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Circular Letters:

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Streptomycin in the Treatment of Tuberculosis: The effects of streptomycin administered to tuberculous patients have been shown to be strikingly beneficial in some phases of the disease, equivocal in some, and quite insignificant in others. Toxic damage by the antibiotic has been of frequent occurrence, but this can be minimized by limiting the dose and the length of treatment. A more serious disadvantage, insurmountable thus far, is the development of bacterial resistance to streptomycin which often nullifies its further use.

The purpose of this paper is to suggest some clinical interpretations which, although somewhat tentative, seem reasonable at this time.

In dealing with a disease as variable in its clinical manifestations as tuberculosis, it is not possible to distinguish precisely those changes which occur in its natural evolution from those influenced by treatment; this is particularly true after the disease has become chronic. It was partly for this reason that the authors chose to study streptomycin in some cases of relatively early and severely acute tuberculosis.

When the maximum effects of treatment with streptomycin occur in patients suffering from acute febrile tuberculosis, they often experience a feeling of well being and a return of energy and strength within three or four days. This may antedate the subsidence of fever. In a few cases high fever subsides abruptly, almost by crisis, within a week after treatment is started; but in most there is a more gradual defervescence; this, however, is at a distinctly steadier and more rapid rate than is usually observed under rest treatment alone. These patients, if previously malnourished, may gain weight and, in the space of a few months, acquire an outwardly healthy, well nourished appearance. The erythrocyte sedimentation rate, however, may remain accelerated for several months after the disappearance of subjective symptoms.

The effect on local symptoms is sometimes quite pronounced. Tuberculous laryngitis, causing severe pain and dysphagia, may respond so quickly that often within the course of a few days the patient is able to eat with little or no discomfort. Cough and expectoration often subside rapidly. In genitourinary cases there may be partial or complete relief of frequency, dysuria, and other symptoms of bladder irritability.

Relief from constitutional symptoms, and sometimes also from local symptoms, usually occurs before any change in local lesions can be demonstrated; thus, the early cessation of the pain of tuberculous laryngitis may antedate any visible change in the appearance of the larynx. Presumably this is due to the retardation or arrest of active inflammatory edema, thus lowering the tension in the tissues and easing the irritation of sensory nerves. Within from a few days to one or two weeks, if deep destruction has not already occurred, edema and redness of the laryngeal tissues may diminish, shallow ulcers may be seen to regress, and in time the structures may assume a superficially normal appearance. Similarly, tuberculous inflammatory changes in the mucosa of the bladder

may be observed cystoscopically to diminish, and the capacity of the bladder increases toward normal. Concerning the lungs, a rather common manifestation of subsiding inflammation is a decrease in purulence and amount of sputum daily, and roentgenograms, taken at intervals of from a few days to several weeks, often show rapid clearing of soft mottled shadows indicative of this resolution.

This checking of active tuberculous inflammation and subsequent resolution of the inflammatory exudate is observed most strikingly in acute cases. When the duration of tuberculous pneumonia is only three or four weeks and a prompt arrest of the inflammatory process is induced by streptomycin, the subsequent resolution sometimes seems to become almost complete. The factor responsible for this resolution appears to be the suppressive effect of the antibiotic on bacterial growth before caseous necrosis has occurred. A conclusion that complete resolution has occurred may be erroneous, for minute caseous foci, roentgenographically invisible, may still exist, as evidenced sometimes by the persistence of fine rales.

In a number of cases of early tuberculous pneumonia there has been a prompt symptomatic response to the administration of streptomycin but a considerable lag in the resolution of the lesions; resolution proceeded then to a striking degree during two or three or more months after the completion of the course of streptomycin. It is apparent, therefore, that the failure of lesions to resolve promptly is not necessarily an indication to continue the administration of the drug beyond the allotted time.

As far as the morphology of the lesion is concerned, it is known that the extent of caseous necrosis, which in turn depends upon the type and duration of the inflammation, limits to a great degree the response to streptomycin. Severe tuberculous pneumonia of two or three months' duration is usually widely caseous; there may be a temporary symptomatic response but with little or no demonstrable evidence of resolution and, in such instances, early relapse is to be expected as probable. The same is true of caseous lesions in other sites. Tuberculous abscesses in soft tissues may persist as such. Nodular, presumably caseous, lesions in the epididymis and prostate usually do not show any striking change. This is not surprising in view of the fact that caseous lesions are organized slowly, with or without sloughing or ulceration. To what extent such healing is favored and accelerated after the use of streptomycin remains to be determined by further observation.

The presence of caseous lesions goes far to explain many observed phenomena. The frequent relapse and fatal course of tuberculous meningitis after an initial striking response to streptomycin therapy seems in some cases to be explained by the presence of caseous lesions in the cortex of the brain, which are the sources of renewed invasion of the meninges some time after the drug has had its effect. Similarly, streptomycin may promote temporary clinical recovery

from generalized miliary tuberculosis and resolution of numerous non-necrotic metastatic lesions while the caseous focus of origin remains little affected and may later seed the blood stream again, with a fatal result. In pulmonary cases, renewed progression of the disease by bronchogenic dissemination is more often related to persistent caseous foci containing viable tubercle bacilli than to any other single factor. Unless these residual necrotic lesions can be held in abeyance by prolonged and careful rest treatment (to allow for the slow process of fibrous organization) relapse is almost inevitable.

However impressive may be the immediate effects of streptomycin, there is as yet no reason to think that the time required for the ultimate healing of residual caseous lesions and lasting clinical recovery is shortened. Initial recovery under streptomycin from acute progressive tuberculous pneumonia should be regarded only as a respite for the patient whose natural resistance has failed to cope with the infection; a favorable balance can be restored but slowly, if at all. The patient should have perhaps a year or more of bed rest, and another year or so of convalescent care in order, as far as possible, to promote permanent recovery.

Caseous necrosis, as a rule, is not as deep and massive in structures such as the larynx, bronchi, intestine and bladder, as it is in structures like the lungs or kidneys, and the prompt improvement in lesions in the former locations, as well as in the skin, is on the average more striking than in deeply involved viscera such as the lungs or the kidneys.

Even though ulcerated caseous lesions are sometimes affected little, if at all, by streptomycin, the exudation and discharge from them may be at least temporarily diminished, as indicated, for instance, by an improvement in the amount and character of the sputum or in the degree of pyuria. Such changes are frequently observed without any appreciable difference in the size of the pulmonary cavity or the renal defect. Nevertheless, even a partial control of purulent exudation may be a desirable thing, particularly to help avoid further dissemination of the infection through the bronchi in the case of the lung, or through the ureters in the case of the kidneys. This may help prepare the way for other needed treatment such as pneumothorax or surgical intervention. On the other hand, the disappearance of tubercle bacilli from the sputum or the urine may be misleading, for this is not good evidence of healing unless there is also a simultaneous obliteration of the ulcerated lesions from which the organisms were discharged.

In several cases of tuberculous pneumonia the authors have observed the lesions to break down and become excavated rapidly during the course of streptomycin treatment; yet new bronchogenic lesions were not demonstrated.

The importance of vital resistance in the final outcome in each patient is recognized; it is clear from brief experience that relapse after streptomycin treatment is more frequent, and occurs earlier and with greater severity, in

those with poor native resistance. The implication is clear, therefore, that in such cases facilities should be available for long and rigidly controlled rest treatment, perhaps aided by collapse therapy, in order to gain the most from any temporary benefit of the drug.

It has been shown that resistant variants of the bacillus are recognized in cultures of sputum or other exudates within four weeks after the start of treatment; and after from three to four months of streptomycin therapy, 70 percent or more of the patients harbor bacilli with resistance so strong that the usual therapeutic doses of streptomycin are no longer effective. The development of resistance seems to be more closely related to the duration of treatment than to the daily dose employed. Cumulative evidence suggests that this bacterial resistance may be permanent. There is some evidence that strains of bacteria of varying resistance occur in different lesions in the treated patient and that in such cases a renewed dissemination of sensitive bacilli may be controlled by re-treatment with streptomycin. Because of these observations a number of studies are under way to determine the optimum dosage of the drug and the optimum period of time over which it should be administered. The authors' study of 40 cases of acute tuberculosis, 18 treated with 2 grams of streptomycin daily and 22 with 1 gram daily for 42 days, indicates that this relatively short period may be as effective in some instances as a longer period of administration. In these regimens, development of drug-resistant variants is approximately from 25 to 30 percent, including a number of cases in which drug resistance has continued to increase after the termination of treatment. Such a regimen, therefore, provides a possible therapeutic margin for re-treatment should the first course of the drug prove to be inadequate. It also has the advantage that patients who, after a period of rest cure, require surgical intervention for the tuberculosis, may then expect some protection and benefit under a renewed course of streptomycin.

Damage of the labyrinthine apparatus is most common and serious when the drug is administered in high dosage for long periods of time. A study of relatively smaller doses given for six weeks indicates that 1 gram of the drug a day does not destroy vestibular function, as shown by caloric tests, although there may be occasional partial impairment. By contrast, 2 grams daily for the same period has caused complete loss of function in 12 of the 18 patients treated. The damage is persistent and presumably permanent, although the patient may be able to compensate. It should be emphasized that complete loss of vestibular function, as determined by caloric tests, may occur although the patient may experience no vertigo or other symptoms as long as he remains in bed.

Because it seems important not to exhaust the effectiveness of the drug during the initial course of treatment unless the indications are very urgent, the treatment schedules that follow are recommended.

In cases of acute tuberculous pneumonia known to be of short duration (from two to four weeks) benefit can usually be expected with 1 gram of streptomycin, intramuscularly, daily for a course of six weeks. If, after a short interval, the

symptoms recur and the disease progresses, re-treatment is sometimes effective. If the tuberculous pneumonia is of longer duration and presumably extensively caseous, a longer period of continuous treatment is probably justified, although it is questionable whether larger doses will prove to be more effective. In these cases the incidence of relapse can be expected to be high and eventually no further effect can be anticipated from streptomycin.

