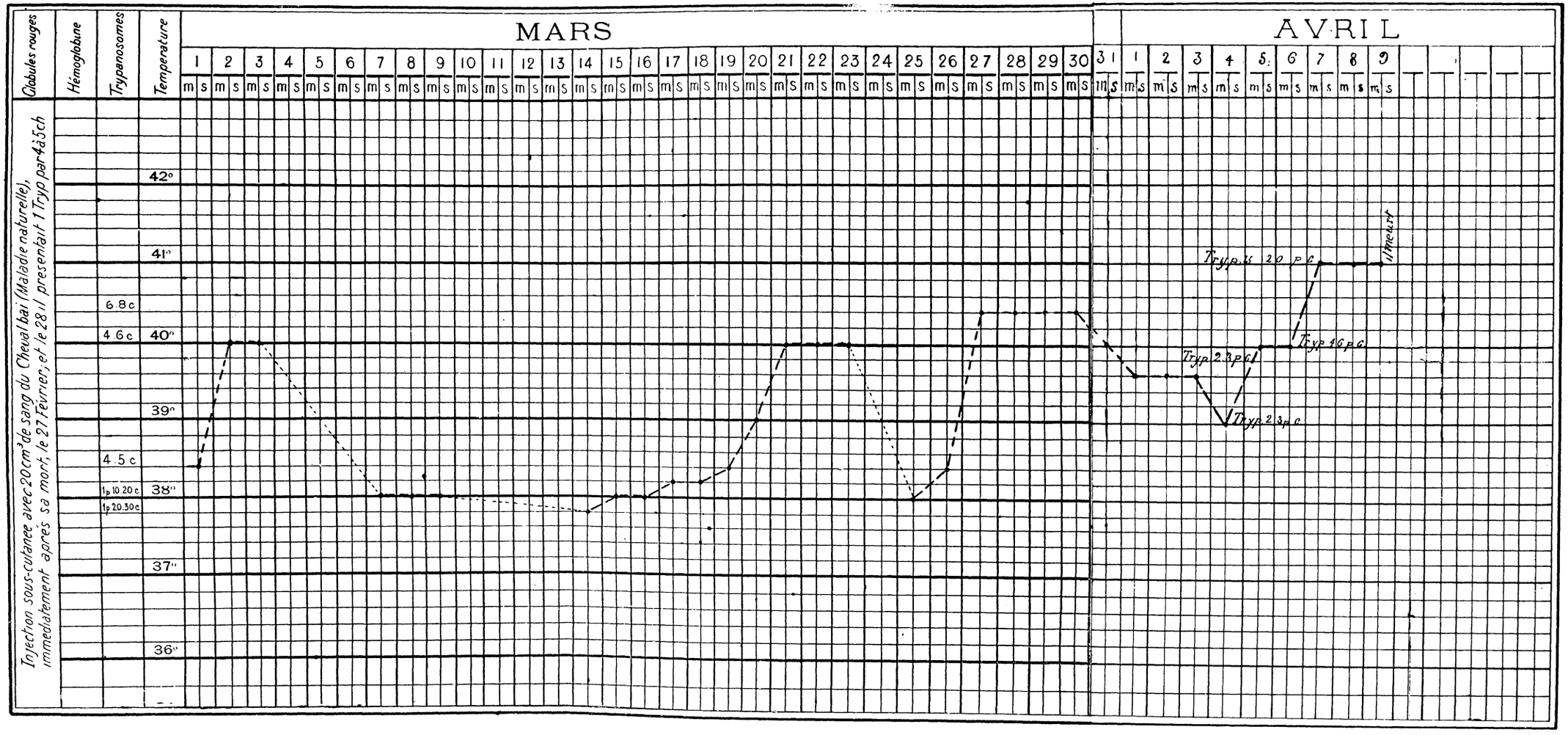

FIG. 153.—"Surra americain" of cat. (After Sivori and Lecler, 1902, Pl. XX, Pt. 1.)

BUREAU OF GOVERNMENT LABORATORIES.
BIOLOGICAL LABORATORY.

ANIMAL RECORD.

Cat *No* 266
May 26, , *190* 3
Weight *Age* *Sex* *Color* *Inoculation* Surra
History Medium-sized healthy cat.

TREATMENT	34	35	36	37	38	39	40	41	42	Date	RESULTS
1 c.c. surra blood subcutaneously										May 26	
										27	
										28	
										29	
										30	
										31	Tryp. pos.
										June 1	
										2	
										3	Few tryp.
										4	
										5	
										6	Few tryp.
										7	
										8	
										9	
										10	
										11	
										12	
										13	
										14	
										15	Weak, watery eyes.
										16	
										17	Few tryp.
										18	Few tryp.
										19	
										20	
										21	
										22	
										23	Marked catarrhal conjunctivitis.
										24	
										25	
										26	Dead.

FIG. 155.—Temperature record of surra in a cat.

nounced. The spleen is enlarged, but assumes more nearly the type of acute splenic tumor, while subserous hemorrhages are numerous.

TRYPANOSOMIASIS OF RATS AND MICE.

Tr. lewisii, the common *Trypanosoma* of rats, has already been described. Most writers agree that it is harmless for rats and noninfectious, by inoculation or otherwise, for other animals.

Large numbers of rats have been found naturally infected in various parts of the world; a partial list of the regions is as follows: Lewis in Calcutta found 29 per cent infected; in Bombay Carter found 12 per cent infected and Lingard 30 per cent; Koch in Africa, 41.7 per cent; Crookshank in London, 25 per cent; Rabinowitsch and Kempner in Berlin, 41.8 per cent; Laveran and Mesnil in Paris, 4.6 per cent; Raillet in Alfort, a large percentage; Chemette at Lille, a large percentage; Sivori and Lecler at Buenos Ayres, 3 per cent; and Chalachnikow and Danilewsky in Russia found the infection present. In Togo eight rats examined were negative (Luman). Voges in South America did not find these animals naturally infected. In a personal letter Kitasato in Japan states that many of the rats there harbor the parasite.

In Manila rats *Tr. lewisii* has been found in from 20 to 65 per cent of the individuals examined, varying according to the season and the locality from which they were received.

Van Dyke Carter inoculated dogs, cats, horses, and monkeys with rat *Trypanosoma,* and always obtained negative results. Koch failed permanently to transfer the infection to other animals. He gave a rat *Tr. lewisii* and *Tr. evansii* and afterwards found both in its blood. He then inoculated a dog with some of this rat's blood and the animal contracted the disease, but its blood was found to contain only *Tr. evansii.* The efforts of Rabinowitsch and Kempner to inoculate other animals with *Tr. lewisii* proved unsuccessful. In their experiments they used white and gray mice, field mice, guinea pigs, rabbits, dogs, goats, horses, and hamsters.

Lingard, on the other hand, inoculated twelve horses with infected rat blood, and four of them, after an average of seven days, died of a virulent form of surra. He argues that some *Tr. lewisii* are infectious for other animals, as demonstrated by his experiments. This statement has caused considerable confusion and his work has been questioned. Judging from our observations in Manila, it would appear, however, that Lingard's mistake consisted in considering these pathogenic parasites *Tr. lewisii.*

Kanthuck, Durham, and Blandford showed rats to be refractory to a second inoculation with *Tr. lewisii.* Rabinowitsch and Kempner noticed that some rats are absolutely refractory to these parasites, but that most of them are susceptible. After inoculations into the abdominal cavity, *Trypanosoma* were found to be present in the blood after

from three to seven days, and occasionally at the end of twenty-four hours. In rats inoculated in the abdominal cavity they found multiplication forms to be numerous in the exudate during twenty-four to thirty-six hours, at the end of which they disappeared permanently from the abdominal cavity to reappear in the blood. Rats could not be given a second infection, no matter how large the dose of infected blood used; and they employed the important fact that some of the animals are refractory as a basis for the preparation of a specific serum.

Laveran and Mesnil in general confirmed Rabinowitsch and Kempner's work and in addition showed that the young born of immune mothers are very slightly if at all immune. They also demonstrated that the agglutinating properties of the blood are not transferred to young. In immune rats *Trypanosoma* are destroyed in the abdominal cavity, and the agglutinative power of the blood lasts no longer than the preventive. In their opinion the treatment of rats with serum is unsuccessful. They state that as a rule the parasites appear in the blood at the end of twenty-four hours, and that in not a few cases, especially in young rats, they are found in considerable numbers before this time. However, many cases came under their observation in which the parasites did not appear in the blood until two to seven days after inoculation, and, indeed, in a few instances no infection resulted at all.

Adult parasites are the first to be seen in the blood, then there is a period, rarely extending beyond the eighth day, when multiplication forms may be observed, after which adult parasites are visible throughout the course of the disease. They believe multiplication to take place in the abdominal cavity during the period from the first to the fourth day, and in the blood between the fourth and the eighth days, after which time multiplication forms are no longer present.

Infection of these animals with *Tr. lewisii* lasts from twenty days to four months or more. In old ones the *Trypanosoma* often disappear in two to ten days, and in these no active immunity is established. Subcutaneous inoculations, according to these authors, give infections which are less severe than those produced by other methods.

Blood infected with *Tr. lewisii* and kept on ice does not give an increased incubation period or produce any alteration of the infection, as long as motile parasites are found to be present. If, however, the blood is allowed to remain for a considerable length of time (forty-seven days), the incubation period is increased from six to nine days, and the infection is less severe. After fifty-one days or more on ice the blood no longer contains living parasites, but is still infectious for rats, with an incubation period of twenty-seven days. All writers agree that rats infected with *Tr. lewisii* show no symptoms of illness. The constant anatomic lesion is hypertrophy of the spleen.

Our work as a whole has been in conformity with that of others. In the thousands of rats found to be naturally infected with *Tr. lewisii* and

in those inoculated, we have never observed either apparent illness or death which could positively be attributed to infection with this parasite, although it was present in enormous numbers in the circulating blood. Our observations have been exceptionally easy on account of the great number of rats furnished the Laboratory for examination to determine the possibility of their infection with plague, since this disease has become endemic in Manila.

Very little is found in literature relating to the clinical manifestations and morbid anatomy of *surra* in rats. We have not seen a specific reference to the natural infection of these animals by *Tr. evansii,* though from our experience, which is to be described later, it is believed that Lingard must in some of his experiments have been working with such an infection.

Lingard states that the latent period in *Mus decumanus* as developed by the subcutaneous inoculation of 0.1 to 0.2 c. c. of virulent blood varies from one to two days; and in *Nesokia providens,* by subcutaneous inoculation of 0.2 c. c., from two to five days.

Kanthuck, Durham, and Blandford state that rats, when inoculated with nagana-infected blood, often exhibit convulsive seizures just before death, but otherwise show no symptoms of the disease, except dullness in the later stages. Transmission from one animal to another by coition, by suckling, or by any other method than by direct inoculation was not observed. Infected mice lived from eight to twenty-five days and rats from six to twenty-six days.

As the morbid anatomy of nagana in rats and mice they describe lymphatic hyperplasia, most noticeable near the point of inoculation, congestion, edema, and occasionally hemorrhages of the glands, great enlargement of the spleen, which is generally firm, friable and dark in color, enlargement and fattiness of the liver, and occasionally a small amount of fluid in the pleural cavity.

Laveran and Mesnil state that in rats and mice of all varieties, including white ones, nagana has a perfectly regular course. No symptoms are manifest, the animal appearing well until near death. Mice appear sleepy and die without suffering from dyspnea. One mouse had convulsions two hours before death. Some rats die with the same symptoms as mice, but most of them show great agitation just before death, crying out and dying in severe convulsions. There are no sensible variations of temperature in these animals. Parasites appear in the blood twenty-four hours or more after inoculation in the abdominal cavity, and on the second or third day after subcutaneous inoculation; they progressively increase in number until death. In white rats and mice death occurs in two and one-half to three days after intraperitoneal inoculations, and after three and one-half to five days following subcutaneous inoculations. Wharf rats (*Mus decumanus*) die in about the same length of time as white rats (*Mus rattus*).

According to Rouget, mice inoculated with *Trypanosoma* of dourine show no symptoms until near death, when the hair becomes rough and the cornea cloudy. The post-mortem changes observed are hyperemia of the abdominal layers, inflammation of the liver and spleen and of the lymphatics near the point of inoculation. Parasites are found in all of the organs and fluids, except the intestines and the urine.

Voges says that death may occur without any preceding signs of illness. In rats and mice inoculated with the *Trypanosoma* of mal de caderas there may be a few hours of comatose condition. The duration of the disease in these animals is given at about four weeks.

As has been stated above, the natural infection of rats with the *Trypanosoma* which cause the disease in domestic animals has not before been reported, except perhaps by Lingard, who, if such was the case in his work, misinterpreted his results.

In a preliminary report on Trypanosomiasis in the Philippine Islands, published as Bulletin No. 3 of the Bureau of Government Laboratories, 1903, Musgrave and Williamson reported that a certain number of rats in Manila were found to be infected with the *Trypanosoma* which in this country causes surra in horses. This discovery was brought about by accident, while the authors were attempting to immunize a monkey with a parasite supposed to be *Tr. lewisii*. As a result the animal contracted surra and died. At first, following Lingard, we thought this to be a pathogenic *Tr. lewisii,* or supposed accidental infection with *Tr. evansii* to have occurred; but more careful study and the repetition of the experiment with the greatest precautions has demonstrated that a small percentage of these rats harbor the parasite causing the disease in the horse. This *Trypanosoma* has the same morphologic characteristics, and upon inoculation is infectious for the same animals, producing the same disease with the same incubation period, course, termination, and lesions.

Wild rats are very unsatisfactory material to work with, because so many die after being in captivity a short time. The duration of life is so uncertain that but little confidence can be placed in results, even when control animals are used. The ones which live for a week or more after caging are likely to survive for some time, and, in order to obtain the best results, these have been employed as far as possible in our experiments.