In milder cases, if streptomycin seems indicated at all, there is strong reason to use small doses for relatively short periods of time. The dose probably should not exceed 1 gram a day for six weeks and in many cases the course could well be terminated earlier than six weeks if the desired effect is being approached. Such a regimen may achieve limited goals such as the improvement of a bronchial lesion or the closure of a cutaneous sinus. In every case, a careful evaluation of the situation should be made, particularly to prognosticate whether more critical episodes might arise in the future. It is generally agreed that patients who may be expected to respond to conventional rest treatment should not be treated with streptomycin even though this might hasten early symptomatic improvement.

In desperately severe cases of tuberculosis such as generalized hematogenous miliary tuberculosis and tuberculous meningitis, usually fatal in a few weeks or several months, streptomycin should be administered intramuscularly in daily doses totalling 40 mg. per kg. body weight (2 Gm. per 110 pounds) for a period of 90 days regardless of likely toxic effects. In addition, in meningitis, 50 mg. should be given intrathecally at from 24- to 72-hour intervals during the 90 days. In most cases there will be at least a temporary remission of the disease, although relapses occur at a rate which, in the case of meningitis, is exceedingly high; i.e., approximately 80-percent fatality. In these situations, the reports of Lincoln and her associates suggest that the addition of promizole may be beneficial. The place of the sulfones, para-aminosalicylic acid and other agents, as supplements to streptomycin, can be established only by further investigation. (Ann. Int. Med., Aug. '48 - J. B. Amberson and W. H. Stearns)

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Pneumoperitoneum in Tuberculosis: A great divergence of opinion regarding the indications, effectiveness, and usefulness of pneumoperitoneum in the treatment of tuberculosis continues to exist in spite of the fact that well over a decade has passed since the procedure was first recommended by Banyai and since a number of sanatoriums and clinics began to use pneumoperitoneum in selected cases.

It can scarcely be denied that pneumoperitoneum is capable of favorably influencing the course of tuberculosis in certain patients. The general experience is that no physician who has used pneumoperitoneum adequately on enough patients for a sufficient period of time has then discarded it as a procedure of

no value. There is no longer reason to doubt that, in competent hands, pneumoperitoneum is a relatively safe procedure and that serious complications are relatively few. Moreover, a logical rationale for its use can be constructed, not merely from roentgenographic and fluoroscopic observations regarding the affected diaphragms of patients, but also from lung volume studies, recently carried out by Wright, in which several extremely pertinent observations were made:

1. The degree of relaxation of pulmonary tissue produced by a given therapeutic procedure is best determined by studying the effect of the procedure upon the lung volume at mid-capacity, i.e., the air content of the lungs at the end of an ordinary quiet expiration. It is this volume, not the volume at the end of forced inspiration or expiration, which most accurately indicates the usual volumetric status of a patient's lungs during the twenty-four hours of the day. (Trimble has similarly pointed out the importance of studying the relative position and mobility of the diaphragms fluoroscopically during quiet respiration if the relaxing effect of pneumoperitoneum is to be estimated radiologically. This effect cannot be accurately estimated merely from conventional roentgenograms made on deep inspiration.)

2. When a patient, with or without pneumoperitoneum, changes from the erect to the recumbent position, lung volume at mid-capacity is reduced by from 25 to 50 percent.

3. In the study of a limited number of cases, Wright found that the effect of pneumoperitoneum without phrenic paralysis varied considerably and was sometimes extremely slight. In general, however, volume at mid-capacity in both the erect and recumbent position was reduced by from 15 to 40 percent of that measured with the patient in a corresponding position prior to pneumoperitoneum.

4. Observations on patients with phrenic paralysis and pneumoperitoneum were too limited to justify generalizations. In 2 patients with pneumoperitoneum, the addition of phrenic paralysis further decreased volume at mid-capacity to a marked degree (50 percent over the expected levels in both positions).

5. In the cases studied, pneumoperitoneum produced little reduction in maximum breathing capacity (not over 10 percent).

It may still be debated whether or not relaxation of diseased tissue is the principal factor responsible for the beneficial effects of collapse therapy in pulmonary tuberculosis. It is a commonly accepted theory that relaxation is, at least, a desirable therapeutic objective, and this theory has much evidence to support it. Wright's studies show that relaxation can usually be achieved by pneumoperitoneum, and both clinical and physiological observations indicate that pneumoperitoneum is less likely than pneumothorax to produce serious impairment of ventilatory function.

What, then, shall be the tentative appraisal of pneumoperitoneum at this time? This is bound to be a somewhat personal matter, influenced, in part, by one's own case material and experience, and by the attitudes, preferences and special skills of the surgeon with whom one works. The following is the author's tentative evaluation of pneumoperitoneum:

Pneumoperitoneum is a useful and valuable therapeutic procedure, which is relatively safe and which can be well tolerated by most patients. It can often be successfully applied when bed-rest alone is inadequate and when pneumothorax and thoracoplasty are not well suited to the problem. When not completely successful, pneumoperitoneum can usually be abandoned without impairing the patient's suitability for an alternative procedure. An anatomically satisfactory pneumothorax or a thoracoplasty is, however, generally preferable to pneumoperitoneum when there is a good indication for one or the other of these procedures, and when the risks involved are not excessive.

Pneumoperitoneum is especially valuable in patients with active and progressive exudative or caseous pneumonic tuberculosis, who are too ill for thoracoplasty and in whom the risk of complications from pneumothorax is high. Pneumoperitoneum will often produce sufficient improvement to bring such patients successfully to thoracoplasty even when it is inadequate, alone, to produce arrest of disease. Pneumoperitoneum also often deserves a trial following unsuccessful pneumothorax, provided that the extent of disease and the severity of pulmonary damage is limited, so that one is reluctant to proceed immediately to thoracoplasty. In both these situations, pneumoperitoneum is much more likely to prove effective if the distribution of disease is such as to warrant the combination of phrenic paralysis with the pneumoperitoneum.

The value of pneumoperitoneum is limited in patients with extensive old fibrocaseous or fibrocavernous tuberculosis. This is also true when tuberculous bronchitis with bronchostenosis or tuberculous bronchiectasis is prominent. In such patients, either permanent collapse by thoracoplasty or pulmonary resection is usually preferable. When disease of these types is bilateral, so that thoracoplasty or resection is not feasible, one can scarcely raise a strong objection to a trial of pneumoperitoneum. Clinical improvement is, apparently, often observed. It can hardly be expected, however, that the use of pneumoperitoneum will frequently produce complete and sustained arrest of tuberculosis in such patients.

Bed-rest remains the basic treatment in tuberculosis, and pneumoperitoneum, when indicated, should be used in addition to bed-rest, not instead of it. (Am. Rev. Tuberc., July '48 - Editorial by K. S. Howlett, Jr.)

Medullary Nailing for Arthrodesis of the Knee Joint: George Chapchal of Utrecht, Holland, reports that the use of intramedullary nailing for arthrodesis of the knee shortens the period of treatment, gives better fixation immediately after arthrodesis, and makes the use of a plaster cast unnecessary. He used this method seven times in six patients.

The fixation obtained by means of a long intramedullary pin, which enters into the femur and the tibia, is so stable that the plaster cast can be omitted. The fixation by such a pin is so strong that it will even be possible to shorten the after-treatment to just the period necessary for healing of the operative wound. The primary stability achieved by this pinning is much better than that obtained by nailing the ends with different nails, because of the length and the better construction of the pin. In other methods in which nails are used for fixation in arthrodesis, they are placed in the spongiose tissue of the condyles of the femur and of the tibia. This tissue is soft, so that the nails can change their position as a result of slight trauma. The advantage of using the medullary pin in arthrodesis of the knee is that the pin is fixed in the hard cortex of the bone. Dislocation is then possible only by trauma sufficient to bend the pin or to break the bone.

A further advantage of this method is that proper care can be given to the other joints and the muscles of the extremity during the patient's rest in bed necessary to the healing of the wound.

The operation is performed under general anesthesia or epidural analgesia. An anterior approach to the knee is chosen. The straight incision of from twenty-five to thirty centimeters (from 10 to 12 inches) runs on the ventral side of the thigh, over the patella to the tibial tuberosity. By this incision, the femur is exposed and the joint is opened after excision of the patella. The ligaments of the knee are cut, and the surfaces of the joint are exposed by maximal flexion of the knee. The joint cartilage is removed by chiseling until cancellous bone appears and a good adaptation of the pieces is possible. Then a hole, three centimeters long, is made lengthwise in the femur in the upper part of the incision. By this hole the medullary cavity of the femur is opened, so that the medullary pin can be introduced. A medullary pin, from twenty-five to thirty centimeters in length, is chosen to fix the femur and the tibia. It should be as thick as the medullary cavity of the tibia will allow. The medullary pin is introduced into the cavity very carefully, so that the femur will not crack. When the pin appears in the joint, the tibia is put in front of it, so that the pin enters the medullary cavity of the tibia as shown in figures 1-A and 1-B on the next page. This is possible only when the knee is in slight flexion (approximately from 6 to 10 degrees). Then the capsule of the joint and the skin are sutured.