As has been shown in other countries during the study of the disease in these animals, the infection is not evidenced by any symptoms of moment until just before death, when convulsions often occur. Too much importance should not be attached to this symptom, for time and again we have seen our control animals die in the same manner. Wild rats suffer such great excitement during the taking of temperature that no conclusions can be based upon the results. We must there-

fore believe that rats and mice infected with surra show no constant symptoms of practical significance. Some of the rare manifestations are cloudiness of the fluid in the anterior chamber, falling out of the long hairs about the head, and in a few cases edema and a tendency to paralysis of the hind parts. The incubation period, as determined by the appearance of parasites in the peripheral circulation, varies from a few hours to five days or more, and the duration is from two to twelve days.

The post-mortem examination shows an enlarged spleen, which may be hard and friable or more nearly approach acute splenic tumor with the organ usually dark in color; and there is generally enlargement of the lymphatics, especially of the inguinal regions, which may be hemorrhagic. The changes in the other organs are not significant, except in a small number of cases which show gelatinous infiltration of the subcutaneous and subserous tissues.

These lesions, particularly the enlarged spleen, are found in rats dying from *Tr. lewisii,* which is considered harmless. After discovering that a number of rats harbor *Tr. evansii,* we suspected the ones which died supposedly from *Tr. lewisii* and showed enlarged spleen, etc., on post-mortem to be in reality infected with *Tr. evansii*; but animal experiment absolutely disproved this theory.

The study of Trypanosomiasis in rats has not been completed. It is certain that rats in Manila may be infected both with a *Trypanosoma* harmless by inoculation to other animals and with one pathogenic for them. These parasites correspond microscopically to the descriptions respectively of *Tr. lewisii* and of *Tr. evansii.* We are not fully convinced that *Tr. lewisii* is always harmless for rats, or that some of the rats in Manila do not even harbor a third species of parasite.

TRYPANOSOMIASIS OF FROGS, FISH, AND FOWLS.

Trypanosoma have been found in *frogs* obtained from points scattered over a large area of the world, but they are usually considered harmless in these animals. The infection, so far as we have been able to determine, is not artificially transferable from frog to frog or from frogs to other animals. As already mentioned, we have not been able to find *Trypanosoma* in the blood of frogs in this country, and these batrachians have not been proved to be susceptible by inoculation with any of the *Trypanosoma* we have studied.

A number of observers have found *fish* harboring *Trypanosoma,* but all agree that no symptoms are produced. The species reported as infected are mudfish, trout, pike, redeyes, soles, and salt-water fish of the Mediterranean (species not given). The different species of these parasites have already been discussed.

Laveran and Mesnil, whose work is the most important in this line, found the infection of the redeye with *Trypanoplasma* to be very com-

mon, but proved the young rarely to be infected. In the sole, however, Trypanosomiasis is uncommon, being found in only four cases out of a large number of fish examined. They did not observe any symptoms of disease in fish caused by *Trypanosoma,* and were unable to transfer the infection by inoculation. Doflein, during a fatal epidemic in fish, found *Trypanosoma* in a number of the diseased ones, but he was not sure of any pathogenic action of the parasites.

We have examined a number of fresh and salt water species of fish in Manila, but have been unable to find *Trypanosoma* in any of them, nor have we been able to infect them with *Tr. lewisii* or *Tr. evansii.*

It has already been shown in the discussion of *Trypanosoma* that some *birds* are occasionally found to harbor a specific *Trypanosoma,* which, however, does not appear harmful to them. With reference to the inoculation of *Tr. evansii, Tr. bruceii, Tr. rougetii,* and *Tr. elmassianii* into birds, the evidence is somewhat contradictory for the different species. Most writers agree that birds are not susceptible to infection, but Voges, writing of mal de caderas, considers turkeys, ducks, and chickens susceptible by inoculation. He says that chickens die in from two to three weeks in great agony, from either subcutaneous or intraperitoneal injections. The only symptom noticed is emaciation, and parasites are very few in number in the circulation.

We have so far experimented with several varieties of birds, including maya, pigeons, doves, and chickens, but have been unable to infect them. No symptoms are produced, parasites are not found, and the blood proves noninfectious when inoculated into susceptible animals.

TRYPANOSOMIASIS OF MAN.

In 1898 Nepveu published an account of the occurrence of *Trypanosoma* in human beings. An extract from his article, translated, reads as follows:

> So far *Trypanosoma* have been found only in the blood of animals. In India they have been found in the blood of the rat (Lewis), the horse (surra epidemics), the dog, and the domesticated elephant. In Africa they have been discovered in the disease caused by the tsétsé fly, and in Europe in the blood of the rat, the rabbit, various birds, and the frog. No one seems to have as yet observed them in man, although Laveran states that Barron found certain flagellated protozoa of an undetermined genus in the blood of an anemic woman. In 1890, while making researches on malarial parasites in Algiers, I found flagellates in the blood of a patient, besides *Laveranii,* and I was able to count three to each preparation of 18 square millimeters. At about that time (see Nepveu, Etudes sur les Parasites du Sang chez les Paludiques, 21, 1891, in Bulletin et Memoires de la Société de Biologie) I published some of the drawings I had so far collected. I hoped then that I might be able to complete my first observations by a more detailed study, but since then I have rarely been able to find the parasites. I have therefore decided to publish the following facts in the hope of drawing the attention of such naturalists and physicians as will have the opportunity of completing these researches. * * *

In over 200 patients, mostly malarial, of whom I have examined the blood, I have found these various forms of *Trypanosoma* in only six, three of whom were suffering from quotidian fever (Khill, Langevelle, and Bichielli), one from double tertian (Hendrick), and two from pernicious comatose fever (Cabane and Ginestet), while the seventh observation was made on Dr. X., who was apparently in good health. In none of these patients have I been able to observe any symptoms characteristic of this special parasitic invasion. They were almost all suffering from the effects of *Laverania*, which prevailed everywhere in its various forms. This seems, therefore, purely a coincidence, which has appeared to me worthy of notice.

His article attracted very little attention, some writers mentioning his work with the remark that his descriptions were inaccurate, and many overlooking it entirely. He did not attach clinical importance to the appearance of these parasites in the blood, but his remarks regarding them seem to us perfectly clear as to the occurrence of *Trypanosoma* in the blood, sufficiently so as to entitle him to the credit for priority in the discovery of *Trypanosoma* in the human blood. His description does not appear sufficiently ample to designate the species of his parasite, but when one considers the confusion which exists even at the present time regarding the classification of these organisms, Nepveu can not be denied credit because in 1898 he failed to classify his *Trypanosoma*. The parasites more recently discovered in human blood, as in his case, have not been clearly classified. Nepveu observed seven cases.

The eighth case of Trypanosomiasis in man is published in the British Medical Journal for January 1, 1902, in an editorial and telegram from Dutton, in which he announces the discovery of a *Trypanosoma* in a European, who displayed peculiar symptoms. The same Journal for January 11, 1902, contains a letter from Ross, in which he gives Dutton credit for the following clinical data:

The patient has been suffering from a form of relapsing fever with peculiar edema of the eyelids and puffiness of the face, also edema of the legs, general weakness, abnormal frequency of pulse and respiration, and enlarged spleen. There was no organic lesions of the heart and kidneys, and no malarial parasites were found after repeated examination. The relapsing fever recalls that of horses suffering from the same parasite. It is not yet certain whether the parasite approximates *Tr. bruceii* or *Tr. lewisii*.

Dutton considers the most valuable features presented by his case as (1) its chronic course, (2) the general wasting and weakness, (3) the irregular rise of temperature, which is never very high, and of a relapsing type, (4) the local edemas, (5) the congested areas of the skin, (6) the enlargement of the spleen, and (7) the constant increased frequency of pulse and respiration (hurried breathing).

He examined the blood of one hundred and fifty healthy children between the ages of one and fifteen years, natives of Gambia, and says that he found *Trypanosoma* apparently identical with those observed in the European in the ninth case. The child is reported as showing no clinical evidence of the disease.

Forde (Journal Tropical Medicine, September 1, 1902) publishes the case already described by Dutton. He deals particularly with its history and symptoms previous to Dutton's personal observations.

The patient was a European, 42 years old, and at the time he came under Dr. Forde's care, May 10, 1901, at the Colonial Hospital, Bathurst, was a man of robust constitution, living a regular and steady life.

He was at first thought to be suffering from malarial fever, but quinine produced very little change in the course of the temperature. His blood was examined and malarial parasites were not found, but in nearly every specimen Forde found "small worm-like bodies," which he at first considered a species of *Filaria*. After repeated observations, however, the diagnosis became doubtful, and he associated these bodies with the symptoms of the disease.

The patient was invalided to Europe and returned to Bathurst in December, 1901. At this time Dr. Dutton, being informed of the case and examining the patient's blood, again found parasites, and immediately recognized them as *Trypanosoma*.

Forde gives as the chief characteristics of this case: (1) The irregular intermittent temperature, (2) the edematous condition of the face and lower extremities, (3) the rapid and variable pulse and respiration, unaccompanied by any evident cause, (4) the loss of weight with marked debility, wasting and lassitude, (5) the persistence of these symptoms and their resistance to treatment.

In the Journal of Tropical Medicine for November 1, 1902, is published "A Case of Trypanosomiasis in a European," under the care of Dr. Manson—the tenth case. Manson had been struck by the peculiar clinical features of Forde's case, its chronic irregular fever, the enlargement of the spleen, the edema, especially of the face, and the very well-marked erythema multiforma scattered over the trunk and limbs.

The patient under Manson's observation was the wife of a missionary, who had resided on the Upper Congo for about a year and had been sent to Manson by Habershon. She had been suffering while on the Congo from an irregular fever, which was still present when she came under observation, though she had been living in England for the past eight months and had been drugged with quinine and arsenic.

On examining her Manson recognized the same grouping of symptoms he had seen in Forde's and Dutton's case. The patient was admitted to the hospital and her blood was examined daily for two weeks, but no *Trypanosoma* were found. While arrangements were being made to test the tentative diagnosis by injecting blood into animals, Dr. Daniels, while making a blood count, found a *Trypanosoma,* and on subsequent examinations more parasites were observed. In the British Medical Journal, May 30, 1903, this case is accurately described by Manson and Daniels.

Manson published the eleventh case of Trypanosomiasis in human beings. The patient was a European lady who had resided on the Congo. In this case an erythematous rash was a prominent symptom, preceding or accompanying the attacks of fever, which occurred every ten days and lasted each time for about three. The cause of the disease is attributed to the bite of some insect on the foot. Manson is inclined to attribute significance to a tick (*Argas moubata*) as a transmitter of the infection.

Broeden, according to a letter received by Dr. Manson, has discovered two more cases in human beings—the twelfth and thirteenth. Both of these were Europeans. Baker has recently reported three more cases in human subjects in Uganda.

Of the sixteen cases of Trypanosomiasis in man, two have been in apparently healthy persons, six associated with malarial fever, and eight have shown clinical symptoms apparently entirely due to the infection with *Trypanosoma*. In these five cases the clinical picture, which has already been reviewed, was peculiar and quite similar.

Castellani has reported the discovery of a *Trypanosoma* in the cerebrospinal fluid of twenty out of thirty-four cases of sleeping sickness. He has described the parasite and proposed the name *Tr. ugandense*.

Bruce has continued Castellani's work and has reported to the Royal Society the discovery of *Trypanosoma* in the fluid obtained by lumbar punctures in all of the thirty-eight cases examined, and in twelve out of thirteen of these cases he found the *Trypanosoma* also in the blood. The importance of this discovery can hardly be estimated at the present time, but it is certainly additional evidence of the increasing importance of this subject. Lieshman has also recently reported the possible appearance of *Trypanosoma* in the blood of patients suffering with "dumdum" fever in India.

Since the beginning of the present work in Manila constant vigilance has been observed in order to discover the infection in man, but so far with negative results. Neither the clinical symptoms nor the parasites have been found. The blood of hundreds of cases of persons ill and in health has been examined, particularly that of persons who have come in close and frequent contact with animals suffering from the disease. Both writers of this article have repeatedly performed post-mortem examinations on animals which had been but a few minutes dead of the disease, and have been bitten by flies covering the infected organs, but without the slightest inconvenience. A number of assistants during the course of the work have often exposed open skin wounds to infection both by blood directly and by biting flies, but all with negative results.

The reported cases show conclusively that human beings may become infected, and we shall continue our observations in this country, where the constant presence of the disease in animals, the sanitary conditions and the anemic state of most of the inhabitants would lead to expect a case eventually to occur in a human being.

Here we shall briefly mention the notes found in literature relating to such animals as have contracted the disease but in the case of which the clinical manifestations have been given but little detailed discussion and on which, owing to the lack of animals, no observations can be made by us.

Bruce proved by animal experiments nine out of thirty-five wild animals examined in South Africa to be infected with *Tr. brucei*. The positive ones included one buffalo, three *niedbeuste,* three koodoo (*Strepsiceros kudu*), one buch-buck, and one hyena. Many of these animals showed no clinical evidence of disease.

Laveran and Mesnil, in mentioning the animals susceptible to nagana, give several species of antelopes, the dromedary, the hare, the mullet, the hyena, the lapian, the hedgehog, the racque. Bruce mentions the babale and Brumpt the chamois. Lingard and others say that buffaloes and elephants are susceptible. Sivori and Lecler refer to the carpincho and Voges to the nutria (*Myopotamus coypus*) among animals subject to the infection.

Voges considers the nutria extremely susceptible. Death occurs suddenly about ten days after inoculation, without symptoms.

Laveran and Mesnil say that wolves have an incubation period of two to three days and that death takes place in from five to twelve days after inoculation. Parasites vary in number, but are usually to be found throughout the disease by microscopic examination of the blood. Cachexia and irregular fever are the prominent symptoms.

In strong, healthy animals the course of the disease is much longer, being twelve to fourteen days or more, and the period of incubation is from four to five days. The blood is always infectious, but parasites are not usually found in it by microscopic examination. Local symptoms appear in twenty to thirty days. Emaciation is not noticed until just before death.

The prominent symptoms when once established are conjunctivitis, coryza; edema, particularly of the head, the legs, and the genitals; congestion of the testicles, or even a true orchitis; falling out of the hair about the eyes, nose, and base of the ears; opacity of the cornea, sometimes purulent conjunctivitis and blindness in the late stages; ulcers around the eyes, nose, and other parts of the body, similar to those seen in dourine. In animals dying from twenty to thirty days after inoculation the marked clinical symptoms are not observed. English writers give the incubation period at eight days and the duration of the disease at twelve to fifty-eight (average, thirty) days.

Several writers mention hamsters as susceptible.

Hagger states that surra runs a very chronic course in camels and that the natives believe that a small portion of those surviving for three years to recover. He gives as the principal symptoms fever, swelling of the

right side of the chest, in the scrotum, and sheath of males and in the udder of females, frequent abscess formations in these regions, progressive anemia, and rapid emaciation. The appetite remains good. Parasites are present in the blood during fever, which sometimes reaches 42° C., and are absent during intermissions.

The several forms of the disease are said to run a chronic course, somewhat similar to that of the goat and the deer.

IX. COURSE, DURATION, AND PROGNOSIS.

The course of the disease varies in the same and considerably more so in different species of animals. In the language of Laveran and Mesnil, "it always shows the general characteristics of blood infection."

A temperature of remittent, intermittent, or relapsing type is present in nearly all animals, including man. Progressive anemia and emaciation are also constant manifestations. It is rarely a very acute infection, although in exceptional cases it becomes so intense as to suggest septicemia.

The duration is also variable both in like and unlike animals. Schilling says that the surra of South Africa lasts from thirty-six days to eight months in horses. He considers the acuteness of the disease to be influenced somewhat by the number of parasites in the blood. Bruce says that horses live for weeks and months with nagana.

In the Philippine Islands the duration of the disease in horses does not show a greater variation than it does in other countries. It is from fourteen days to three months, and is about the same for American, Australian, Chinese and native horses.

The length of time the disease lasts in cattle is usually somewhat longer. Bruce had a cow sick with nagana under observation during eighteen months.

The prognosis is influenced to a certain extent by the species of the animal infected. Most writers agree that it is invariably fatal in horses, but there are some exceptions. Schilling believes that some horses recover; and Laveran and Mesnil say that recoveries have been reported in South America, although they have seen none. A varying percentage of cattle, according to careful observers, recover. Bruce says that cattle occasionally recover from nagana, and Laveran and Mesnil have had similar results. Lingard believes that a large proportion of cattle recover. Voges, on the other hand, considers the cattle of South America immune.

The annual report of the Division of the Chief Quartermaster of the Philippine Islands for the year ending June 30, 1902, records the death of 3,693 horses and mules out of a total of 17,220 on hand. He adds that most of this havoc was produced by surra and glanders.

The course, duration, and prognosis of the disease have been considered somewhat in detail under the discussion of the different species of animals.

The duration in particular varies so much with environment, the constitution of the animal, and probably with other conditions which we do not understand, that it can not be fixed except within wide limits. The prognosis is always grave, the mortality in most species of animals being 100 per cent. The only exception to this fact among domestic animals of economic importance is found in cattle, a varying percentage of which recover.

X. COMPLICATIONS.

Broncho-pneumonia, observed especially in horses, has been mentioned by writers as a frequent complication. In this country edema and congestion of the lungs is common, while broncho-pneumonia, more or less extensive in character, is occasionally seen.

Nephritis, hydropericardium, and hydrothorax sometimes explain unusual symptoms. Tuberculosis and surra are not infrequently associated, especially in monkeys. We have had two cases of surra and glanders in the same animals. Filariasis and surra often occur together in dogs. Rinderpest sometimes develops in cattle suffering with surra.

Other diseases which we have found associated with surra are foot-and-mouth disease, pseudoactinomycosis, pseudofarcy, malignant neoplasms, and at least two septicemic conditions not fully understood.

XI. DIAGNOSIS.

In order to carry into effect methods looking to prevention an early diagnosis is very desirable in all cases. Fortunately, in the horse, the most frequently infected of all animals, this is in the majority of cases easily done by a microscopic examination of the blood, which consists in examining a specimen prepared in the same manner as one to be examined for malarial parasites. The *Trypanosoma* are readily observed with a Zeiss DD or AA and ocular 4, and are usually in sufficient numbers to be quickly seen. In many cases, however, they may be so few as to require considerable time and the examination of several specimens before they are found; and as has already been said, they may not be observed at all for several days at a time by this method.

When infection is suspected and parasites are not found in the blood, there are two courses open. First, microscopic examination, carried on for several days if necessary, will usually suffice for making the diagnosis in horses and in several other animals in which the parasites are but rarely absent for more than a few days at a time in the early stages of the disease. The second course is to test the blood by animal experiment. For this determination any of the smaller animals, particularly dogs, monkeys, and white rats and mice, are satisfactory. A few drops to 1 c. c. of blood from the suspected animal may be injected under the skin, or, preferably, into the abdominal cavity on account of the shorter incubation period, after which the parasites may be demonstrated in the usual way.

The objection to the latter method is the expense of the animal and the length of time necessary for the appearance of the parasites. On the other hand, results are certain, and in the case of some animals time is saved. This method, however, is absolutely necessary in many cases of infection in cattle, goats, sheep, and some other animals, and should be employed in all cases of doubt from any cause.

Whatever the method used, a determination of the blood infection is absolutely the only way to make an early positive diagnosis of the disease in any species of animal, and it is well constantly to bear this in mind in performing work which means so much in suppressing an epidemic.

As has already been said, the early clinical manifestations are slight. The temperature, always highest in the afternoon, is constant in most animals immediately after the incubation period, but may drop to normal again very quickly and remain so for days. When present during an epidemic it is significant, but its frequent absence leaves much to be desired. The next symptoms to appear are catarrhal discharges from the nose and eyes and a beginning pallor of the mucous membranes. Even with all of these symptoms, which may not be fully developed for a week, the diagnosis is still not absolutely certain without a determination of parasites in the blood.

With the development of other symptoms, such as edema and incoördinations, in addition to those already mentioned, a diagnosis upon appearance alone is justifiable.

XII. DIFFERENTIAL DIAGNOSIS OF SURRA, NAGANA, DOURINE, AND MAL DE CADERAS.

Very little convincing work has been done to solve this important question, for the reason that very few workers have had the opportunity of studying more than one of the affections. In most cases authors have contented themselves with the conclusion that if not identical they are closely allied. Koch, who worked particularly with *surra* and *nagana,* considered the parasites and the resulting infections identical, and many others have formed similar conclusions, while Voges and Laveran and Mesnil and others maintain certain differences to exist.

Writing of *nagana* and *mal de caderas,* Laveran and Mesnil consider them distinct morbid entities, which can not be separated by their clinical symptoms, and they further maintain that species of animals which are susceptible to one can also be infected by the other. They classify their reasons for considering the two diseases to be distinct under three headings: (1) Constant morphologic differences between *Tr. brucei* and *Tr. equinum;* (2) animals immunized against *nagana* do not have for *Tr. equinum* the same activity that they possess for *Tr. brucei,* and (3) animals immunized against *nagana* are susceptible to *mal de caderas.*

The morphologic differences between the two *Trypanosoma* have already been considered, and regarding the other points of difference Laveran and Mesnil explain themselves in substance as follows:

A deer recovered from *nagana* at the end of eight months, and, having received during the interval fifteen inoculations of 10 to 60 c. c. of the blood of a dog affected with *nagana,* without contracting the infection again, was inoculated in the skin with 1 c. c. of dilute blood of a rat suffering with *mal de caderas.* Blood taken from the deer five days after this inoculation was infectious for mice by intraperitoneal injection.

A sheep cured from *nagana* after a period of one month and which had received during this time inoculations of 10 c. c. to 20 c. c. of blood from a dog suffering with *nagana,* was inoculated subcutaneously with 0.5 c. c. of diluted blood from a mouse sick with *mal de caderas.* The blood of this sheep, obtained five days after the last inoculation and injected into the peritoneum of a rat (with a dose of 3 c. c.) and of two mice (with doses of 0.25 c. c.) gave to them an infection caused by the *Trypanosoma* of *mal de caderas* with an incubation period of less than four days.

Blood taken again after fifteen days from *mal de caderas* and injected into the peritoneum of a rat and a mouse conveyed the disease with an incubation period of four to six days. The blood of a control sheep, which had not yet received an injection of *Trypanosoma* of *nagana,* examined on the fifth and thirteenth days after an inoculation of *mal de caderas,* showed the same virulence as the blood of sheep recovered from *nagana* and infected with *mal de caderas.*

The question as to whether the serum of animals immunized against *nagana* is active for *Tr. brucei* and without action for *Tr. equinum,* is discussed by Laveran and Mesnil as follows:

I. The serum of a deer immunized against nagana, when given in a dose of 1 c. c. containing from one-fifth to one-twentieth c. c. of blood of *mal de caderas,* showed no action on the incubation period or on the progress of the infection in mice inoculated with the mixture. The same quantity of this serum, mixed with corresponding doses of blood of nagana, prolonged the incubation period of the disease about five days.

II. The serum of a sheep which had recovered from *nagana,* when given in a dose of 1 c. c. or even 2 c. c. mixed with doses varying from one-tenth to one-twentieth c. c. of diluted blood of a dog having *mal de caderas,* had no action on the incubation period or on the progress of the infection in mice inoculated with the mixture. The same serum, in a dose of 0.5 c. c. mixed with one-tenth c. c. of diluted blood of a dog, prevented all infection in the rats inoculated with this mixture. We also experimented with a mixture of 1 c. c. of the serum with 0.5 c. c. of the same diluted blood.

Bruce considers *nagana* and *surra* analogous, if not homologous, diseases. Weber and Nocard have concluded that *surra, nagana,* and *dourine* are the same disease with slightly different symptoms. Schilling con-

siders them all closely related or identical. Curry believes *surra* and *nagana* probably to be the same, but does not know with which to place the Philippine epidemic.

Salmon and Stiles state that the majority of writers consider *surra* and *nagana* the same disease, but that they maintain *dourine* to be different. Sivori and Lecler from their studies think that the parasites of *surra* and *nagana* are identical.

Voges will not venture a decision as to whether *mal de caderas* and *dourine* are the same disease. He points out in detail their great similarity. He considers these diseases different from *surra* for the following reasons:

(1) "*Dourine* and *mal de caderas* can not be transmitted to cattle, which animals are directly attacked by *surra*." (2) "In regions where *mal de caderas* exists cattle do not die from *surra*." (3) "We have no reason to believe that *Trypanosoma* show the same irregularities of virulence as bacteria, so that the different forms of the disease may be said to be produced by different degrees of virulence in the same *Trypanosoma*. On the contrary, during our four years of experimentation, the latter have shown a constant virulence." The fourth reason, which he considers decisive, is based upon the morphologic differences in the parasites, which have already been discussed. In conclusion he says: "I think these four proofs are entirely sufficient to establish for all time the difference between *surra* and *dourine* as well as between *surra* and *mal de caderas*."

In another article Laveran and Mesnil give extensive consideration to the differences between *surra* and *nagana*, which in substance is as follows:

The same animals are susceptible to both of them: the horse, the ass (except perhaps certain races), the mule, the goat (in the Dutch East Indies they are refractory to *surra*), the sheep, the cow, the camel, the dog, the cat, the monkey (long-tailed macayo), the rabbit, the guinea pig, and the rat. In the horse, the course of the disease is the same, whether *surra* or *nagana*. The animal dies at the end of the same time (30 days on the average). In the case of experimental inoculation, the incubation period is the same, there are the same lesions of the eye and lids, the same edema, the same degree of anemia, the same emaciation, followed by final paresis preceding death. The fever is of the same type, except that it is perhaps more clearly intermittent in the case of surra; besides, during the intermissions, which may last from one to six days, the parasites are not seen in surra by microscopical examination, whereas they are very rarely absent in *nagana* (Lingard insists particularly on this difference). In short, the differences are minimum.

The other equides, the goat, the sheep, and the dog die of the two diseases in the same length of time and with practically the same symptoms. * * * Rabbits, guinea pigs, and rats (*Mus decumanus*) succumb to surra with about the same symptoms as to nagana.

Cows remain to be considered. Few survive nagana (according to Bruce, Koch, and African explorers in general). On the contrary, they generally recover from surra. According to Lingard, death from this disease is in fact exceptional. The

animal becomes considerably emaciated, but recovers its health; and a second inoculation does no harm. This appears to be a sharply marked difference between the two diseases. Perhaps this is owing to a difference of race, as Rogers has supposed, recalling the experience of Koch relating to the asses of Massai. In any case the question should be settled by experimental methods. If the supposition of Rogers is considered incorrect, the question may be determined by proving whether cows inoculated with several doses of *surra* blood are susceptible to *nagana*. Not until these experiments have been made can a positive conclusion be given.

Mal de caderas.—Passing next to *mal de caderas,* Laveran and Mesnil believe that in most of its principal symptoms—

It does not differ at all from *surra* and *nagana*; but hematuria is frequently present. Paralysis of the posterior extremities, * * * a marked symptom of the South American disease, * * * is undoubtedly more pronounced than in surra or nagana.

The dog, the sheep, the goat, the cat, the monkey, the rabbit, the guinea pig, the rat, and the mouse succumbed at the end of various periods, according to the species of the animal (five to twelve days for the rat, four to eight days for the mouse, ten to fifteen days for the monkey, and three months or more for the goat and the sheep). In the rabbit the course is slow, and the animal presents the same symptoms of the eyes and genital organs as we have noted in nagana.

Cows are absolutely refractory; Argentine scientists mention a bull which was inoculated every eight days for a year and a half with 200 to 300 c. c. of blood from a sick horse, without showing any signs of the disease. They do not say whether an examination of the blood was made or a susceptible animal inoculated with it, especially during the month which followed the first injection.