It is recognized that many orthopedic surgeons like to perform arthrodesis of the knee in from 20 to 25 degrees of flexion, being convinced that a better functional result will be obtained by so doing. Even then, it is quite possible to use intramedullary pinning for arthrodesis of the knee, since the degree of flexion

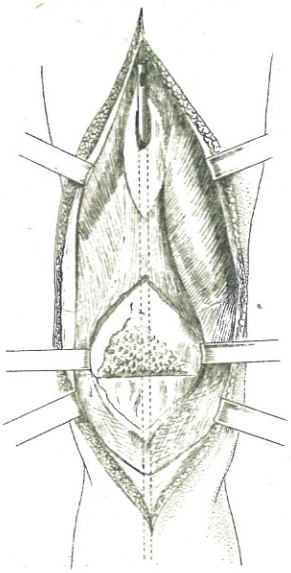

Fig. 1-A

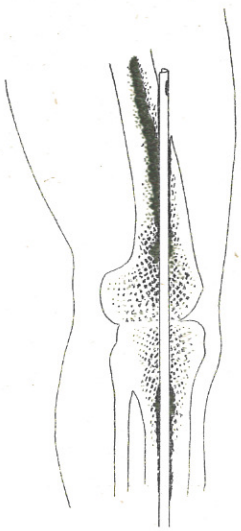

Fig. 1-B

Operative technique of intramedullary pinning for arthrodesis of the knee joint.

pends upon the place where the pin enters the femur. This is demonstrated in figure 5-A below in which the arthrodesis was performed in 20 degrees of flexion because the patient was employed in an office and did his work sitting.

Because excellent stability of an arthrodesis of the knee is obtained by a medullary pin, it is sufficient to use a bandage on the wound for from ten to fourteen days. During this time the patient stays in bed. After the sutures have been removed, he is allowed to leave his bed for increasing periods. Massage should be used for treatment of circulatory troubles, and to avoid postoperative edema when the patient gets up. After some days the patient is allowed to leave the hospital; at that time he is given a plaster splint, to be used only when walking and to be taken off when resting. Six weeks later the patient returns for a roentgenographic examination. He is allowed to resume work after three or four weeks more, according to his occupation.

To promote osseous union of the fragments, cancellous bone chips taken from the iliac bone are sometimes used. They are introduced into the joint before a stable union of the pieces has been caused by the medullary pin, and are fixed in the coagulum obtained by injecting a hemostatic preparation into the hematoma caused in the joint by resection of the cartilaginous covering. The use of cancellous bone bhips marks an important progress in orthopedic surgery, and their strong osteogenetic power is able to produce a quick osseous union.

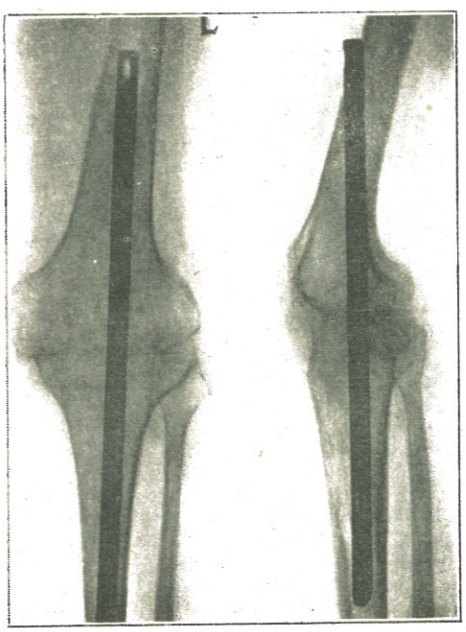

Fig. 5-A

Two kinds of medullary pins are used - thick straight pins for the femur and curved thin ones for the repair of other bones. In case 1 the patient was treated with thin curved pins, as used for fractures of the tibia. They were introduced from a separate incision on the ventral side of the leg, from the tibia, through the knee, into the femur. After a period of rest, the patient was allowed to walk. One knee, arthrodesed by a curved intramedullary pin, showed a favorable result. The other one did not show osseous

union, and consequently the pin broke. This experience suggested the use of stronger pins, introduced as described, through the incision used for the arthrodesis.

The advantage of using a thicker intramedullary pin is clearly evident. It gives better stability and better fixation of the knee. A warning is necessary against the use of pins which are too weak. These pins usually bend when introduced into the medullary cavity. The wall of the pin should be at least two millimeters thick. The pin must be resistant because in the first period it has to carry the whole weight of the patient and withstand all possible strains.

After a period of from four to six months, the pin can be removed if the arthrodesis of the joint is complete. A small incision in the old scar is sufficient to enable one to find the end of the pin and to remove it with the instruments used for this purpose. No difficulties have arisen in pin removal which is done under local anesthesia, and the patient is allowed to leave the hospital a few days later. The sutures can be removed at a subsequent date.

In some cases, the pins remained in situ for a long period of time without causing any reaction. When the pin was removed, no changes in bone tissue or in the pin were observed. It is possible, therefore, to allow the pin to remain in place for more than six months, without any trouble occurring, if the patient asks for delay in removal.

The question of when to use a medullary pin is dependent only upon the indications for an arthrodesis of the knee. Of course, intramedullary pinning of the knee is not possible in case of inflammatory diseases of the joint, when arthrodesis of the knee is indicated. Here another technic has to be employed. All other cases are suitable for the use of intramedullary pinning, such as arthrodesing the knee for arthrosis deformans, creating a stable limb through arthrodesis of the knee for a total infantile paralysis of the lower limb, or correcting bony ankylosis of a knee joint united in a bad position, as after a shell injury or after gonitis.

In all cases of incomplete union or of fibrous ankylosis of the knee joint, arthrodesis with intramedullary pinning and cancellous chips should be employed.

It does not seem advisable to pin the knees in growing children, although the author has had no personal experience with the method during this period of life. On the other hand, it is not necessary to wait until the epiphyses have closed. No growth difficulties were seen after pinning in patients eighteen years old. However, this operation should be performed in adults or at the end of the period of growth.

In all but one of the cases in which intramedullary pinning of the knee was performed for arthrodesis, the results were favorable. No complications have

been observed, except in the case in which the curved intramedullary pin, used in the tibia, broke because it was too thin.

No important shortening of the leg was observed, because it was necessary to remove the cartilage of the joint only enough to get good union. The patients were permitted to move about early, and no difficulties arose. The fact that a postoperative plaster cast, so often the cause of circulatory trouble, could be avoided, was very satisfactory. The patients walked without pain from the very day they were allowed to get up. After removal of the pins, the stability of the knee and mobility of the patient were not affected. Doctor Chapchal concludes that this method of arthrodesing the knee is superior to the methods formerly used. (J. Bone and Joint Surg., July '48)

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Concerning the Definition of Inoperability of Cancer: The greatest margin of error in reporting the end-results of treatment for cancer may be found in the classification by the surgeon who reports a regional or histologic type of cancer as operable or inoperable. The difficulty in correcting this fault is apparent when one realizes that three variable factors interplay in the pronouncement of a given cancer as nonresectable by any surgeon, namely: first, the condition of the patient as regards his age, the coexistence of degenerative diseases, and the complications attendant on the presence of the cancer; second, the extent of the disease, meaning the degree of local or organic involvement, the specific organ or tissue implicated, the extension to and incorporation of neighboring viscera by the cancer, and metastases to regional and distant sites; and third, the surgical philosophy, moral point of view, courage, and experience of the surgeon.

The author's purpose is to present certain arguments for extending the scope of operability for cancer. The very nature of this disease, the infirm and often aged patients in whom it so frequently develops, and the radical character of the numerous operations designed to combat it, all conspire to make the surgical treatment of cancer a hazardous venture for the patient and often an ordeal for the surgeon. With the knowledge of the inevitability of death from cancer that is not treated, no surgeon can refuse a patient the slightest chance for cure or even relief because of a fear of criticism for failure or because of the probability of an increase in his figures for operative mortality. Nor should any surgeon decide arbitrarily that a certain patient with cancer had lived a sufficiently long life or that he had so few remaining years of even normal life expectancy that operation at best would hardly be worth while.

Many operations designed for the cure of cancer achieve in too many instances only a palliative end-result. If inoperability were an absolute state, and not a variable one, dependent in some cases on the criteria of the surgeon, the term would be synonymous with incurability. The unpredictable behavior of cancers and the immeasurable host resistance of organs and tissues to the growth

of cancer combine in creating many intangible factors that make the early cancer occasionally incurable and the advanced cancer sometimes controllable. Assuming that a given cancer is not suitable for radiation therapy, operative removal becomes the only recourse. At the time of laparotomy, for example, a surgeon may be compelled to render judgement absolutely governing the life of the individual, the decision necessitating a matter of a few minutes as compared with days and weeks of courtroom deliberation by judge and jury. The closure of an abdominal wound on a cancer that is obviously hopeless is always done reluctantly, but the abandonment of an operation that is of questionable accomplishment must plague the conscientious surgeon for many sleepless hours. He must worry whether his definition of inoperability is in his state of mind or moral courage or in the actual stage of the cancer. An aggressive attack on cancers presenting almost insuperable technical difficulties will sometimes result in palliative relief and occasionally in cures, but with mounting operative fatalities. Under these conditions, no one would impugn the good intent of the operator.

A distinction should be made between absolute inoperability due to distant dissemination of the cancer, and relative inoperability due to local technical difficulties. No surgeon should perform an exploratory operation unless he is qualified to proceed with the actual removal of the tumor if encountered. Excisional surgery should be available for cancer patients of advanced age if they can be prepared for such an ordeal, for, old age alone is not a sufficient excuse to deny these patients the only opportunity to overcome an otherwise fatal disease. The condition of the patient may present seemingly serious hazards from the surgeon's viewpoint, but with the latest improvements in preoperative and postoperative management, the dangers are often reduced to a point at which major surgical procedures may be safely performed. The stage and extent of the cancer complicate the judgement of the surgeon, but if the cancer is removed whenever technically possible, occasional cures are surprisingly obtained. Palliative resections of the stomach, colon, and rectum afford a great deal of relief to many patients even though small metastatic foci are detected in the liver. Involvement of multiple organs by cancer has been given as a reason for inoperability, but one should attempt by every means possible to remove such cancers which are adherent to any adjacent structures or viscera that may be sacrificed by excision in continuity with the organ involved. Some patients who have had exploratory laparotomy for cancer with abandonment of the operation and pronouncement of incurability are entitled to another chance or effort by a different surgeon if the former surgeon classified the cancer as inoperable because of technical difficulties. The author gives numerous case reports to illustrate the arguments throughout his thesis. (Ann. Surg., June '48 - G. T. Pack)

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Rotation X-ray Therapy - Theory and Clinical Applications: Rotation therapy is a technic of irradiating deep-seated lesions by rotating the patient in the beam or by moving the tube about the patient. Within certain limitations this method

offers a more symmetrical distribution of radiation and a more advantageous ratio of depth to skin dosage than cross-firing with stationary fields.

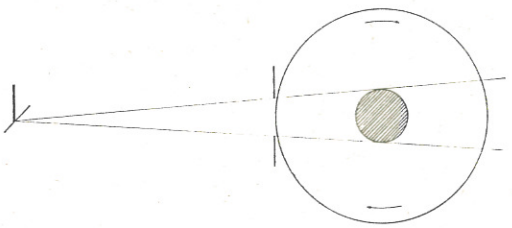

Fig. 1. Diagram of principle of rotation therapy.

The object of the procedure is always to have the lesion in the beam while every other part of the body is irradiated only as it passes through the beam on the tube side of the lesion and on the opposite side (Fig. 1). This is easily accomplished by rotating the patient in the erect posture on a simple turntable with the beam horizontal and perpendicular to the axis of rotation. The patient may sit on a stool or stand up, depending upon the part of the body being treated (Fig. 2). Support is rarely necessary. Moving the tube about the patient presents formidable and expensive mechanical problems.

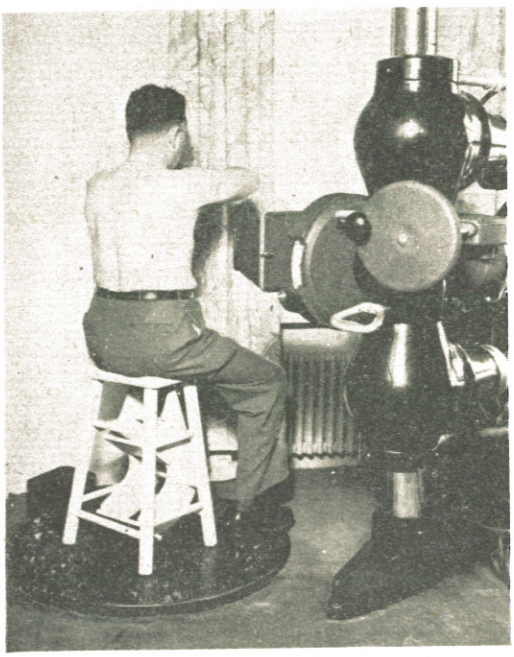

Fig. 2. Patient in position for treatment of the lower third of the esophagus.

The turntable need not be elaborate or expensive. A disk of wood or metal, supported around the edge on roller bearings, and driven by a worm gear and a quarter horsepower motor, is all that is needed. It should be at least 3 feet in diameter and of strong enough construction to accommodate heavy patients. The rate of rotation is immaterial as far as dosage distribution is concerned.

European workers have made elaborate set-ups so that the position, particularly in the treatment of carcinoma of the esophagus, may be continuously controlled by fluoroscopy. They have used very small fields. Although such an arrangement may be desirable, it is considered not necessary. The small fields offer certain disadvantages because peripheral parts of a lesion, particularly an infiltrating carcinoma, cannot be located accurately. The field, therefore, should be wider than the known lesion. If the patient is turned very slowly, a small change in position will produce a serious disturbance in distribution. If, however, the patient is turned from fifteen to twenty-five times during a treatment, a small change in position during one revolution, or part of one, will have little effect. One complete turn a minute is a satisfactory rate. It is slow enough so that the patient does not get dizzy and allows an adequate number of turns per treatment.

The distribution of radiation in the body during rotation differs from that with stationary fields. To illustrate this, in an ideal situation in which a cylindrical

body is irradiated through a portal which is narrow in proportion to the diameter, the distribution may be represented by a bell-shaped curve (Fig. 4).

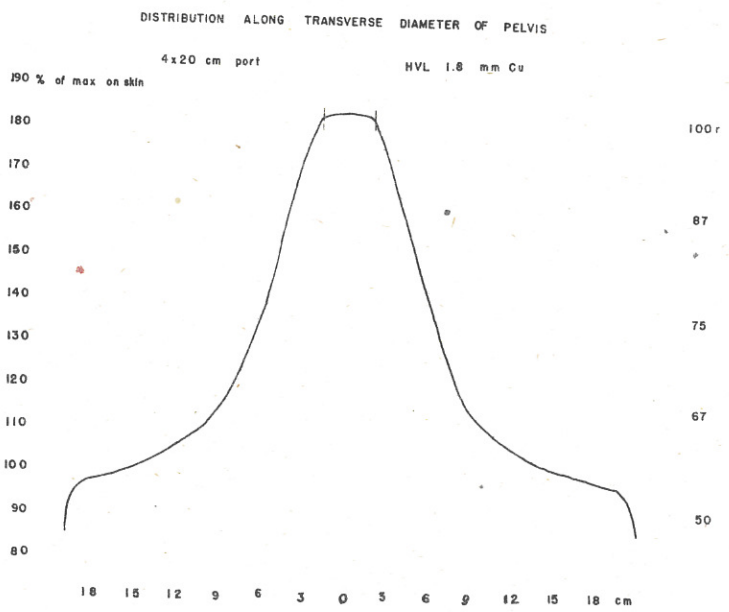

Fig. 4. Distribution curve for narrow port.

The greatest amount of radiation is delivered to a cylindrical volume of tissue about the axis of rotation. With narrow fields, the distribution is practically uniform across this cylinder. At the edge of the beam the amount of radiation received falls off rapidly to a plateau, which gradually descends to the surface. The surface receives the least amount of radiation. Under ideal conditions the dose at the site of the lesion may be as much as three times that on the surface. During treatment, in which ideal conditions cannot always be had, the curve will be modified to some degree, but the basic pattern remains the same.

The shape of the curve and the ratio of deep to surface dosage are altered by changing the width of the field and by changing the shape of the body being irradiated. As the field is widened, the height of the curve, in other words the ratio of the deep to the surface dose, decreases. When the width of the field equals half the diameter of the body, the advantageous ratio disappears and the dose is nearly the same all across the body.

Treatment by rotation was given to a total of 71 patients. At first, because of the possibility of injury from such a large amount of radiation to large volumes of tissue, small doses only were given. These were gradually raised when no adverse reactions were observed. The first 20 patients selected are not included in this report because their disease was so far advanced and such small doses were given. Of the remaining 51, 36 were treated for carcinoma of the uterine cervix, 8 for carcinoma of the esophagus, 5 for carcinoma of the fundus of the uterus, and one each for carcinoma of the bladder and hemangioma of the brain.

Of the patients with carcinoma of the cervix, 14 received radium therapy also. These were given relatively small doses by rotation, ranging from 1,200 r to 2,550 r to the cervix, with corresponding air doses of 8,000 and 15,000 r. Three were treated five years ago, and 2 have remained well for five years. Three were treated four years ago, and all of these have had recurrences. Eight were treated three years ago, and 2 of this number have shown recurrences requiring further treatment.

The other 22 patients with carcinoma of the cervix were all far advanced and were treated with x-ray rotation therapy alone. The dosage varied from 1,944 to 4,032 r to the tumor; from 15,000 to 24,460 r in air, in from four to six weeks. Although none of this group was cured, palliation was satisfactory by present-day standards.

The 8 patients with carcinoma of the esophagus received from 2,100 to 4,000 r to the tumor; from 11,000 to 23,400 r in air. The one who received the largest dose, and was also the most favorable to start with, has remained free from carcinoma as far as can be determined for three years, though he has a cicatricial stenosis at the site of the lesion. In all the other cases there has been a recurrence of the neoplasm.

Of the 5 patients with advanced carcinoma of the fundus, only two received large enough doses to mean much - one 3,600 r and the other 2,400 r to the tumor; 35,700 r and 24,000 r in air, respectively. These two patients were subjectively free from symptoms for one and a half and two years, respectively, though the growth of the cancer subsequently recurred. The others had only short periods of palliation.

The one carcinoma of the bladder disappeared for a period of eight months and then recurred. This was one of the early cases in this study and the dose was relatively small, 2,000 r to the bladder, 10,100 r in air.

In the case of hemangioma of the brain a gratifying result was obtained. A wide portal was used, equal to half the average diameter of the skull, and 1,000 r were given across the cranium, 6,000 r in air, in a period of four weeks. The dosage figures are calculated, as no measurement has been made on phantoms so small. At the height of the reaction all the patient's hair came out and there was a faint erythema over the cranium. His hair subsequently grew back. He returned to work after three months and remained symptom-free for two years.

Although the number of patients treated is not adequate for evaluation in terms of five-year cures, it is sufficient to estimate the effect of rotation therapy on the patient and to some extent on the disease. The patient tolerates large daily doses without difficulty. Practically any will tolerate from 1,000 to 1,250 r daily without symptoms. This is not incomprehensible when it is realized that only a small volume of tissue receives a large dose, and the great volume of tissue receives a small one. Superficial reactions are minimal in spite of the large doses. No evidence of damage to normal tissues has been observed outside of the tumor zone. In cases in which treatment was given over the pelvis there was only slight bladder and rectal irritation, not at all comparable to that often seen in cross-firing with stationary fields. So far, the results have not been materially better than those in comparable cases in which treatment was given by conventional cross-firing methods, though the response is equally good. There is some evidence to indicate that the tumor response was better in the patients who received large doses. (Radiology, Aug. '48 - S. J. Hawley)

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Presence of Neutralizing Antibodies of Newcastle Disease Virus in Human Sera: In 1926 a highly infectious and fatal disease of fowls was first recognized in the Dutch East Indies by Kraneveld, and also by Doyle at Newcastle-on-Tyne, England. In 1927 Doyle isolated a filter-passing agent that he designated as Newcastle disease virus (NDV). Similar outbreaks among poultry were soon described from various parts of the world with the exception of the United States. It was not until 1941 that Beach and in 1942 Stover both recognized a respiratory central nervous system disorder of chickens in California that became known as avian pneumoencephalitis. By means of the serum neutralization test Beach in 1944 established the serological similarity of this strain with that of the British Newcastle disease, and in the following year the same virus was recovered from fowls in a series of outbreaks in the eastern United States. Systematic surveys during the past three years have demonstrated the presence of the disease, either by virus isolations or serum neutralization tests, in all but four states in this country. Therefore, it has become of major importance to poultrymen throughout the United States as well as other parts of the world.