In short, Laveran and Mesnil consider *mal de caderas* very closely related to *surra* and *nagana.*

Continuing the discussion with reference to *nagana,* Laveran and Mesnil say:

We have already shown * * * that the *Trypanosoma* of *dourine* presents morphological differences from that of *nagana.* This is an important argument in favor of the nonidentity of the two diseases. * * * The etiology is completely different. Contagion by coition seems to be the only natural mode of infection for dourine, as no spontaneous cases are known in geldings and mules. Insects, then, play no part in the propagation of *dourine.*

May *nagana* be contracted by coition? It is not probable, as no contagion results from depositing the virus on an unbroken mucous membrane. Nevertheless the experiment should be made, especially in the case of the rabbit.

The first symptoms (in the horse) appear ten to twenty days after the infecting coition. * * * In the male there is edematous enlargement of the foreskin, then of the extremity of the penis, and a slight muco-purulent oozing from the urethral mucous membrane, which is inflamed. In the female there is an enlargement of the two lips, or of one alone, with a muco-purulent discharge from the inflamed vaginal mucous membranes.

When this has persisted for a short time, other phenomena are manifested, as edema of the limbs and abdominal regions, progressive anemia, constant emaciation in spite of good appetite, weakness of the muscles, especially of the posterior extremities, and often sharp flexions of the joints. Certain symptoms are pathognomonic, so to speak, as the cutaneous patches seen on various parts of the body. There is hardly any fever; the temperature rarely passes 30° C.

The disease generally lasts from four to ten months, and has never the acute character of nagana or surra.

Toward the end of life ocular troubles (conjunctivitis, ulcerative keratitis) are sometimes noticed; the pareses are accentuated; there may be pronounced or very nearly complete paraplegia; and at autopsy foci of softening of the medulla may be observed, which is never the case in *nagana* or *surra*. * * *

The common symptoms of *dourine* and *nagana* then are striking. As to the special symptoms of *dourine* (cutaneous plaques, foci of softening of the medulla), they are not constant (the cutaneous plaques, for example, generally being absent in the ass) and may be considered in accord with the slower course of the disease. Nocard "has been able to kill horses in four, six, and eight weeks, with a temperature curve identical to that which characterizes *surra* and *nagana*."

Considering dourine in their animals, they say:

The dog, the rabbit, the rat, and the mouse are susceptible, but with exceptions and degrees of illness that show variations in the virulence of the infecting agent. * * * Rouget killed white mice in five to ten days with a general infection like *nagana* in its course. Only a small number of sewer rats succumbed, others recovered after having a sanguinary infection, while some were absolutely refractory. In the beginning of their studies, Buffard and Schneider had the same experience as Rouget on rats and mice; but Nocard, who their *Trypanosoma* after passage through a dog, found rats and mice almost absolutely refractory, and it was only with the greatest difficulty that the virulence was sufficiently increased to make rats sensitive. In the rabbit and the dog the course of the disease is much the same as in the horse, and contagion may take place by coition.

We wish to call particular attention to the lesions in the infected rabbit, already well described by the authors we have cited. They are much like those of rabbits infected with *nagana*. * * * With *nagana*, however, they never live longer than two months after inoculation, while in the case of *dourine* they may survive for more than six months with characteristic lesions. Experimental methods, therefore, do not show a sharp difference between *dourine* and *nagana*. * * * Cows are scarcely susceptible to *surra* and absolutely refractory to *mal de caderas*, the two diseases which we have shown to be so closely related to *nagana*.

Finally, a recent experiment of Nocard shows that there is a difference between *dourine* and *nagana*, * * * which corroborates our morphological observations. A number of dogs highly immunized against *dourine* were incoulated with a very small quantity of blood taken from one of our mice and rich in *Trypanosoma* of *nagana* at the same time as a control. The two immunized dogs died of *nagana* in eleven days, the control in fourteen days.

The statement of Weber and Nocard and others that dourine is found naturally only in horses and donkeys has been used as an argument for the individuality of this disease. In looking over the work of these writers, however, it will be noticed, as has been pointed out by others, that their statements are based upon observations made in localities free from other forms of the disease, and in at least one case in a country free from the known insects of transmission. When dourine is transferred to a country where surra is prevalent, it has recently been shown that transmission takes place just as it does in this disease; so that it appears that Schilling's remark that coition is the natural mode of transmission only in the absence of the usual insects and other necessary environments,

is rational and goes a long way toward refuting one of the arguments for the individuality of this disease.

We have studied surra with special reference to the particular points brought out by writers in various other countries and have been unable to find any clinical evidence that it is materially different from the description of any one of the other diseases already described or that they differ sufficiently from each other to justify the continuation of so many names.

A comparative study of the *Trypanosoma* has already been discussed in a chapter devoted to that subject and it is unnecessary to repeat conclusions here.

In summing up the whole matter it appears to us, when we take into consideration the work done by others and add our own results, that we are justified in believing *surra, nagana, mal de caderas,* and probably *dourine* the same disease, and that all are caused by *Tr. evansii.*

We recently received from Java a cow suffering with surra when it arrived. Rinderpest also developed in this animal shortly after landing, and the surra not yet having been discovered, the blood of this animal was used by Dr. Jobling, Director of the Serum Laboratory, in the immunization of three other cattle, two of which promptly developed Trypanosomiasis. We have studied the parasites in these animals and the course of the infection in different animals, and have satisfied ourselves that it is the same disease with which we are working in Manila. If the transfer of surra from Java to this country causes such a change in the nature of the infection in cattle, it is not at all surprising that similar ones may be brought about by transferring it in other countries.

Laveran and Mesnil found that the parasite of nagana is not so virulent for their cattle in France as it is usually reported to be for those of Africa.

The immunization of animals against one form of the disease with attempts to prove them susceptible to another has been undertaken by several authors, and most flattering results have been reported; but on going over the work it does not appear that the presence of the first disease was disapproved by animal experiment in some of the so-called immune animals before the second one was administered.

A discussion of the very interesting and important question of the identity or difference of these various diseases, to be of any great value, must take into consideration two factors: (1) The morphology of the parasites and (2) their pathogenesis in full.

It is the old story of parasitic infections over again, the zoölogist paying particular attention to the first of these considerations without full investigation of the second, and the strictly medical men doing the opposite.

In this case both points deserve careful consideration, but as the value of conclusions in sanitation and therapeutics are enhanced more by what

the parasite does than by what it is, we acknowledge the pathogenesis to be of the greater importance and shall so apply it in our discussion.

A number, if not all, of these diseases show a special tendency to lesions of the genitals, and if, as asserted, dourine is transmitted only by coition, this fact would serve merely to emphasize a symptom shown as a tendency in the others and therefore does not place the diseases so far apart as might appear at a glance. Competent observers have shown, however, that in this disease as in all others of Trypanosomatic origin the infection may be transferred by inoculation and the typical disease reproduced in this manner.

The supposed natural transmission of dourine only through coition has been explained by a recent writer as probably owing to the absence of the usual transmitting insects in the regions affected. In any event it does not appear to have been demonstrated that insects are not capable of transmitting the infection. The other described characteristic manifestations of the disease—the peculiar skin lesions—are found by a careful review of literature not to be confined entirely to dourine and not to be constant in this disease, especially when produced by inoculation. So far, unfortunately, but little work appears to have been done with a view to determining the probability of transmission of the other forms through coition and the study of the disease so produced.

In the early reports on *surra* by Evans and others it was stated that the disease was very fatal for cattle as well as for horses, but in late years most of the writers say that these animals are somewhat more resistant and that many of them recover. So, too, with *nagana,* in certain parts of Africa the disease is reported to be very fatal for cattle, but in other sections of that country and in other countries a greater resistance has been shown, and, as with *surra,* a certain number recover. When we look over carefully the literature relating to these diseases in cattle, we fail to find the marked differences so strongly emphasized by some authors as being diagnostic points in differentiating the two diseases; and indeed there are as great variations reported for the action of either of these diseases in cattle as there are reported for any two of the diseases in them, so that we are justified in concluding that there is nothing in the course of the various forms of trypanosomiasis in the same or different animals to warrant considering them distinct pathologic entities; in fact, the contrary would appear reasonable.

Absolute proof of the identity or individuality of these infections as they exist in various countries can be obtained only by importing infected animals for each individual disease into one place and carrying on their study under like environment. Until this is done we are inclined, as before stated, to regard *surra, nagana, mal de caderas,* and probably *dourine* as the same disease. This is a very interesting question and one which should be settled; but as far as providing means to combat the infection is concerned, a solution of this problem would not be likely to

add anything of value. Means which prove efficacious for one form of the disease will probably do so for all.

XIII. SUSCEPTIBILITY AND NATURAL IMMUNITY.

A full discussion of this subject would involve a great deal of repetition, but owing to its importance in dealing with epidemics it will be briefly reviewed.

On the whole there is a most remarkable similarity in the degrees of susceptibility and immunity of various animals to surra, nagana, and mal de caderas. There are individual differences, but it must be remembered that many factors contribute to such differences, since experimentation is carried on in various parts of the world.

Schilling mentions pigs as the only animals refractory to African surra; others, however, have shown that they may contract this disease, and they are considered to be susceptible to the other forms of Trypanosomiasis as well. Penning says that the cattle of Java do not contract surra, while Schat considers them susceptible. The chronic course of surra and nagana in cattle and the reported natural immunity of these animals to mal de caderas are not sufficiently at variance to justify the statement that the difference is diagnostic.

Lingard considers buffaloes susceptible, but says they may recover from the infection. These results do not differ from those reported in relation to the same animals in other countries. He also cites the case of a horse which he cured of surra with arsenic, iodide of arsenic, and mercury; but twelve months after the cure the animal died of the disease from the inoculation of one drop of virulent blood.

Sivori and Lecler were unable to find *Trypanosoma* in carpinchos, tapirs, peccaries, stags, small deer, pumas, tigers, and the *Lutra brasiliens.*

Birds, according to Foa, are absolutely refractory to large doses injected subcutaneously, abdominally, or through the eye. Voges, on the other hand, claims that chickens, ducks, and turkeys are susceptible by inoculation to mal de caderas. Later reports state that the birds of South America are immune.

Voges believes that the cow is the only animal naturally immune to mal de caderas. He proved horses, mules, donkeys, sheep, goats, rabbits, dogs, guinea pigs, white and grey rats, and white and grey mice to be susceptible.

Rouget determined birds, bats, and guinea pigs to be resistant to *Tr. equiperdum.* Sewer rats also showed a partial immunity. Kanthuck, Durham, and Blandford consider the sheep and deer of Africa resistant to *nagana,* and Koch says that the asses of Massai and the crosses of these asses with those of Mosket are immune to the same disease.

Salmon and Stiles mention horses, asses, mules, camels, elephants, cats, dogs, cattle, buffaloes, sheep, goats, rabbits, guinea pigs, rats (*Mus decumanus* and *Nesokia providens*), and monkeys as susceptible to surra.

They say that birds, reptiles, amphibia, and fish are immune to the *Trypanosoma* of mammals. The gaur (Indian bison) and the tsaing, according to Evans, have never been observed to have surra.

Ducks, roosters, doves, sucking pigs, and kids (a short-legged variety of goat found in Togo) were inoculated by Ziemann and recovered permanently from the disease.

Curry considers chickens immune by inoculation. He found horses, cows, carabaos, monkeys, dogs, cats, and rats susceptible to infection with *Tr. evansii* of the Philippines.

The only animals naturally susceptible to *Tr. lewisii* are wild and grey rats and mice; white rats and mice and tachetes may acquire the disease by inoculation. Laveran and Mesnil and others have shown that guinea pigs inoculated in the abdominal cavity are temporarily infected in a certain percentage of cases. To these may be added monkeys and puppies.

Rouget showed that white and grey rats and mice, rabbits, and dogs inoculated subcutaneously, intraperitoneally, in the abdominal cavity or by dropping infected blood into the conjunctivæ, are susceptible to *Tr. equiperdum*. Wasielewski and Senn found *Tr. equiperdum* in horses and asses, and successfully inoculated horses and dogs with it.

Voges mentions dogs, horses, rabbits, rats, mice, and guinea pigs as susceptible by inoculation to dourine. Weber and Nocard say that this disease may be inoculated subcutaneously, abdominally, or in the serotum or vagina in the case of the dog, the horse, the donkey, the rabbit, and the mouse.

Bruce proved the horse, mule, ass, cow, dog, cat, buffalo, hyena, bobale, and several other animals susceptible to nagana.

Laveran and Mesnil mention among the animals which may contract mal de caderas horses, asses, mules, cattle, sheep, goats, rabbits, guinea pigs, dogs, cats, rats, camels, elephants, and monkeys. Brumpt found the chamois susceptible.

There is no doubt that cattle have a relative natural immunity, which seems to vary somewhat in different countries; but this variation is not great enough to be of especial diagnostic significance.

The value of keeping in view the relative immunity of certain animals, in addition to its scientific interest, lies in its practical significance in providing measures for the suppression of an epidemic. The animals showing this tendency in the greatest degree are those which also give the least physical evidence of infection, and consequently are dangerous in that they provide hosts for its perpetuation. It is in these animals that parasites are often present only in small numbers in the peripheral circulation, necessitating animal experiment fully to establish a diagnosis.

XIV. PROPHYLAXIS.

The question of prophylaxis constitutes the next important part of this subject. All efforts to cure the disease having failed and there

being but slight prospect of working out methods which will be successful in the treatment of an animal once infected, our highest hope lies in being able to bring about a practical and at the same time efficient condition of prevention.

A curative treatment of animals suffering with this disease is not at all necessary to the welfare of the community which has the infection in its midst. It is a disease belonging to the class readily controlled by preventive measures, just as the case with many of the infectious diseases of man for which we have no cure. Practical rules for the control and even for the suppression of an epidemic may be prepared and enforced with no great difficulty; and the failure to do so shows a lack of progress in proportion to that evidenced in the control of the less important diseases.