Burnet and Ferry in 1934 were the first to propagate NDV in the embryonated hen's egg, but it was not until 1942 that Burnet demonstrated its ability to agglutinate chicken red-blood cells and thus place it with the respiratory group of viruses, such as influenza and mumps. The NDV has long been considered of primary importance for birds; yet in 1947 Reagan and co-workers demonstrated its adaptability to certain mammalian tissues. They were able to make serial passages in the Syrian hamster and likewise infect a rhesus monkey by the intracerebral but not by the intranasal route. Mice, guinea pigs, and rabbits were relatively insusceptible.

Although much has been written about Newcastle disease in poultry, only four reports in the literature mention invasion of human tissues. All of these cases are concerned with eye manifestations. Burnet in 1943 described a laboratory infection in Australia due to accidental entrance of live virus into the eye, followed by a conjunctivitis, headache, chills, and general discomfort. Newcastle disease virus was recovered from the conjunctival fluid, and antibodies for the latter were present in the patient's serum. In 1946 Anderson reported two other laboratory infections in Australia. Both patients developed conjunctivitis and NDV was isolated from the tears.

In 1946 Shimkin recorded a case of conjunctival hemorrhage in a worker at the Governmental Poultry Laboratory in Palestine. In the same year Yatom described a small epidemic of NDV infection among kitchen workers handling poultry in the Agricultural School, Mikveh-Israel, where an outbreak had recently occurred among the fowls. Seventeen people developed a conjunctivitis which disappeared in from 10 to 14 days.

Although NDV was first recognized in California about 1941, it was not reported for the eastern states until 1944 and 1945, which time would roughly correspond to the appearance of certain atypical cases of disease in human beings in

Tennessee. The disease in fowls spread rapidly over the country after the first recognition, but was not recorded in Alabama and Tennessee until 1947, although it may have been present earlier in an inapparent form. It was in 1948 and perhaps in late 1947 that infections in human beings in Alabama were found.

Except for these reported eye manifestations there has been no mention of any particular association between this disease in fowls and human infection among the general population.

From the gradually increasing evidence, it is apparent that during the past 3 or 4 years a hitherto undifferentiated disease entity is beginning to be recognized, particularly in communities of the South. Because children are often affected and manifest certain poliomyelitis-like symptoms, the disease is often reported as poliomyelitis. On the other hand, some cases, in which there are pronounced meningeal irritations, may be called meningitis. In still others there may be pneumonitis. Although the clinical symptoms may not be quite uniform and may vary according to the individual physician's interpretation, yet in general there is an agreement among all cases in showing a sudden onset, abrupt febrile course and rapid recovery without paralysis or other sequelae. An outbreak of this type, recognized as a meningo-encephalitis, was reported in 1947 by Humbert, Tucker, Mosley, and Bishop for Giles County, Tennessee. About 209 children and adults were seen with this acute disease, probably of viral nature, which usually lasted from 24 to 48 hours, although the fever, headache, and malaise might continue for from 5 to 10 days. There were no fatalities.

Sera were received in 1947 and 1948 from various groups of children in Alabama and Tennessee suffering from this mild central nervous system infection of short duration and without sequelae. Because of the frequent association with chickens and the absence of antibodies for the common neurotropic viruses, serum neutralization tests were done against the virus of pneumoencephalitis (Newcastle disease) of fowl.

Of 15 sera from children in Tennessee with the ND syndrome, 12 were positive to NDV. One patient with encephalitis and one with poliomyelitis-like symptoms had antibodies for this virus, but all other sera were negative, including 78 that were taken from children in 1944-1945 without this atypical syndrome. Two chickens from the premises of one of the patients showed both the pathological lesions of Newcastle disease and the presence of neutralizing antibodies in the blood.

Of 10 sera from human beings in rural Alabama showing this mild central nervous system syndrome, 8 had definite neutralizing antibodies for NDV; the result of tests in 2 were equivocal. Chickens with NDV antibodies were in association with several of the patients.

Subsequent to starting work with the virus in the laboratory, an acute influenza-like infection developed in 6 of the laboratory personnel. Antibodies

in high titer against NDV were found in the sera of these 6 persons. Antibodies were also found in 4 out of 11 sera of laboratory personnel without symptoms. The sera taken from 19 people in 1947, before working with the virus, were negative for NDV antibodies. The blood of 3 individuals who had typical symptoms before association with the laboratory contained definite neutralizing antibodies for NDV.

Although no virus has been isolated, it seems probable from the evidence that the Newcastle disease virus of fowls is the agent responsible for many of the atypical central nervous system infections that have been reported in man during the past few years, and that, as in the fowl, the manifestations are neurological in young individuals and influenza-like in the adult.

The data suggest that the virus originating with the fowl has subsequently spread to man, so that now in many instances it may be transmitted from man to man as well as from fowl to man. Poultrymen have long recognized the air-borne transmission of the virus, but it was only recently that DeLay, DeOme, and Bankowski, by means of a special apparatus, recovered NDV from the air of poultry houses containing infected birds. Because NDV is both air-borne and quite resistant to adverse conditions, a rapid dissemination from fowl to man could be readily explained. (Am. J. Pub. Health, Sept. '48 - B. F. Howitt et al.)

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The Application of a Silver Carbonate Stain for the Diagnosis of Uterine Cancer by the Vaginal Smear Method: H. S. Yue et al., working at the University of Michigan Hospital, Ann Arbor, Michigan, have modified Del Río-Hortega's silver carbonate method for staining nervous tissue and adapted it to the study of vaginal smears in the diagnosis of cancer. The several noteworthy advantages claimed for this technic are as follows:

1. Chromatin elements are heavily impregnated with silver carbonate. Because the nuclei of malignant cells are often hyperchromatic, they become focal points in the microscopic field.

2. Cellular outline is sharply delineated and cytoplasmic detail is preserved.

3. Good preparations are not dependent upon immediate fixation.

4. Only one stain is required for differentiation of nucleus and cytoplasm.

5. The possibility of erythrocytes obscuring significant cellular elements is avoided.

6. The fatiguing nature of intensive smear examination is lessened, due to generalized light absorption.

7. The procedure is relatively simple and rapid.

Method of Taking the Smear. Smears are obtained by using a glass pipette with a rubber bulb attached to the distal end as a means of providing suction. Customarily, a drop of water is drawn into the pipette first. This is deposited at the cervical os and the area is manipulated slightly as material is drawn up into the pipette. The droplet of water aids in making thin spreads. Very thick smears are to be avoided, because they do not stain uniformly.

Fixation. The smear is allowed to air-dry and is then immersed in 10-percent formalin for at least fifteen minutes. The smear may remain dry for twenty-four hours without impairment of subsequent staining qualities. Satisfactory results may also be obtained by immediate fixation of the wet slide.

Fixation with 10-percent formalin results in a loss of red blood cells due to hemolysis. However, the erythrocytes can be preserved by a slight modification of the fixation procedure. After drying, the smear is placed in an alcohol-ether solution (equal parts of ether and 95-percent alcohol) for five minutes. This is followed by immersion in 10-percent formalin for five minutes. The exclusion of red blood cells by formalin fixation is ideal for diagnostic purposes because erythrocytes, when present in large numbers, tend to obscure the less numerous epithelial cells.

Staining. After fixation, the slide is rinsed successively in two jars of distilled water and then stained for from two to three minutes in freshly filtered, weak, Hortega (silver carbonate) solution. Any excess of silver carbonate solution is removed by touching the side or end of the slide to absorbent paper. The slide is next placed in a solution of 1-percent formalin for one minute, where reduction of the silver carbonate occurs. Following reduction, the slide is rinsed in distilled water. At this time the smear may be examined under the microscope for staining quality. In the event that the stain is too light, the slide may be returned to the Hortega solution for from two to three seconds and then reduced once more in 1-percent formalin. This reinforcement of color takes place very rapidly, and care should be taken to prevent excessive impregnation with the silver carbonate. After rinsing in distilled water, the slide is dried in air, rinsed in xylol, and mounted in clarite.

It has been found practical, when only a few slides are being stained, simply to cover the surface of the slide with Hortega solution. This may be accomplished readily by pouring a small quantity of the solution into a funnel with filter paper in place. With the funnel held in position over the slide, the necessary amount of staining solution may be deposited on the surface of the slide and the remainder of the solution returned to its container. This procedure results in little loss of silver carbonate solution.

Undiluted Hortega solution should be stored in a brown bottle and can be kept available for ready use for from three to four weeks. The stock solution is prepared by adding ammonium hydroxide until the solution becomes clear to 100 c.c. of 10-percent silver nitrate plus 300 c.c. of 5-percent sodium carbonate. The weak Hortega solution is prepared by adding 275 c.c. of distilled water to 100 c.c. of stock solution; it should be filtered immediately before using.

Staining Characteristics of the Vaginal Smear. All the cellular components of the vaginal smear are readily identified following silver impregnation. In general, the cells are in marked contrast to those stained by other methods, for they are less transparent and stand out in bold relief against a clear or pale gray background. The increased absorption of light by the silver-treated smear reduces the disturbing glare which usually characterizes a thinly spread smear preparation.

Leucocytes. These cells are frequently a conspicuous feature of the vaginal smear. The nuclei stain intensely black, while the cytoplasm stains a pale yellow.