With the aggregate of the findings on the nature and mode of transmission of this disease before us and considering the practicable manner in which this knowledge may be applied efficiently to control the infection, one can not help wondering that the annual loss of millions of animals from this scourge is permitted.

With the possible exception of rinderpest, it is the most important disease of animals with which a large part of the tropical world is infected. From an economic standpoint, measures looking to its control are of greater importance to the public welfare than are many of the diseases of man on which annually are spent millions of dollars.

Quarantine regulations governing the importation of animals are obviously the first point to consider in the discussion of preventive measures. Very few countries have efficient quarantine laws. France prohibits the importation of animals from infected countries and the United States does not allow animals to be imported from the Philippines. Recently a few other countries have been considering similar steps.

Leveran and Mesnil state that "the importation of animals from infected countries should be prohibited or greatly restricted. All animals arriving at a port should be examined, and if any are found to be infected, these should be killed and the others isolated. If the disease gains entrance to a new country, preventive measures, if established early, should prove efficient."

In a preliminary report, Bulletin No. 3, Bureau of Government Laboratories, Musgrave and Williamson in part say as follows:

1. Prevention of reinfection of the country by proper quarantine laws.
2. Eradication of the present infection by enforcing efficient sanitary regulations.

It is believed that the methods to be described are practicable and, if adopted, will prove sufficient to control the epidemic and eventually to eradicate it from the country, but to give the best results work should be begun at once, during the dry season, while the cases are comparatively rare and before the wet season comes with its great increase in the number of biting flies and the consequent spread of infection.

Had vigorous methods been adopted when the disease first appeared in this country in 1901, there would not have been an epidemic, and even now, were proper procedure followed persistently, the disease should be eradicated from the Islands. If, however, no more efficient course is adopted than the one in use now, the disease will go on spreading until the whole country is involved and the epidemic becomes perpetuated, as it has been in Africa, South America, India, and other countries.

The subject is an all-important one to the country, and it is imperative that facts and suggestions as to remedies be placed before our legislators. Without legal authority, municipal sanitation (as history so well demonstrates) must always be a failure, but with the authority given by proper ordinances, a disease such as Trypanosomiasis of horses should be controlled from the start and finally eradicated from any country in which it has obtained a foothold.

In considering quarantine regulations against the introduction of Trypanosomiasis into a noninfected country, a safe but hardly justifiable procedure would be to forbid the entrance of any animals from an infected port, as was so promptly done by the United States against the Philippine Islands when the disease was first reported here. Whether our home country enforces the same stringent laws against all others infected with Trypanosomiasis and against all animals which have been in infected countries but are shipped to America from noninfected ports, can not, without full knowledge of the quarantine laws, be stated, but, granting this to be so, there still remain reasons for stating that there must be forces other than quarantine laws which prevent the introduction of Trypanosomiasis into the United States. Wild animals for circuses and other purposes are certainly admitted in considerable numbers from infected countries,, and when we consider the fact that many of these animals harbor the parasite without inconvenience, the introduction of the infecting agent into America at some time or other seems very probable. Not alone quarantine laws, but other factors, such as possibly conditions of temperature, moisture, and carrying agents, probably play a part in preventing the spread of the disease.

However, Trypanosomiasis has gained admission to the Philippine Islands, and so far as we are concerned, there is no need of discussing the quarantine laws necessary to prevent infection in a virgin country. It would have been entirely feasible, as is shown by accumulated experience, to have prevented the introduction of the disease into the Philippine Islands with its subsequent disastrous results by the enforcement of proper quarantine regulations without actually prohibiting the importation of animals. That this was not done is owing to the fact that the disease was not recognized until after its introduction and to our inexperience in dealing with tropical conditions, but it would appear in place to sound a note of warning to other countries, especially those within the geographically infected zone, and which are as yet without the disease. It is a question of economic importance second to none in a large area of the world, and deserves the closest attention and prompt action of the sanitary guardians of the public welfare.

In framing quarantine laws particular attention should be paid to circus animals and to wild animals in general.

It has already been shown in discussing the etiology and modes of transmission of the disease, that every case of infection is entirely dependent upon exposure to biting insects, and that this brings us in the outset face to face with the necessity of (1) *destroying all infected animals,* (2) *destroying biting insects,* (3) *employing a combination of these methods, or* (4) *rendering susceptible animals immune.*

Before beginning a discussion of these points, we shall review somewhat fully the recommendations of Voges, of South America, and Schat, of Java, who have written in detail upon this subject.

Voges considers preventive measures under two headings—general means and specific means. The burning of cadavers need no longer be recommended, since we know that twenty-four hours after death the tissues and fluids are no longer infectious. It is sufficient to protect the bodies from biting insects during twenty-four hours. When the disease breaks out in pastures, the animals should be transferred to high dry grounds, and those already infected should be killed. Animals should not be allowed to run at large, but should be kept in stalls; and especially valuable ones may be protected from biting flies by screens.

Voges compares mal de caderas to malaria in the manner of its spread, etc., and suggests preventive measures along the lines used for the latter. He states that there are two methods of preventing malaria, that of the Italian school, which bases its work upon the destruction of the intermediate host, and the other, that of the German school, as recommended by Koch. Continuing, he writes as follows:

Quite different is Koch's system, which strikes the evil at its roots. Koch fights the cause of the disease, the plasmodium; he seeks to remove it, and in effecting his purpose does essentially nothing different from what has been done with considerable success in other infectious diseases.

If I am working in the laboratory with a culture and wish to transmit it, I use a platinum point. If the platinum point is taken away from me, for the time being I can make no inoculations, for I must first make a new point. If, on the other hand, my cultures are taken away from me and every crack and corner where these might be is ransacked and I am deprived of every possible opportunity to make a new culture, then my inoculations are at an end and I can not proceed with them even with the best of points.

I always use this illustration when I wish to explain Koch's malaria theory. In malaria the mosquito serves as the point; and I no sooner kill thousands of them, than hundreds of thousands again appear.

The reagent glass, the holder of the culture, is the person; the nourishment (agar, bouillon, etc.) is the blood. R. Koch puts into the reagent glass—the human being—a disinfectant, quinine, and the culture is destroyed. If, then, I disinfect everybody who has been inoculated with the virus of malaria, all the cultures are destroyed, and no matter how much virus (blood) the point (mosquito) takes from the reagent glass (human being), the transmission of the disease is no longer possible. Could anything be simpler and at the same time more effective? Is it not, therefore, an outrage and a shame that even in our day civilized nations place their hands in their laps, at the most raising themselves to a few efforts, while they allow their subjects to die before their eyes?

Should not Koch's results, then, be applicable to mal de caderas? We know that the blood of horses suffering with mal de caderas harbors parasites. We know further that the infection is transmitted only through the bite of a blood-sucking insect. We also know that the infection occurs during times of rain and flood. And finally, we know that the virus maintains its vitality in horses for from two to five months and in donkeys and mules as long as one year, and can nearly always be detected during this time.

In malaria the conditions are such that we must seek the proper host in the human being, and in the mosquito the intermediate host. In the human being the virus maintains its vitality for years, but in the mosquito only a short time. Evidently the conditions are very similar in mal de caderas. We have not yet discovered the intermediate host, but we presume that it is a blood-sucking insect, while the horse is the proper host. I draw this conclusion from the fact that in the case of the horse, and especially in that of the donkey and mule, sick animals are found throughout the year. Virus can be obtained at all seasons, although the disease occurs periodically, a fact which can be attributed only to the periodical appearance of the intermediate host (insect). With a knowledge of the intermediate host this would be still more evident, but for our object we really do not need this. Its periodical appearance is one of the most favorable preliminary conditions possible for a successful fight against the epidemic.

We shall next state that there are certain periods, dependent upon the rains, during which the transmission of the disease through the intermediate host does not occur. The virus exists then only in the proper host. * * * The rainless season is the period of which we should take advantage to destroy the *Trypanosoma*, for it is then that their distribution is most confined.

For our purpose we need only two things—first, a means of detecting the presence of the *Trypanosoma*, and, secondly, a disinfectant with which to destroy them. The second thing we do not yet possess, at least not one that will work in the same manner as quinine does in malaria. There remains only one possible solution, that is to destroy the *Trypanosoma* cultures; in other words, to kill the diseased horses.

This measure is radical and yet very practicable, for such horses are of no value, and this is almost universally true with native horses, for when once sick a horse may as well be considered lost, and it is useless to continue feeding him. Thus, if we have killed all the diseased horses, mules, and donkeys during the season which is free from the epidemic, when, with the beginning of the rainy season, the intermediate hosts return, there will be no more *Trypanosoma*, and the disease will at once have been stamped out, just as Koch exterminated malaria by poisoning the plasmodia with quinine. This is not only possible but absolutely certain. It depends on searching out all the animals having *Trypanosoma*. If the rainy season were longer, most of the animals affected with mal de caderas, at least horses, would die. Donkeys and mules, however, would continue to live; but they show signs of weakness so early that it would be easy to pick them out and render them harmless.

Kimmerich, according to Voges, successfully combated the disease on his estate by converting the marshy regions into open ponds. He considered running water harmless. A South American company using a large number of horses lost annually the larger part of them for two years, the animals being kept in the fields, as is the custom there. Stalls were then built and the horses were kept and fed in them, as a result of which the epidemic disappeared. If infected herds are removed to high, dry grounds, the disease generally ceases. Horses quartered in stalls seldom contract it. The influence of stalling animals on the suppression of the infection is mentioned also by writers in India and Africa.

So far as we have been able to determine, Java is the only country which has adopted and enforced regulations for the suppression of the

infection, and as a result the disease is well under control in that country.

Referring to the statement that it is impossible to destroy biting insects, Schat (Java) says:

It is the opinion of Voges that blood-sucking insects are the carriers of the infection, but he has not proved it, probably because he considers the destruction of the insects as impracticable. Contrary to his opinion, we think it both desirable and possible to do so, nor is the measure to be left out of consideration. To search out all the hosts, that is the animals suffering with chronic surra, is, in the Tropics, where sufficient expert assistance is lacking, not yet entirely feasible; the more so, since Dr. Bruce, of South Africa, has found that the tsétsé fly may become infected by sucking the blood of wild animals. The detection and destruction of all infected animals is therefore under the circumstances almost impossible in the Tropics. We should look for other measures, such as to insure the coöperation of the owners of cattle and in general of all laymen; we should make warfare on all flies found on horses and cattle.

In the prevention of an epidemic of surra by veterinary means, the three following measures should, in our opinion, be particularly observed.

1. Limit the extent of influence of the flies which carry the infection.

2. Protect the sick as well as the healthy animals from the bites of flies in places infected with the disease.

3. Destroy the hosts, that is the diseased animals, or else render them harmless.

These measures alone should have a good chance of success, if the following rule of preventing the spread of an infectious disease at its first appearance is observed. The rule may be given as follows: Whenever an infectious disease appears, the cases of sicknes sand death should be reported as soon as possible. This applies to all infectious diseases in general, but it is particularly necessary in the case of surra, because its detection is often difficult and requires a great deal of time.

Let us now, with special reference to surra, discuss the three above-mentioned measures one by one and with more detail.

First measure.—To limit the extent of influence of the flies which carry the infection. Whenever a case of surra is determined by the clinical symptoms or by the discovery of *Trypanosoma* in an examination of the blood, or by animal experiment, the sick animal should first of all be isolated, or killed and buried. The animals which are kept on the same ground, as suspects, should not be transferred to any other place. In this way a spread of the disease as well as of the flies found on the animals will be prevented; for, as is known, flies swarm with horses and cattle when they are quickly removed.

For the purpose of making it as certain as possible that no infected flies shall be transferred to other places in this manner, the transfer of cattle from grounds bordering on those where surra has been discovered should be forbidden. This measure may, according to the circumstances, be extended to the entire inhabited part of a district or to a portion of it. In short we would recommend the prohibition of the importation, exportation, and transference of cattle, etc., in the inhabited part of a whole district or in portions of it.

Second measure.—To try to protect the sick as well as the sound animals against the bits of flies.

The sick and the healthy animals should be separated as quickly as possible and transferred to dark, spacious, well-ventilated stalls, since experience proves that in dark places few, if any, flies are found.

This precaution the inland cattle owner can take without great trouble.

Furthermore, the greatest cleanliness should be observed in the stalls, although this would appear to be very difficult in the villages here, even with the greatest perseverance. The fecal matter should immediately be removed and collected in one place, not too close to the cattle stalls, in order to combat not only the flies but also the larvæ; we know that the larvæ of the *Stomoxys* live mostly in manure, where they develop into a light reddish-brown chrysalis, from which after from four to six weeks the young fly appears.

It might perhaps be recommended that the leaves, pieces of wood, etc., found on the spot where a case has occurred be collected and burned. This should be done in the morning, on the wind side of the kraal, so that the smoke will drive away the flies, which appear on the animals just at this time of the day, in order to suck themselves full of blood.

Whenever, in the rainy season, the smoking of the stalls in this manner becomes difficult or impossible, the same purpose may be accomplished by placing earthen or iron pans in them, burning damp wood, leaves, etc., in the containers; the cattle owner may also easily make use of ash-water, with which he will be able to keep the flies from his cattle. In catching flies the inlander can without much trouble make use of sticky twigs, there will always be found on his ground a plant which produces one or another kind of gum or other viscous substance (getah). Getah, mixed with some kind of a treacle (tétés), smeared on a piece of paper or stick of wood and hung up in the cattle stall, serves the purpose very well.

Third measure.—To destroy or render harmless the hosts of the infection, i. e., the sick animals. * * *

Thus far we are obliged to resort to * * * a very radical measure, that of destroying the infectious material in as short a time as possible, i. e., killing the sick animals.

On the outbreak of an epidemic of surra, so long as another and less costly measure is wanting, authority should be requested from the head of the provincial government to take possession of animals sick with the disease and to kill them, in the hope of checking its spread from the very beginning. If, however, too large a proportion of the animals have become infected, so harsh a measure could hardly be carried out; but we would suggest in that event that the spread of the infection may to a large extent be prevented by a strict isolation of animals in spacious, dark stalls, where great cleanliness is observed.

I wish also to call attention to the following point. In the blood of emaciated animals we repeatedly found *Trypanosoma*, while clinically individuals suffer with emaciation for a considerable time, without showing, however, any other single definite symptom. It is just these animals from which a spread of the disease through flies should be feared, since we have been able to determine that whenever such chronic sufferers from surra die their blood contains large quantities of parasites. In the eradication as well as in the prevention of surra it is therefore of great importance to know this fact, in order that the emaciated animals in the district may be looked after. Since this is so and since in the examination of the blood of these animals surra parasites appear to be present, these hosts of the infection should first of all be rendered harmless.

Our purpose is only to put these rules in such a form that they may best be applied to the purpose in view, that is the prevention of surra.

Some of the earlier recommendations for the suppression of the epidemic in the Philippine Islands were not only unsatisfactory but dangerous. Smith recommended isolation of sick animals at a distance of one-half mile.

Curry, in his original communication, recommended (1) the isolation (at least one-half mole) of infected animals, (2) the protection of infected animals from flies, (3) the protection of healthy animals, and (4) the keeping of flies out of the stables.

However, early in 1902 proper advice in regard to measures for the control of the epidemic were prepared by the Director of the Biological Laboratory and given to the public in a popular article in the Spanish press. In a later publication Curry realized fully the weakness of his first recommendations, and made additional suggestions. Had the directions of both these observers been followed at that time, the saving of millions of dollars to the country would have resulted. In substance these were the destruction of all infected animals and of as many flies as possible, and the protection of healthy animals.

Considerable delay in carrying out rules which will control the infection here has been occasioned by the efforts of some to minimize the importance of the agency which flies constitute in the transmission of the disease and to push forward the untenable *theory* that food and water are the principal transmitting agents.

Misguided local efforts have been made in communities, causing unnecessary expense and trouble and utterly failing to accomplish the purpose for which they were intended. Several municipalities have absolutely forbidden the use of native food for animals and have promulgated long, useless rules for isolation, etc.

A set of rules which was adopted by one of the provincial boards of health and which was sent to us for remarks is as follows:

1. All sick horses must be isolated to a pasture separate from the rest of the herd.
2. Inspections must be made daily and sick horses transferred to isolated pastures.
3. The bodies of dead horses must be burned or buried in trenches at least ten feet in depth.
4. Those who attend to diseased horses must not take care of other horses.
5. No efforts must be made to preserve the hides of diseased horses, for their sale will not be permitted.
6. The pasture used for diseased horses shall not be used for other horses or cattle for a period of two years after the epidemic.
7. Diseased horses shall not be watered in running streams, nor shall they be bathed in streams or rivers used for other horses.

Of course such rules need no comment. They show, on the other hand, that the intelligent element of the country is aroused to the necessity of doing something, and not knowing just what is best, follows out the dangerous suggestions of some of the earlier writers in regard to the epidemic in these Islands. These are, however, in substance, the antiquated ones of literature. In the face of all this, it behooves us to reach the root of this subject for the information of the better classes and to suggest regulations

which will place the execution of efficient measures in the hands of the proper officials.

We have already dealt with the methods for preventing infection in a virgin country and reinfection in countries where the disease is already prevalent, and will now take up the discussion of methods looking to the control and suppression of surra in our own country. To be fully efficient recommendations must, of course, be practicable and of such a nature that the coöperation of the public may be obtained. The necessary considerations are:

1. The destruction of all infected animals; (*a*) animals of economic importance; (*b*) rats and mice; (*c*) game and other wild animals.
2. The destruction of biting insects.
3. The protection of contact animals from flies during the incubation period.
4. Miscellaneous measures.

First. The destruction of all infected animals would make other measures unnecessary, but this offers so many difficulties, especially in the provinces and outlying districts, that it will be found advisable to reinforce this measure by the other methods discussed.

(*a*) *Animals of economic importance.*—In Manila and other cities with organized sanitary corps, diseased animals should be located without any difficulty. To do this to the best advantage and to make the work systematic necessitates that the whole matter be placed in the hands of a single bureau, and that bureau should, of course, be the Insular Board of Health. Other points in the accomplishment of this task are matters of detail, which may readily be solved by the Board of Health. There can be no question that this matter properly belongs under the control of the sanitary bureau, just as do the infectious diseases of man. In fact, as already shown, there have been many cases of *trypanosomiasis* in man and the chances are that many more will be found.

The work of detecting all diseased animals will necessitate some kind of a systematic inspection, which may easily be carried out in Manila and other cities by those charged with such duties in guarding the public welfare. In addition to the daily inspection by sanitary inspectors of all horses found in stables, all other officials, such as medical, veterinary, and police officers, might be required to report all sick animals coming under their cognizance to an official of the board of health.

How best to secure the coöperation of the general public in reporting sick animals is a problem open for discussion. Several officials interested in this work have suggested the advisability of the Government's buying all sick animals, arguing that a reasonable offer would cause all such to be brought in and thus prove economical in the end, whereas, if coercion were attempted, the more ignorant people would hide their animals for days and probably for weeks before they could be found by the authorities, thus adding materially to the spread of the disease. This argument has

something in its favor, but it seems to us on the whole a dangerous policy—the purchase of good citizenship—which, although it might give immediate results of a temporary nature, would in the end prove unsatisfactory. The purchase of superstitution or malice, whether it be with candy in the case of children or with money in that of adults and whether in the schoolroom or in the municipal office, invariably leads to disaster.

It appears to us that the recommendations made should be just and equible, and such as will be supported by the intelligent part of the community and in the end will result in the elevation of the standard of citizenship of the ignorant. Undoubtedly right *demands* the coöperation of the public in such an undertaking, and we believe that the law should require owners, agents, and custodians of animals to report those sick, and that the failure to do so should be punishable by law.

The manner and time of inspections and the reporting of sick animals in cities are matters of detail which need no discussion here, while rules applicable to the provinces and outlying districts may be drawn up to meet conditions. The methods best adapted for searching out the infected animals may be subject to discussion, but the disposition of them when once found does not admit of argument. *There is only one thing to do with a horse suffering from trypanosomiasis, and that is to destroy him immediately.* To do this efficiently and quickly necessitates the placing of authority in such a manner as to avoid the loss of time.

Immediately after the death or destruction of an animal suffering from this disease, the body should be protected from flies and other insects and disposed of as soon as possible. This may be done in one of several ways. In cities probably the most satisfactory way is to take the body to the crematory in a fly-proof wagon and have it burned at once. Where means for such disposition are not at hand, which is generally the case in rural districts, the body may be buried at a sufficient depth to keep dogs and flies away from the carcass for forty-eight hours, or it may simply be protected by mosquito netting or otherwise for the same length of time, and then disposed of in any sanitary manner.

It is well to call attention to the care which should be exercised in performing necropsies on animals dead of the disease. They should either be done under protection from flies, or, if this is not practicable, all living animals should be removed from the immediate vicinity and kept away for forty-eight hours. In any event, the blood, organs, etc., should be protected from flies and dogs, in the same manner as the whole body, for from twenty-four to forty-eight hours.

(*b*) *Destruction of rats.*—There is no longer any doubt that a certain number of these pests harbor *Tr. evansii* and that they have a practical significance in the spread of the disease. The annual destruction of thousands of them in Manila on account of the plague, as already mentioned, will no doubt reduce the danger of the spread of surra from this cause to a minimum. In the provinces and other cities, however, where this

wholesale destruction is not carried on, the importance of looking after this work with special reference to surra is more urgent.

Fortunately, whether in the city or in the country, great difficulty is rarely experienced in destroying large numbers of rats by poisoning, and it is recommended that such a procedure be carried out as a matter of routine in methods adopted for the control of the disease under discussion.

(*c*) *Destruction of game and other wild animals.*—In other countries the spread and perpetuation of the infection is undoubtedly carried on by wild animals, and if our work in stamping out the infection here is not prompt and vigorous it will in all probability become one of the conditions that we shall have to face here later on, if it does not already exist to a limited extent. This is a matter to be kept constantly in mind in dealing with this disease, and our plans might well be broad enough to cover this point. This source of danger will, even under the most favorable conditions, rarely become a great menace in cities, but some precautions are nevertheless necessary.

A law which will prevent the reinfection of the country by such animals is of the highest importance. With the prohibition of the admission of circus and other wild animals, except under certain regulated conditions, there still remain for consideration the public animals of our parks. While the disease is constantly prevalent in Manila there is nothing to prevent some of the animals in the Zoological Garden from contracting it, and, on account of the harmlessness of the infection of these animals, they might become an indefinite focus for the diffusion of the disease. It seems to us that the easiest and most practical way of avoiding this danger would be to inclose all such animals in fly and mosquito proof screened areas, as is now being done in many of the large zoological gardens in other countries. Researches of recent years have shown the necessity of this precaution, since many wild animals act as hosts for other parasitic diseases communicable to man, which need not here be discussed.

2. *Destruction of stinging and biting insects.*—As has already been stated, if the destruction of infected animals (the hosts) were carried out systematically and with thoroughness, flies and other insects as carriers of the infection would be harmless. While we have sacrificed the ideal in the disposition of infected animals to the practical, as far as possible within the limits of efficiency, we fully realize that conditions may make still further sacrifices necessary. It is principally for this reason that we have taken up the consideration of auxiliary measures to supply what may necessarily be lost in the efficiency of the more desirable ones.

Insects are becoming of so much importance in the propagation of other diseases, both of man and of animals, especially in the Tropics, that we are urged to recommend their partial destruction on account of surra with more assurance, knowing that the fulfillment of our hopes would be a distinct step in advance in preventive medicine in general.

To illustrate what we shall some day be compelled to face here, the best medical thought of Europe and America is already concerning itself with the effect which fast travel to the Orient is likely to have upon the introduction of yellow fever to this part of the world. The proposed interoceanic canal has brought this subject afresh before the world. The mosquito of yellow fever is one of the most common in the Philippine Islands, and with the shortening of the voyage from fever-infected countries by the proposed canal, and for that matter without the canal by the increased speed of our modern ocean-going vessels, the time required to travel from those countries to the Orient will be brought within the limit in which the disease may be transmitted. Without dealing further with present and prospective problems, depending to a certain extent upon the disposition of certain insects for their solution, we shall resume the discussion in hand.

The most important insects to be destroyed because of the part they play in carrying surra are the biting flies. To accomplish this, in the most extensive manner and with the least amount of work, resolves itself into the destruction of their breeding places by the proper disposition of fecal matter. As has been recommended by various writers, this may best be done by burning all offal during the dry season. Methods upon a smaller scale looking to the same end are too well known to need discussion here. Cleanliness around livery stables and large corrals belonging to the Government and to other persons is particularly desirable, because it is naturally in such places that the danger is the greatest on account of the close proximity of the animals and the large number of flies usually found there.

Recommendations and methods for the destruction of mosquitoes are so recent and so well known that this part of the subject may be omitted.

The destruction of fleas, which are second in importance to flies in the transmission of surra, is so far as we are informed an unsolved problem.

3. *Treatment of contact animals.*—The blood of an infected animal is infectious before the symptons are present or parasites found in the blood by microscopic examination, so that the necessity of protecting contact animals during the incubation period of the disease is evident.

There are several ways of accomplishing this. When surra is found in a stable, contact animals should be quarantined where they are, for at least seven days. The contact horse, after removal, should be protected from flies during the first forty-eight hours, and if several are present they should be protected from each other. Where there are only one or two contact animals, they may be protected by mosquito bars, by smearing with iodoform ointment, washing with solution of creolin, burning smudges in the stables, or by other well-known means. Where there is a large number, as in a livery stable, it will be found easier to destroy or remove the flies by smudges, darkening of the stalls, etc.

All rats around such places should be poisoned and the general sanitation, especially with reference to breeding insects, should be improved.

Temperatures of all such contact animals should of course be taken twice daily during the incubation period, and the animals should be carefully examined for other symptons. It is hardly necessary to repeat here that as soon as an infected animal is found it should be destroyed.

4. *Miscellaneous measures.*—Musgrave and Williamson, in a preliminary report, offered the following suggestions to owners of private stables or individual horses:

When using the animals in the daytime, as much as possible avoid allowing a horse to stand in a group of other horses. To illustrate: Only a few days ago we observed standing in front of a Government building some thirty or forty horses, and one of them, hitched to a public carromata, had a well-advanced case of Trypanosomiasis. Should such a thing happen during the season of biting flies, the danger of infection to all would be very great.

Stables should be kept scrupulously clean and well ventilated and excreta and waste should be promptly removed.

All sores of whatever character on horses should be kept covered with a suitable ointment to keep off the flies.

Especially valuable horses may be provided with screened stalls.

There is no conclusive evidence, so far as Trypanosomiasis is concerned, of any danger from allowing horses to drink the city water or to eat food supplied in the Manila market.

Upon the appearance of illness in a horse, a competent observer should be asked to examine the animal.

All kinds of sores on animals should be kept covered with tar, iodoform ointment, or some other substance disagreeable to insects. The legs and edges of the hoofs should be carefully looked after. Rats should be kept away from stables by systematic poisoning or should be caught with traps. Other little points worth looking after will suggest themselves to the thoughful mind.

That from which the public in general will derive the greatest benefit and which will give results to every stock owner is the moral support of the officials entrusted with the handling of this problem.

XV. SERUM THERAPY.

In this day of scientific advance in medicine, the trained mind naturally turns to the possibility of preparing prophylactic or curative sera for disease, and as all other remedial measures have proved a failure in surra, this seems to be the only hope. Considerable work in this direction has been done during the past few years, and while as yet not successful, the outlook is not altogether discouraging.