Normal Epithelial Cells. The cytoplasm of superficial vaginal squamous cells stain a light yellow or pale brown. The nuclei vary in color from dark brown to jet black. Frequently an intricate network of chromatin is apparent in the nucleus of noncornified squamous cells. The details of the chromatin elements are revealed with striking clarity.

The cytoplasm of the smaller vaginal basal cells, as well as that of endometrial cells, usually appears darker than that of the larger, more superficial squamous cells.

General Features of Malignant Cells. Malignant cells, stained with silver carbonate, are recognized with relative ease due to the intense staining of their hyperchromatic nuclei. The recognition of these cells is further enhanced by the fact that their cytoplasm is frequently more darkly stained than that of the other cellular elements of the smear, this being particularly true for the less differentiated malignant-cell types. In many preparations, the cytoplasmic stain resembles that of the basal squamous epithelial cells. The color is fairly comparable to that of burnt sienna.

Although individual abnormal cells are readily recognized, one's attention is particularly attracted to groups of malignant cells in which the opaque blackness of individual nuclei permits the group to stand out conspicuously from neighboring cellular elements.

Aberrations of Malignant Cells as Seen Following Silver Staining. Various cellular aberrations are reported to be commonly found in the presence of cancer of the cervix or of the body of the uterus. These variations are readily revealed by the silver staining technic.

Because of the distinctness of cellular outline, variations in shape and size of cells are easily observed. Recognition of significant nuclear irregularities is enhanced by the remarkable affinity of the chromatin elements for the silver stain. Thus, variations in nuclear size or shape, disproportion between nuclear- and cell-size, nuclear fragmentation, and nuclear multiplicity are readily distinguished from nondiagnostic elements in the smear. (Am. J. Obst. and Gynec., Sept. '48)

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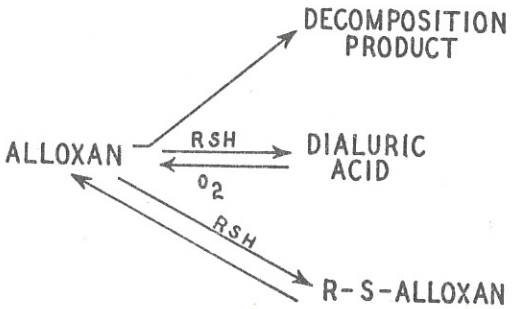
The Mechanism of Cysteine and Glutathione Protection Against Alloxan Diabetes: The suggestion that alloxan may produce diabetes because of inactivation of essential sulfhydryl enzymes of the beta cells of the pancreas was made in an earlier paper by Lazarow. Inasmuch as large doses of alloxan also destroy other cells (liver, kidney, etc.), it also was postulated that the selectivity of this compound for the beta cells might be due to an especially low glutathione content which rendered the beta cells more susceptible to alloxan.

The injection of large doses of glutathione, cysteine, thioglycolic acid, and BAL protected rats against a diabetogenic dose of alloxan. By contrast, large doses of alanine, methionine, thiourea, and other compounds did not modify its diabetogenic effect. Protection against diabetes by these sulfhydryl compounds occurred only when they were given prior to the diabetogenic dose of alloxan. When glutathione or BAL was given 5 minutes after a diabetogenic dose of alloxan, no protection occurred. Since protection failed to occur when the sulfhydryl compound was given after the alloxan, it was suggested that, if the diabetogenic action of alloxan is due to a combination with essential sulfhydryl groups of enzymes, this reaction would not be as readily reversed as would be the case if the SH groups of the enzymes were simply oxidized to SS groups. However, a combination of alloxan with the SH groups would explain the failure to protect against diabetes when the sulfhydryl compound was given following the diabetogenic dose of alloxan.

Inasmuch as alloxan, dialuric acid (reduction product of alloxan), and derivatives of these compounds are unstable, the ultraviolet absorption spectra method was considered suitable for studying the possible reactions of alloxan with sulfhydryl molecules. This necessitated the study of the absorption spectra of alloxan and dialuric acid, which previously were reported as having no maxima.

The data suggest the following conclusions, which are illustrated in the figure on the next page.

Alloxan is rapidly decomposed at pH 7.4. It is also reduced to dialuric acid by sulfhydryl compounds. With alloxan and glutathione (as compared with cysteine), the formation of a maximum at 305 mμ is striking, and is thought to be due to formation of an addition product which would appear to be similar to that described



by Schubert in his study of the reaction of carbonyl groups with sulfhydryl. Because the addition of cysteine will convert alloxan to dialuric acid, the fact that added cysteine slows down the formation of a product with an absorption spectrum maximum at 305 mμ indicates that the mechanism involves a reaction of glutathione with alloxan rather than with dialuric acid. Since oxidized glutathione fails to react, the addition product is believed to take place through the sulfhydryl group of the glutathione.

The mechanism by which cysteine protects against alloxan diabetes is probably due to the reduction of alloxan to a nondiabetogenic compound, dialuric acid. Although dialuric acid can be reconverted to alloxan, this reconversion is also slowed by cysteine, thus preventing the formation of an effective concentration of alloxan. In addition, glutathione removes alloxan from the field of action by forming a new compound with an absorption spectrum maximum at 305 mμ. These results might explain why the administration of a large dose of sulfhydryl, given 5 minutes after a diabetogenic dose of alloxan, fails to protect rats from diabetes. For, if the alloxan has already reacted with proteins as indicated in the data (presumably with the sulfhydryl groups of essential enzymes), the addition of sulfhydryl might not be expected to reverse this reaction. The data also support the contention that dialuric acid itself is not diabetogenic, but that the diabetes observed after the injection of dialuric acid is due to the conversion of dialuric acid to alloxan in the body.

Since it has been reported that an enzyme contained in dog liver can convert uric acid into dialuric acid, and since the injection of dialuric acid produces diabetes, presumably by conversion to alloxan, there is a reasonable chance that alloxan may also occur in man.

In a preliminary note Griffiths claimed the production of diabetes by the injection of massive doses of uric acid into a glutathione-depleted rabbit.

Should alloxan prove to be a factor in human diabetes, the reaction between glutathione and alloxan herein reported would have an important bearing on its cause and prevention. (Science, 17 Sept. '48 - A. Lazarow et al.)

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Proteus OX19 Agglutination in Pregnancy: In 1942 Gratch reported that the serum of pregnant women gave a positive Proteus OX19 reaction without regard to a history of or finding of rickettsial disease. One hundred percent of his group of pregnant women had positive reactions, whereas the only false positive tests in the nonpregnant group occurred in the presence of malignant disease. He

questioned whether the reaction might not form the basis for a diagnostic test in pregnancy. White in 1945 was able to confirm these findings partially, but the author and co-workers have noted no other reports in the American literature on this phenomenon.

Because of the potential value of this finding in the diagnosis of rickettsial infections or of pregnancy, this test was carried out in 402 women of whom 207 were pregnant and 195 were not.

The 207 women were selected at random from those attending the prenatal clinic. The duration of their pregnancies, at the time of the tests, ranged from two to nine months. The nonpregnant women were outpatients of other clinics or inpatients of the hospital. Commercial Proteus OX19 antigen was employed. In all the tests here reported the slide technic was used, questionable clumping being checked under the microscope.

Results. Of the 207 tests on pregnant women, 73.9 percent were positive to some extent, ranging from 1:20 to 1:640. The findings on this group indicate that neither the percentage of positive reactions nor the height of the titer is statistically proportionate to the duration of the pregnancy.

Of the 195 nonpregnant patients some degree of agglutination (from a titer of 1:20 to 1:320) was found in 81 or 41.5 percent.

To a certain extent the number of false positive reactions found in the control group may be attributed to the fact that these women were selected from the clinics and wards of the hospital, with diagnoses ranging from acute infections to malignant tumors. Nevertheless, a considerably higher percentage of the pregnant than of the nonpregnant patients gave positive reactions.

The data indicate that the Proteus OX19 reaction as performed by the author cannot serve as a reliable aid for the diagnosis of pregnancy. It does indicate, however, that the presence of pregnancy may render the test less useful in the identification of rickettsial disease. (Am. J. Clin. Path., Aug. '48 - A. C. Barnes)

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Personal Factors for Developing Safety Consciousness: The foundation of a significant safety consciousness is laid deeper than simple adherence to a code of safe practices. It comes about, in its best sense, when all who are concerned in an undertaking - management, supervision, and the working force - understand all the conditions requisite to efficient production and are willing, by necessary training and standards of practice, to avoid those inefficiencies which lead to accidents and other losses. The personal factors for developing safety consciousness are fully discussed. (Mech. Eng. - W. A. Cutter, through Indust. Hyg. Digest, Aug. '48)

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Taking Odors Out of Air: Bad odors in exhaust air made a serious problem for a manufacturer of vitamins and hormones, as they do in the perfume industry and others. The problem was solved by passing the air through activated carbon in specially constructed canisters. First it is necessary to remove dust which would clog the pores of the carbon. A fairly large percentage of the air can be recirculated. In the installation described, it was necessary to enlarge the operation requiring odor removal. It was found that the 25-percent outdoor supply could be decreased, rather than bring in additional air requiring heating or cooling. Details of placing of canisters, rate of air flow, and data for recirculation are given. (Factory Man. & Maint., Aug. '48 - G. A. Van Brunt, through Indust. Hyg. Digest, Aug. '48)

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Diphtheria and Tetanus Toxoids, Alum Precipitated, Combined with Pertussis Vaccine, Now Available: The following item for use in dependent service is now available for issue in the medical supply system:

> Stock No. 1-602-600 Diphtheria and Tetanus Toxoids, Alum Precipitated, Combined with Pertussis Vaccine, 7 and 1/2 c.c.: Potency 18 months. Unit - Bottle.

One unit is sufficient for 5 complete immunizations, each consisting of three 1/2 c.c. injections. (Materiel Div., BuMed)

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Active Duty Billets Available to Naval Reserve Medical and Dental Officers: There are vacant full-time active duty billets for Naval Reserve medical and dental officers, especially younger officers, at many stations in the United States and beyond the continental limits. To become eligible to receive the additional compensation of $100 per month authorized by Public Law 365, 80th Congress, inactive Reserve officers should apply to BuPers via their district commandants for active duty for a period of one year or longer. Assignments must be made in accordance with service requirements, but, requests for active duty may include a list of three preferences showing localities or areas in which such duty is desired.

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Re Naval Immunization Requirements for Overseas Travel: The attention of the Bureau of Medicine and Surgery has been directed to the fact that civilians, mainly dependents, have arrived at ports of embarkation without proper immunizations required for travel to their destination. Reports have been made that advice on immunization requirements has been furnished to civilians and dependents by personnel of naval medical activities to the effect that certain immunizations were not required, or that immunization may be accomplished at ports of embarkation. Information of this type not only is contrary to instructions in the MMD, Part III, Chapter 5B, but also reflects upon the efficiency of the service provided, causes avoidable delay and hardship to civilians and dependents in travel status, and imposes unwarranted responsibility for immunization procedures upon medical activities at ports of embarkation. In addition to the requirements as set forth in the MMD, travel instructions which contain specific information on immunization requirements are forwarded to Navy dependents contemplating travel.

The immunizations of civilians and naval dependents, traveling outside of the continental United States under the cognizance of the Navy Department, must be completed prior to arrival at ports of embarkation. (Preventive Med. Div., BuMed)

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Opportunity for Reserve Dental Officers for Full-Time Active Duty in the Naval Air Reserve Program: There are several vacant billets available for reserve dental officers at air stations of the Naval Air Reserve Training Command.

These stations are as follows:

NAS, Seattle, Washington
NAS, Spokane, Washington
NAS, Birmingham, Alabama

Applications for this duty are desired from dental officers of the Naval Reserve not above the rank of lieutenant commander. Applications should be addressed to the Chief of Naval Personnel via the District Commandant, the Chief of Naval Air Reserve Training, and the Chief of the Bureau of Medicine and Surgery, listing the stations (in order of preference) at which duty is desired.

Reserve dental officers having previously applied for duty in connection with the Naval Air Reserve Program should resubmit their applications if still interested in being ordered to this duty.

Applicants should volunteer for one year or more of active duty in order to become eligible for the additional compensation of $100 per month authorized by Public Law 365, 80th Congress.

Under the present policy Reserve dental officers accepting these assignments will not be subject to change of duty station. (Dental Div., BuMed)

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Training Program for Entomologists and Malariology Technicians of the Naval Reserve: BuMed Circular Letter 48-105 on page 34 contains information which concerns training planned for entomologists and malariology technicians during their annual tour of duty for two weeks.

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New Forms for Physical Examination and Medical History: BuMed Circular Letter No. 48-103 on page 32 contains information concerning the adoption by the Navy and the beginning use on 1 January 1949 of new forms for recording medical history and physical examination findings.

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BUPERS CIRCULAR LETTER 48-162 25 August 1948

To: All Ships and Stations

Subj: Annual Physical Examinations, Calendar Year 1948

Ref: (a) General Order 191, of 28 May 1943.

1. The following is promulgated for guidance in connection with the annual physical examination required by reference (a):

(a) It is directed that any officer concerned who is not examined prior to 1 February 1949 submit a letter to the Bureau of Medicine and Surgery setting forth the circumstances involved.

(b) Physical examinations conducted during the calendar year 1948 in the cases of officers of the Naval Reserve or temporary officers USN for the purpose of determining physical fitness for permanent appointment in the Regular Navy will obviate conducting an annual physical examination in such cases, during the calendar year 1948.

(c) A physical examination conducted incident to temporary promotion shall be considered as not sufficient to obviate an annual physical examination.

(d) Attention is invited to the provisions of paragraph 21104, Manual of the Medical Department, in connection with the conducting of the annual physical examination. In evaluating fitness for duty, due consideration shall be given action taken on recent reports by boards of medical survey and also to existing waiver of defect or disease.

(e) An electrocardiogram shall be conducted in the cases of all officers who are 45 years of age or over. A complete blood count and sedimentation index, a blood Kahn test, a prostatic examination, and any other special study that may be indicated shall be performed at the discretion of the examiner.

(f) In those cases where a chest X-ray study has not been conducted within the past year as required by paragraph 21103.2, Manual of the Medical Department, a chest X-ray study shall be conducted as a part of the annual physical examination.

(g) There will be no special boards convened for the purposes of examining senior officers.

2. Attention is invited to existing instructions which require that a NavMed-Y, or a NavMed-AV-1 in the case of aviators, be completed and forwarded only in those cases in which defects are discovered which are regarded as sufficient to impair the examinee's ability to perform his duties. When such reports are forwarded the examiner shall indicate the proposed local action to be taken, whether it be observation on active duty; ambulatory treatment; transfer to hospital at once or when later indicated; professional advice intended for correction, arrest, or improvement in disease process; or other appropriate action. Indiscriminate transfer to a hospital should be avoided, but such disposition may be warranted early in the course of a disease such as arterial hypertension to

afford thorough case study and fully considered corrective and preventive therapeutic program. In those cases wherein officers are physically qualified in all respects, an entry on NavMed-H-8 of the health record constitutes an appropriate record of the examination.

3. Attention is invited to the provisions of paragraphs 21104 and 2221.4, Manual of the Medical Department, regarding the forwarding of reports of annual physical examinations. The letter of transmittal required in paragraph 5 of reference (a) shall be omitted.

4. Officers who are hospitalized for study or treatment by direction of the board of medical officers conducting the annual physical examination shall be further examined by a board of medical survey to determine their physical fitness for return to duty.

--BuPers J. W. Roper

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BUSHIPS LETTER
JJ51-(16)(688), EN28/A2-11 25 August 1948

To: All Ships and Stations

Subj: Antifogging Agents for Gas-Mask Lenses, Eye Protectors, and Lenses in the Facepieces of Various Types of Respiratory Protective Apparatus

Ref: (a) BuShips ltr. JJ51-(16)(688), EN28/A2-11, of 22 July 1946.

1. Reference (a) stated that results of tests made on antifogging agents showed that the material issued with various protective apparatus was toxic and a source of dermatitis and that such material should be turned into store at the nearest naval activity for disposition. Reference (a) further stated that this material could be identified by the trade name of "Fogpruf" as manufactured by the Mine Safety Appliances Company.

2. In releasing reference (a) the Bureau inadvertently omitted information that the "Fogpruf" referred to was the type which was in paste form and not the liquid "Fogpruf" which is also made by the Mine Safety Appliances Company.

3. Since reference (a) was released, Navy Department specifications for antifogging materials for the subject purpose have been revised to insure that these materials as procured are nontoxic, nonlachrymatory, and nonirritating. The revised specification is N:51-C-68. Materials procured under this specification are now stocked as "Antifog Kit," Standard Stock No. 37-K-380 and may be obtained on requisition. So far, the brand names and manufacturers of antifogging materials whose product is acceptable under the specification referred to above are as follows:

Trade Name	Type	Manufacturer
Antifog Compound	Paste	American Cynamid Co.
MSA Fogpruf #52	Liquid	Mine Safe Appliances Co.
Ceiling 0	1, 2, & 9	Specialties Incorporated.
Mistoff	Impregnated cloth	O. K. Linck Co., Inc.

-BuShips P. D. Gold, Jr.

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BUMED CIRCULAR LETTER 48-99

17 September 1948

To: MedOfComs, U.S. Naval Hospitals; U. S. Naval Medical Supply Depots; National Naval Medical Center, Bethesda, Md.; Naval Medical Center, Guam, M. I.

Subj: Appointment of Industrial Relations Officers (Civilian Personnel Officers)

Refs: (a) BuMed Cir. Ltr. 47-27 of 27 Feb 1947.
(b) BuMed Cir. Ltr. 48-79 of 15 Jul 1948.
(c) NCPI-125.
(d) NCPI-135.2-3c

1. The most recent revision of reference (c) deletes the requirement for prior approval of the cognizant bureaus for the appointment of Industrial Relations Officers (Civilian Personnel Officers). Accordingly, reference (a) is hereby modified.

2. In the addressed activities the titles "Personnel Officer" and "Civilian Personnel Officer" shall be synonymous since reference (b) requires that responsibility for civilian personnel administration be assigned to the Personnel Officer (Chief of the Personnel Division). The civilian employee assigned as head of the Civilian Personnel Section in accordance with reference (b) shall be designated "Civilian Personnel Assistant." This shall be an organizational title and should not be confused with the payroll title assigned to this position by the Area Wage and Classification Office.

3. The title "Industrial Relations Officer" will not be used hereafter in the addressed activities. Delegation of responsibility to the Personnel Officer and the Civilian Personnel Assistant, including the signing of mail by direction, is a matter for local determination, except that civilian personnel actions shall be signed in accordance with reference (d).

-BuMed H. L. Pugh

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BUMED CIRCULAR LETTER 48-100 17 September 1948

To: All Medical Department Activities

Subj: Navy Day - Medical Department Participation in

Refs: (a) SecNav ltr dated 19 June 1948.
(b) SecNav ltr dated 1 September 1948.

This letter directs, (1) that addressees participate to the fullest extent during Navy Day Week, from 23 to 29 October in accordance with references (a) and (b), and (2) that clippings of press items and photographs published be forwarded to BuMed.

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BUMED CIRCULAR LETTER 48-101 23 September 1948

To: All Medical Officers and Dental Officers

Subj: Selective Service Act of 1948; Procedures for Administration of

Encl: (A) (HW) Army Regulations 40-115 dtd 20 Aug 1948.