Koch professed to have established a successful method of preventive inoculation based upon the attenuation of the parasites by succesive passages through other animals. His experiments are given as follows:

On the 8th of September, 1897, there were inoculated with the defibrinated blood of an ox, rich in *Trypanosoma*, the following animals: One ass of Massai,

1 cow, 2 calves, 2 monkeys, 2 guinea pigs, 2 rats, and 1 dog. The ass of Massai, the monkeys, and the guinea pigs remained in good health; no sign of infection was observed in them. The cow died at the end of thirty-nine days, the calves at the end of forty-one and forty-nine days, the rats at the end of thirty-four and fifty-two days, and the dog at the end of nineteen days.

On the 15th of October, 1897, the blood of one of the rats inoculated on the 6th of September was injected into 2 rats and 1 dog. One of these rats was found dead six days after inoculation, showing the appearance of *Trypanosoma* in the blood; the second rat showed *Trypanosoma* thirteen days after inoculation, but did not die until sixty-eight days thereafter. The dog died at the end of forty-two days, and its blood was utilized for the third passage.

On the 30th of October there were inoculated with the blood of the dog 2 dogs, 2 oxen, 4 asses of Massai, and 3 rats. The dogs died after nineteen and twenty-six days, the rats at the end of sixty-seven, seventy-three, and eighty days, and the asses were not infected.

Laveran and Mesnil criticise Koch's work, stating that a certain percentage of cows are known to recover from both nagana and surra and that the attenuation of *Trypanosoma* by successive passages through different species of animals is very slight.

Nocard immunized a calf that had recovered from nagana with increasing doses of virulent blood until it had received 850 c. c. in all. The animal was then proved free from infection by animal experiment, but its serum had neither preventive nor curative properties in mice, and mixed with infected blood produced the disease with a prolonged incubation. This serum was very agglutinative for *Trypanosoma.*

Rost gave a pony sick with surra 10 drops of normal goat blood subcutaneously, and 10 more drops four days afterwards in the same manner. A temporary dimunition of the parasites and a fall of the temperature followed each injection.

Another pony, which had the disease in an advanced form, was given 20 drops of mule's blood by subcutaneous injection. The parasites temporarily disappeared, but returned in greater numbers, and the animal died on the fifth day after inoculation.

Another pony infected with surra and the blood of which was rich in *Trypanosoma* was given subcutaneously 30 drops of the blood of a goat which had recovered from a single injection of surra blood. The parasites temporarily disappeared. Another injection was given on the twenty-third day and a temporary disappearance of the parasites again resulted. On the twenty-eighth the parasites were again numerous; and another dose of goat serum, which had been highly fortified by injections of surra blood, was given, followed by another fall of temperature and the permanent disappearance of the parasites. The animal continued to grow fat, but on the twenty-third day after the last injection the temperature again rose and death finally occurred from tuberculosis.

Sterilized filtered goat serum caused a temporary disappearance of the *Trypanosoma* in a horse sick with surra, but the disease followed

its regular course and the animal was shot before death. Ten mules were treated with serum without encouraging results; in fact, the contrary was true, for Rost concluded that the sterilized serum of immunized goats produced exacerbations of the disease in mules.

His best results were obtained from normal or slightly fortified goat's serum, for the more highly he immunized his goats the worse were the results obtained. He immunized a goat with surra blood taken from the same species of animals which he afterwards treated with the serum, and during a period of eight days he sterilized it daily for four hours at 57° C. He says that the immunized goat's serum killed surra parasites under the microscope.

Voges inoculated a cow for eighteen successive months with virulent blood, but the serum obtained from the animal was worthless either as a preventive or curative measure.

In Schat's work the serum obtained from cows which had recovered from surra was injected into other cattle and into rabbits, and in some cases it seemed to exercise certain preventive and curative influences on the disease.

He immunized a cow against *Trypanosoma* by increasing doses of defibrinated blood during a period of two months. The serum obtained from this cow was injected in doses of 10 c. c. into two calves known to be nonimmune. Twenty-four hours after the last injection of serum the animals were inoculated with surra blood; a control was inoculated at the same time. On the sixth day parasites appeared in the blood of all the three animals, disappearing from that of the immunized calves at the end of four days and from the control at the end of five days. The protected calves returned to health, but parasites again appeared in the case of the control and the latter went through the regular course of the disease.

A rabbit was protected by 5 c. c. of the same serum, with only a temporary appearance of the parasites. Three rabbits were inoculated with mixtures of cow's serum and blood containing *Trypanosoma*. One of them developed the disease, while the other two, where the mixture was kept from five to fifteen minutes before injection, did not contract the disease.

Laveran and Mesnil, experimenting with mice and rats and a few dogs, state that human serum injected in sufficient quantities shows manifest action on the disease. *Trypanosoma* disappear from the blood at least temporarily, the evolution of the disease is retarded, and sometimes a complete cure results in the case of mice and rats. The serum of adults is more active than that of children, and maintains its activity for a considerable time when preserved aseptically. Pleural effusions are less active than the serum from the blood, while the activity of ascetic fluid is still less. In infected mice they used doses of 0.5 to 1 c. c. and

in rats doses of 1 to 2 c. c., which caused a disappearance of the parasites in eighteen to twenty-four hours after infection.

They had four successful cures out of a very large number of rats and mice so treated, and in all of these cases it was obtained after one or two injections. In those animals from the blood of which the parasites disappeared only temporarily, they were caused to disappear time after time by repeating the injection, and if they recurred after the first injection a complete cure was never produced.

By alternating the injections of human serum with arsenic the influence exercised on the longevity of animals was still more favorable, but there were no complete cures. One rat so treated lived for one hundred and twenty-seven days and a mouse for one hundred and three days.

Human serum was determined to be just as active for mal de caderas as for nagana, but *Tr. lewisii* were unaffected by the treatment. The sera of birds, chickens, and geese highly fortified with *Trypanosoma* blood had no curative power. Large numbers of sheep, cows, and deer recover from nagana, but their sera fail to show either preventive or curative properties, and do not acquire them when immune animals are further protected by large doses of virulent blood.

According to these authors, sheep, deer, and cattle which have recovered from nagana possess an active immunity to this disease.

Human serum has a very weak preventive power. Mice given 1 c. c. of blood mixed with 4 c. c. of human serum show no infection. Sometimes this result may be obtained by injecting serum and blood simultaneously in different parts of the body. If, however, the serum is given twenty-four hours after the virulent blood, the disease appears, the only result noticed being an increase of from five to nine days in the length of the incubation period. If human serum is injected first and infected blood twenty-four hours later, the infection, as before, takes place with a prolonged incubation. In those mammals which do not contract the disease by the injection of human serum and infected blood an active immunity is established.

The sera of dogs, sheep, deer, horses, geese, and chickens, when mixed with Trypanosomatic blood, are still infectious and the disease runs the regular course with a normal incubation. The sera of animals that have recovered from nagana are without value as either preventive or curative agents in the disease. The serum of sheep which have recovered from nagana and have afterwards been further immunized shows neither preventive nor curative properties. Fortified sera from the chicken and the goose are worthless as a means of prevention. Chicken's serum mixed with equal parts of infected blood killed a mouse in fifteen days, while a control lived seven days.

Strong, commenting on Laveran and Mesnil's earlier work, writes:

> We had already previously tried injections of human blood into monkeys suffering from experimentally produced Trypanosomiasis from injections of *Tr.*

evansii, but found, while the parasites disappeared temporarily, after a few days they were always again present in the circulating blood. Goat's blood and bile from monkeys that had died of the disease were also tried, but with like results. Goat's serum was used, as these animals are relatively immune to the parasite. Experiments with the intravenous injection of benzoyl-acetyl peroxide will be performed as soon as the animals for experimental purposes can be secured.

Laveran and Mesnil also showed that infected blood kept on ice or at the temperature of the room until the death of the parasites has almost resulted is still infectious, producing no change in the course or the duration of the disease excepting a prolongation of the incubation period. Similar results were obtained with blood heated to different temperatures for different periods of time. The addition of toluidin blue to infectious blood, in the proportion of 1 to 100 parts, did not modify the virulence, except to prolong the incubation.

They passed *Trypanosoma* through sheep six times and then through a dog, but the blood remained just as virulent for rats and mice as the original control. They failed to confirm Schilling's and Koch's work. The difference in action between their *Tr. brucei* and that of South Africa may be owing to the difference in species of the cattle or to an attenuation of their virus. They suggest the possibility of obtaining practical good by infecting the South African cattle with the milder *Tr. brucei,* from which a large percentage of Paris cattle recover.

Laveran and Mesnil come to the conclusion that all attempts at prevention or cure have, for practical purposes, been negative, and that prophylactic measures which may be found of service in one form of Trypanosomiasis will probably prove equally efficacious for all.

Schilling states that he had attempted to attenuante the parasites by passing them through different animals. He inoculated three horses with *Trypanosoma* which had passed through five dogs; they all contracted the disease and died. He then inoculated two horses with *Trypanosoma* after eight passages through dogs, as a result of which they both contracted the disease and died. Parasites which had been passed through four cows were still virulent for the horse.

In a second paper Schilling writes that he immunized a bull which had recovered from surra. Parasites were found in the blood from nine to twelve days after the first injection of 10 c. c., but none were found after the second of 19 c. c., which was given in the abdominal cavity a month later. A month after this injection the serum in thirty-one minutes killed the parasites in the hanging drop. Further immunization for two and one-half months did not make it more effective in vitro, and when employed in treatment it was useless. After about eight months the animal died of hemorrhagic enterocolitis, but *Trypanosoma* were not present.

Schilling simultaneously inoculated three calves with the peritoneal exudate of a dog which had been infected by an abdominal inoculation of

Trypanosoma after they had been passed through the peritoneum of other dogs. After twenty-one, twelve, and fifteen days, respectively, parasites were no longer found in these calves. The serum showed no reaction with *Trypanosoma*. These animals were then transferred to an infected region, one dying during transportation, while the other two were well at the end of three months.

The same author immunized a steer in a similar manner, except that as a first inoculation the peritoneal exudate of a dog inoculated directly from a horse was used, and a like injection was given sixteen days after the first. Five days after the first injection the serum showed no reaction with the *Trypanosoma,* but four days after the second one it agglutinated them, only a few motile ones being left at the end of thirty minutes.

Two young steers were immunized with doses consisting of from 3 to 10 c. c. of the peritoneal exudate of dogs, which seven days before had been inoculated in the abdominal cavity with virulent blood. On the fourteenth and fifteenth days after the last injection the serum of both these steers showed marked antiparasitic action on the *Trypanosoma,* killing them in thirteen to twenty-five minutes. Parasites were absent in both of these animals.

Schilling later immunized thirty-six cattle with the peritoneal exudate of dogs which had been given intraperitoneal inoculations of *Trypanosoma* attenuated by passing them through seven dogs and rats and then through eighteen to twenty-one dogs. The peritoneal exudate of dogs used on cattle always showed numerous *Trypanosoma.*

Of twenty-four cattle twelve showed parasites in the blood on the tenth day after inoculation. The number in all of these cases, however, was very small, and in ten animals they disappeared in from one to two days. In one out of nine cows one *Trypanosoma* was found in a preparation made on the ninth day after the second inoculation, while the others were negative. The temperature rose to 40.3° C. on the fifth day after the first injection in the case of one of these animals, but it fell to normal within three days. On the same day a single parasite was seen, but after that none were to be found; indeed, following the second injection of large numbers of *Trypanosoma* the temperature remained normal and parasites were constantly absent from the blood.

Eight of the animals previously used were examined (subsequently to the last injection) to determine the parasiticidal power of the blood serum. In five cases the parasites were killed in twenty minutes, in one the reaction was very weak, while in two there was no reaction whatever. What the factors in the production of such differences were he could not then say, because of the limited time and the small amount of material at his disposal. He believed, however, that the cause lay neither in the quantity of injected parasites nor in the time which had elapsed between the first and second inoculations.

Of the animals used 19 remained in Sokode, 9 were taken to the station of Ataxpane, and 8 to Mishche and the experimental station of the cotton expedition of the Colonial Scientific Committee in Tove—all places at which, during the year before, animals had died of surra. According to reports, at the beginning of October the inoculated animals were well and in Tove five oxen were doing their usual work in the fields. The time had not been sufficiently extended for him to come to any definite conclusions.

In Sokode Schilling found a naturally infected ass, which he watched for twenty-five days. It has already been stated that the ass of Soudan is susceptible to surra. Attention should here be called to the fact that there are some racial differences between these asses and those of east Africa, with which Koch worked and which he did not succeed in infecting. In one of his experiments, however, the inoculation of surra blood into a small wound in the skin of the ear proved negative. Passages of blood taken from the naturally infected animals mentioned above were made through several asses by the subcutaneous injection of large doses. Altogether five animals died between the eleventh and fifteenth days after inoculation, with all the symptoms of a severe general infection (fever of remittent type.) Post-mortem showed nothing that might be called typical. The parasites increased very rapidly (incubation about four days), reaching enormous numbers. From this we may conclude that the Soudan ass is even more susceptible than the horse.

This writer inoculated the parasites obtained after passages through five asses into a small, healthy horse. The animal suffered an acute attack of surra, but the course was somewhat unusual. According to a letter received from Dr. Kersting, the animal was fairly well on the twenty-first day after inoculation. On the eighteenth day no parasites could be found.

He believed that the principle of successfully immunizing animals against the African tsétsé-fly disease (nagana) had been discovered. The peculiarities of the nágana parasite with reference to its ever-present host were utilized in weakening its virulence for certain kinds of animals.

In looking over literature carefully one is struck by the relative immunity to surra of certain animals that are susceptible to other diseases.

Mr. Harford, British consul to the Philippine Islands, informs us that when he was stationed in Africa it was a recognized fact that "salted" animals were less susceptible to the bite of the tsétsé fly than others and that the Government paid increased prices for such animals for the African service. By "salted" horses are meant those that have recovered from a peculiar disease of horses prevalent in Africa and by "salted" cattle those that had recovered from rinderpest.