1. In connection with the procedures for administration of the Selective Service Act of 1948, the Army Regulations are to be used as representing the physical standards and physical profile method of classification in connection with induction and discharge of all male enlisted and inducted personnel.

2. Enclosure A represents the physical standards and procedure in relation to classification of an individual's functional ability to perform duty in connection with induction and separation from service for physical disability insofar as the administration of the provisions of the Selective Service Act of 1948 are concerned. The enclosure is furnished for your information and guidance in advance of the regulations which are to be promulgated shortly by BuPers, BuMed, and MarCorps in connection with the administration of the Selective Service Act.

3. In interpreting the contents of the enclosure the references to Army Regulations or Department of the Army will be interpreted as being representative of the Naval Service.

--BuMed H. L. Pugh

NOTE: The enclosure, Physical Standards and Physical Profiling for Enlistment and Induction, contains 57 pages.

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BUMED CIRCULAR LETTER 48-102 23 September 1948

To: All Holders of the Bulletin of Bureau of Medicine and Surgery Circular Letters, NavMed-937.

Subj: BuMed Circular Letters, Cancellation of Several

By this letter, several BuMed circular letters are cancelled. The reason for cancellation are indicated.

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BUMED CIRCULAR LETTER 48-103 23 September 1948

To: All Ships and Stations

Subj: Report of Medical Examination, Standard Form 88; and Report of Medical History, Standard Form 89; Use of

Refs: (a) BuMed C/L 47-156 dtd 12 Nov 1947; AS&SL July-Dec 1947, 47-1064, p. 250.
(b) Para 2115, Manual of the Medical Department.

Encls: (A) (HW) Completed sample copy of Standard Form 88 (Report of Medical Examination).
(B) (HW) Aviation adaptation of Standard Form 88 (Report of Medical Examination).
(C) (HW) Completed sample copy of Standard Form 89 (Report of Medical History).
(D) (HW) Vision Conversion Chart.

1. The standard forms referred to herein shall be placed in use effective 1 Jan 1949 in order to comply with instructions issued by the Bureau of the Budget.

2. The Report of Medical Examination, Standard Form 88, enclosures (A) and (B), replaces the present Report of Physical Examination, NAVMED-Y, and the Physical Examination for Flying, NAVMED-AV-1, and shall be executed in all instances now requiring the use of these forms. It is permissible to use the NAVMED-Y and AV-1 forms if there is a delay in receiving the Standard Form 88. Existing stocks of NAVMED-Y and AV-1 forms should be destroyed upon receipt of the initial supply of Standard Form 88.

3. The Report of Medical History, Standard Form 89, enclosure (C), replaces several medical questionnaires now serving the same purpose, including enclosure (A) to reference (a); and a report shall be executed in ink in the following cases:

(a) Original applications from civilian or military personnel for appointments in the regular Navy, Naval Reserve, Marine Corps or Marine Corps Reserve, and for transfer from the Naval Reserve to the regular Navy, or from the Marine Corps Reserve to the Marine Corps. The completed Report of Medical History (S.F. 89) on officer applicants should be forwarded with the Report of Medical Examination (S.F. 88) to the Bureau of Medicine and Surgery.

(b) Applications of all men and women for enlistment in the regular Navy, Naval Reserve, Marine Corps, or Marine Corps Reserve. Men and women with prior regular Navy or Marine Corps service re-enlisting in the USN, USNR, USMC, or USMCR will be required to execute this form only when enlistment is not effected under conditions of continuous service; i.e., within 3 months following date of discharge. The completed Report of Medical History, Standard Form 89, on applicants for enlistment should be forwarded with the Physical Examination, NAVMED-H-2, to the appropriate training station which will in turn forward the papers to the Bureau of Medicine and Surgery.

(c) Applications of all candidates for Officer Training Naval Academy, N.R.O.T.C., Midshipmen Merchant Marine Reserve, Marine Corps Officer Training programs, and Naval Aviation Cadets). The completed Report of Medical History (S.F. 89) should be forwarded with the Report of Medical Examination (S.F. 88) to the Bureau of Medicine and Surgery.

4. The Manual of the Medical Department, reference (b) in particular, will be revised to reflect the changes brought about by the introduction of subject forms. Adaptations to meet present requirements should be made locally; e.g., under Item 28, Report of Medical Examination (S.F. 88), indicate chest expansion, and, in the blank space under Item 18, Report of Medical History (S.F. 89), give the answer to Question 24 on enclosure (A) to reference (a) in order to complete the information now included therein. Enclosure (D) is an aid for the recording of eye examinations on the Report of Medical Examination (S.F. 88).

5. Subject standard forms will be stocked by all District Publications and Printing Offices and should be requisitioned by all activities concerned in sufficient time to assure receipt of stock prior to 31 December 1948. Requisitions should be carefully scrutinized by responsible officers in order to eliminate ordering an excessive supply. Normally, the supply of forms should not exceed a three months' requirement.

6. The standard forms are considered to be in a trial status for the first year. During this period the Bureau desires comments and suggestions for revisions which will be considered by a Federal interagency committee on medical forms.

--BuMed H. L. Pugh

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BUMED CIRCULAR LETTER 48-104 28 September 1948

To: Medical Officers in Command, All Naval Hospitals

Subj: Pictures for Use in the Nurse Procurement Program

Addressees are requested to furnish BuMed with approximately 12 pictures which show nurses performing various professional duties, in and around their living quarters, in recreational areas, etc.

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BUMED CIRCULAR LETTER 48-105 28 September 1948

To: All Naval Districts (Continental) and PRNC

Subj: Training Program for Naval Reserve Entomologists and Malariology Technicians

Encl: (A) Proposed Program of Activity for Annual Tour of Duty (2 Weeks) for Naval Reserve Entomologists and Malariology Technicians

1. The Commanding Officer, Naval Air Station, Jacksonville, Florida, has informed this Bureau of the establishment of a Training Program for Naval Reserve Entomologists and Malariology Technicians. This program will provide an opportunity for Reserve personnel to receive two weeks annual training duty in an area where insect control problems are encountered throughout the year. The existence of a major mosquito problem and the presence of staff, equipment and large scale operations of the Malariology and Pest Control Unit at the Naval Air Station, Jacksonville, provide uninterrupted and excellent facilities for a course of instruction at this station.

2. The training periods are scheduled to begin on the first and third Wednesday of each month as required but if applicants for training find these dates cannot be met, other dates may be arranged during such periods as no regularly scheduled classes are convened.

3. The attention of addressees is invited to this training program and it is desired by this Bureau that its utilization be given consideration where quotas and funds permit.

--BuMed H. L. Pugh

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BUMED CIRCULAR LETTER 48-106 29 September 1948

To: All Ships and Stations

Subj: Hospitalization and Medical Care of Dependents of Armed Forces Personnel Under Auspices of the Medical Department of the Navy

Refs: (a) Sec. Defense ltr dtd 12 Aug 1948 to SecNav, SecArmy, and SecAirFor.
(b) Pt IV. Ch I Sect II Manual Medical Department.
(c) BuMed Circ Ltr No. 45-78
(d) BuMed Circ Ltr No. 48-69

1. The Secretary of Defense in reference (a) has declared it to be the policy of the National Military Establishment that the several Services afford medical care for dependents on a reciprocal basis, within the limits of facilities, funds, and personnel and to an extent consistent with the over-all preparedness and efficiency of the National Military Establishment; and that the rates charged for medical care of dependents be uniform throughout the National Military Establishment.

2. The terms "several services" and "National Military Establishment" as used herein, are defined as comprising the U. S. Navy, U. S. Army and U. S. Air Force. The term "medical care" is defined as including in-patient and out-patient care.

3. Effective 1 October 1948, those naval activities having facilities for medical care of dependents are authorized to provide medical care for dependents of active duty personnel of the Army and Air Force in like manner as now provided for dependents of naval personnel, as set forth in reference (b) and (c), under the following conditions, emergent cases excepted:

(a) The Navy has medical facilities available for the care of dependents, and
(b) The Army or Air Force has no medical facilities for dependents reasonably available in the Area.

4. Dependents of active duty naval personnel only may be provided medical care at Army and Air Force medical facilities in like manner as now provided at naval medical activities, under the following conditions, emergent cases excepted:

(a) The Army or Air Force has medical facilities available for the care of dependents and
(b) The Navy has no medical facilities for dependents reasonably available in the Area.

5. Dependents of naval personnel will be required to present a Dependent's Identification Card NAVMED-562 in making application for medical care at Army or Air Force medical facilities. Dependents of Army and Air Force personnel will employ a current Commissary or Post Exchange Permit as a

means of identification in making application for medical care at naval medical facilities. In the absence of a Commissary or Post Exchange Permit, such other official identification as will establish identity to the satisfaction of the medical officer will be accepted.

6. The per diem charge for in-patient hospitalization of dependents of Army and Air Force personnel at naval medical activities within and outside the continental limits of the U. S. and Alaska will be $1.75. Monies so collected will be accounted for in the same manner as set forth in reference (d) for dependents of naval personnel. There will be no charge for out-patient treatment.

7. Naval hospitals shall report dependents of Army and Air Force personnel on line 77 of the Monthly Ration Record, NAVMED HF-36, including an analysis under "Remarks" of the above report, indicating the number of sick days applicable to dependents of Army and Air Force personnel separately. Necessary detailed financial data applicable to these patients should be reported on line 8, Section G, of the Monthly Ration Record, in accordance with the same instructions that apply to the reporting of this data for dependents of Navy and Marine Corps personnel. At other than naval hospitals, all naval medical facilities shall submit only one report of hospitalization of all dependents. However, an analysis should be included in the report, indicating the number of days applicable to dependents of (1) Navy and Marine Corps, (2) Army, and (3) Air Force personnel, separately. Separate reporting on Monthly Summary Medical Care of Dependents, NAVMED-669, is not required.

8. Appropriate changes in the Manual of the Medical Department will be issued separately.

--BuMed C. A. Swanson

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