G. H. Evans, quoted by Lingard, says:

> The gaur (Indian bison) and tsaing suffer from rinderpest and foot-and-mouth disease, yet these animals have not up to the present time been observed with surra, although a careful search for the disease has been made. They live in

a jungle where the flies are so annoying to them that they have to go into the open to escape their attacks.

In India a large percentage of cattle are "salted"; that is, they have recovered from rinderpest or from the "serum simultaneous-inoculation method" against rinderpest, which, when successful, results in a mild attack of the disease.

These points and the fact that the injection of rinderpest blood into dogs prolongs the incubation period somewhat suggest a possible antipathy between surra and rinderpest. We have performed a number of experiments fully to determine this matter and have come to the conclusion that animals suffering from rinderpest or recovered from it are just as susceptible to surra as others.

The attempts of Schilling, Koch, and others to attenuate the parasites by methods already described, in which they believe they have succeeded, have been repeated by us, but we have been unable to verify their conclusions. In fact, we have failed to attenuate *Trypanosoma* by any of the methods employed. Attempts of all conceivable kinds have been made to immunize animals, but usually without success.

In the beginning of our work, when we were less familiar with our subject, we believed that we had immunized a goat, because parasites could not be found in the blood, but it was later discovered that the blood was infectious by inoculation.

We have succeeded in bringing a cow up to the point where the injection of 3,000 c. c. of blood produced but little effect, although it contained large numbers of *Trypanosoma*. This animal was infected and ran a chronic course after the first injection of 10 c. c., and the blood remained infectious until about one month after the last injection of 3,000 c. c.; but since that time, now three months, the blood of this animal has not been infectious by inoculation, and it has fattened and appears to be in perfect health. Serum taken from this cow at different times has been absolutely valueless either as preventive or curative in several species of animals.

Similar negative results have attended all our extensive work. We have followed the suggestions of others and have conducted many original experiments, but we have had no results which seem to offer hope for either a preventive or a curative serum.

XVI. TREATMENT.

Many drugs have been used in attempts to cure this disease, but so far without results offering any hope for future work along this line.

Braid, in a letter written in 1858 to the British Medical Journal, suggested the use of one to two grains of arsenic daily in cattle suffering

from the bite of the tsétsé fly. This letter was called to the attention of Dr. Livingstone and he agreed to follow out the suggestion at the next opportunity.

In a letter to the British Medical Journal, published March 13, 1858, Balfour indorses Braid's suggestion as to the use of arsenic but recommends Fowler's solution as a more desirable preparation, provided it is used in large doses.

Referring to the letters mentioned, Livingstone himself writes in the British Medical Journal, May 1, 1858, as follows:

> The very same idea with respect to the employment of arsenic in the disease which follows the bite of the tsétsé occurred to my own mind about the year 1847 or 1848. A mare belonging to Mr. Gordon Cumming was brought to Kolobong, after prolonged exposure to the bite of the insect; and, as it was unable to proceed on the journey southward, its owner left it to die. I gave it 2 grains of arsenic in a little barley daily for about a week, when an eruption resembling smallpox occurred. This induced me to discontinue the medicine, and when the eruption disappeared the animal's coat became so smooth and glossy that I imagined that I had cured the complaint; for, after the bite is inflicted, the coat stares as if the animal were cold.
>
> The mare, though apparently cured, continued lean. This I was rather glad of, as it is well known between the latitudes of 20° to 27° south that, when a horse becomes fat, he is almost sure to be cut off by a species of pneumonia commonly called "horse sickness." About two months after this apparent cure, the coat began to stare again; but this time it had remarkable harshness and dryness. I tried the arsenic again; but the mare became like a skeleton, and refused to touch the barley. When I tried to coax her, she turned her mild eye so imploringly, and so evidently meaning, "My dear fellow, I would rather die of the disease than of the doctor," that I could not force her. I got her lifted every morning to feed, and saw her at last perish through sheer exhaustion; and this was nearly six months after the bite was inflicted.

Since that time the treatment of Trypanosomiasis by arsenic has frequently been mentioned in literature. It has been given in various ways and in all reasonably sized doses, by mouth, subcutaneously, and intravenously. The pure acid as well as many of the salts have been used. Some writers mention its previous use in the treatment of the disease, while others, judging from their writings, thought that they were trying something new.

In a circular letter from the headquarters of the Division of the Philippines, as late as January 11, 1902, we read as follows:

> The board ordered to inquire into and to investigate the disease of animals called surra have found Fowler's solution of arsenic, given intravenously, to destroy the parasite in nearly every case, and animals so treated are doing well, but such treatment is not as yet conclusive as to cure.

Lingard has given minute directions for the use of arsenic to accomplish the best results. Some writers assert that arsenic delays the course of the disease and a few that cures may result, but the concensus of opinion is against this, and without doubt justly so. The statement that

arsenic destroys the parasite in circulation is without a particle of evidence to support it. That the parasite may not be found by microscopical examination after such an injection is true, but the same results are just as likely to happen after the injection of any other substance; or for that matter, it is occasionally difficult or even impossible to find the parasite for days at the time, when no treatment whatever has been given. However, it has been shown by others, and the observations have been confirmed by us, that the blood at this time is infectious when injected into susceptible animals, and that in such cases the parasites always reappear.

Laveran and Mesnil conclude that human serum and arsenic are the only substances that have shown any definite activity, and that under certain conditions arsenic may be used to prolong life.

They treated animals sick from nagana with arsenious acid, arsenite of soda, arrhenal, corrosive sublimate, Donovan's solution of arsenic and mercury, potassium iodide, quinine, a solution of arsenious acid, toluidan blue, methylene blue, and several of the newer silver salts, as silver lactate, fluoride, or trachiol, and carseinate of silver, or argonin, without curative results.

They quote Edington as having caused a disappearance of the parasites in animals by injecting one part of the bile of animals dead of the disease mixed with two parts of glycerine, and state that he obtained immunity in healthy ones. Laveran and Mesnil used this treatment on dogs with negative results. In rats and mice it did not influence the course or duration of the disease.

Bruce used arsenite of sodium intravenously in large doses. He concluded that this treatment would cause a temporary disappearance of the parasites and somewhat prolong life, but that it would not cure the disease.

Lesur employed subcutaneous and intravenous injections of Fowler's solution, cacodylate of sodium, and arrhenal without definite results.

Deixome made use of arsenic, cacodylate of sodium, arrhenal, and corrosive sublimate, but to no purpose.

Curry tried quinine subcutaneously and intravenously, methylene blue and salt solution intravenously, arsenic subcutaneously and by mouth, as well as various tonics, iron, cinchona, etc., but the animals died with the usual regularity in spite of treatment.

Schilling determined quinine, corrosive sublimate, and bile to be useless.

Voges used intravenous injections of large doses of quinine and methylene blue with negative results. He also employed the following (without any benefit: Enteral, sodium salicytate, turpentine, potassium permanganate, potassium iodide, and corrosive sublimate. He observed, as have so many others, a temporary improvement under the treatment of arsenic, life being prolonged, but no cures effected.

Three native ponies were treated with daily intravenous injections of large quantities of 1–1,000 solution of acetozone. A temporary drop of the temperature often followed treatment, and, as in the case of almost any kind of an injection, the parasites sometimes disappeared for a short time from the circulation, but definite or permanent results were not obtained, although the course of the disease was somewhat shortened.

As has already been shown, several substances have a destructive action for *Trypanosoma* in the hanging drop, but no such favorable action was obtained from any of them in treatment, whether by mouth, subcutaneously, or intravenously. The following have been used by us in the treatment of animals ill of the disease, but in none of them with hopeful results:

Lysol, creolin, infusion of pepo granatum, santonin in the form of freshly prepared santonate of soda, strychnine arsenate, Fowler's solution, spigellia, copper arsenite, pelleterine, eucalyptus, quinine hydrochlorate and urea, and combinations of several other salts and quinine, thymol, chloral hydrate, glycerine, methyl alcohol, acetic alcohol, barium chloride, calcium chloride, magnesium chloride, picric acid, oxalic acid, and various strengths of salt solutions alone and in combination with other drugs, carbolic acid, formalin, potassium permanganate, cyanide of potassium, urotropin, turpentine, cuprous sulphate, cupric sulphate, eosin water soluble, eosin alcohol soluble, potassium acetate, potassium chlorate, corrosive sublimate, arsenious acid, methylene blue, and several other aniline dyes.

The following serums have also been used: Antidiptheritic, antistreptococcic, antirinderpestic, antiplague, antidysenteric, antitetanic, and all available prophylactic preparations.

Toxins, toxic cultures, and fresh cultures of numerous organisms have been used, including plague, dysentery, typhoid, paracolon, malta fever, streptococcus cholera, and several strains of colon bacilli.

Blood parasites have been inoculated, including malaria and two varieties of filaria.

Extensive use has been made of human blood taken from fresh necropsics and in the following diseases: Cholera, dysentery, plague, malaria, typhoid, Bright's disease, leprosy, and malignant neoplasms.

Blood from the lower animals, both in health and in disease, has been employed; from healthy cows, as well as those suffering from rinderpest and foot-and-mouth disease; from sheep, goats, deer, rabbits, guinea pigs, frogs, chickens, ducks, pigeons, and several other species of animals.

Bile and other excretions and secretions, including urine from both healthy and diseased animals as well as from those dead of surra, have been used.

Use has been made of the extracts from the lymphatics, the adrenal,

and the thymus, as well as from organs of animals affected with surra and other diseases.

Recourse has been had to X-ray and other light treatments, various emulsions and preparations of blood, and attempted attenuations of parasites.

As already mentioned under serum therapy, considerable time has been devoted to the preparation of specific sera; and numerous injections of aspirated serous fluids and the contents of collodion sacs have been kept in the abdominal cavity of susceptible animals for varying lengths of time.

In all this work we have not obtained a single recovery, nor have we been able to bring about conditions that would indicate the slightest hope of effecting a cure in animals when once they have contracted the disease.

In conclusion, we see no hope whatever for curative treatment along lines so far investigated, and the outlook for preventive treatment is hardly more encouraging.

From a casual observation the conditions seem unfavorable, but if we go more deeply into the matter we find that they are not so bad after all. The disease is one which can certainly be prevented in a country not yet infected and can as surely be eradicated from one where it is already epidemic by means which are thoroughly practicable. There is presented to us in the Philippine Islands to-day an opportunity to accomplish results which will be gratifying to the scientific world and which should save the country from the annual loss of thousands of dollars.

XVII. SUMMARY AND CONCLUSIONS.

Trypanosomiasis is considered to be a general infection caused by *Trypanosoma*. The term *Trypanosomiasis* in a general sense is used to designate all varieties of the infection as found in different animals. The long list of vernacular names now in use, except *surra,* should be discarded or else allowed to fall merely as synonyms, save in those cases where the infecting parasite is shown to be a species distinct from that of *Tr. evansii.*

A study of the history of the disease shows it to be of remote origin, records of it in some countries dating back for centuries.

It is distributed over large areas of the tropical and subtropical world, corresponding closely in its dissemination to the malarial zones.

Trypanosoma in general are discussed with reference to history; methods of study; general characteristics, including modes of multiplication, agglutination and involution forms; distribution in the body and outside the body; life cycle.

The life cycle is as yet unknown, but is believed to be acted out entirely within the animal economy.

A *tentative* classification has been adopted for purposes of study, and each *Trypanosoma* of importance has been discussed with reference to its principal characteristics, habitat, and pathogenesis.

The differential diagnosis of *Trypanosoma* of mammals, like the life cycle, is left an open question, but the weight of evidence in literature and our own observations tend to the conclusion that at least three of the species to which separate names have been given are in reality identical with *Tr. evansii.*

Under the discussion of modes of transmission and infection, the only point upon which emphasis need be placed is the conveyance of the disease through wounded surfaces, in which biting insects, particularly flies and fleas, serve as the principal agencies. It is clear that the prevalence of the disease is dependent upon the presence of a host for the *Trypanosoma* and of insects for their transmission. The animals which serve as hosts for the perpetuation of the disease through the dry season vary in different countries. In Manila sick horses exist in sufficient numbers to carry the infection from one rainy season to another. Cows and rats may also aid in its perpetuation.

Statements concerning the infection of pastures and water and the transmission of the *Trypanosoma* through sound mucous membranes have nothing to support them.

After describing the general pathologic anatomy and symptomatology we have taken up the discussion of the infection in various species of animals, paying particular attention to the disease in those of economic importance. The manner in which the symptoms vary in different animals has made this necessary, in order to enable us to make satisfactory diagnoses and intelligently to control the epidemic.

The course, the duration, the prognosis, the complications, and the diagnosis have all received a general consideration.

A chapter has been devoted to the consideration of the identity or individuality of surra, nagana, dourine, and mal de caderas. This is an important subject from a scientific standpoint, but as an aid to the evolution of means of prevention or cure it is of little consequence. As in the case of the parasite, we have with most other writers left the subject open, but we are strongly inclined to believe them the same disease, in which case *surra* would be the only vernacular name allowable. There is certainly nothing in the clinical study of these diseases to differentiate them. The only real arguments in favor of their individuality are based upon morphologic differences in the parasites, and, as has already been said, these appear to us to be so slight that a positive classification can not be founded on them.

The study of prophylaxis has included the consideration of quarantine laws intended to prevent the infection or reinfection of a country, as the case may be, and of methods for the control and eradication of the disease in territories where it already has a foothold. In discussing this matter

we have limited ourselves almost entirely to the consideration of means adapted for destroying the hosts and supplemented by those suitable for combating the carrying agents. It has been thought necessary to go into this subject with considerable detail, and miscellaneous conditions have been given full consideration.

Prophylactic and curative serum therapy have thus far failed to give successful results, but if recent reports from Africa are to be trusted, preventive inoculation is not *wholly* without promise of success.

All methods tried for the treatment of the disease have been without results of practical importance or significance.

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