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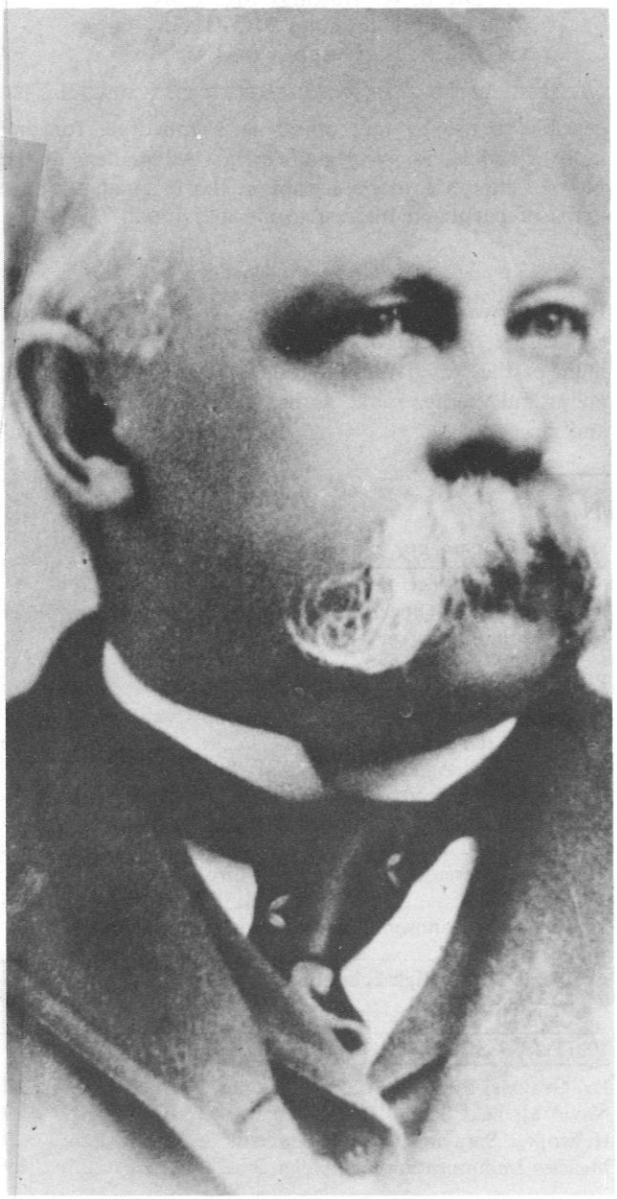

Surgeons General of the Past

(The fifteenth in a series of brief biographies)

Newton L. Bates, fifteenth Chief of the Bureau and eleventh Surgeon General, was born in New York in 1838 and received medical training in that state. He received his appointment as Assistant Surgeon in the Navy from President Abraham Lincoln 30 July 1861. After first being attached to the New York Naval Hospital he had duty in the Seneca in the South Atlantic Blockading Squadron, and later went to the Benton of the Mississippi Squadron. From 1864 to 1867 he served at the United States Naval Laboratory in New York, the forerunner of the Naval Laboratory and Department of Instruction, which later became the Naval Medical School (1902) and the Naval Medical Supply Depot (1906). Founded in 1853, Surgeons B. F. Bache and E. R. Squibb had carried on the manufacture here of chloroform and ether for the Navy. Doctor Bates was promoted to Surgeon on 16 September 1865. After the Civil War he had extensive sea duty, serving on the Portsmouth, the Swatare, Miantonomah, Pawnee, Brooklyn (as Fleet Surgeon), and the Minnesota. He commanded the naval hospital in Yokohama, Japan for 2 years and was attending surgeon in Washington, D.C. from 1884–1887, being promoted to Medical Inspector in June 1881 and Medical Director in September 1888. After commanding the Mare Island Naval Hospital and serving at the Naval Museum of Hygiene, he was appointed Surgeon General of the Navy by President William McKinley on 1 October 1897. Doctor Bates was a close personal friend of the President and was the McKinley family physician. His term of office was shorter than that of any other Surgeon General. He was ill when appointed, took the oath of office at home, was unable to go to his office in the Navy Department, and died on 18 October 1897.

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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

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The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

FROM BOARDWALK TO BEDSIDE—CLINICAL RESEARCH IN AMERICAN MEDICINE

An Editorial Reprinted from Ann Intern Med 66(2):437–440, February, 1967.

Every year in the first week of May the boardwalk in Atlantic City is the site of a very special agglutination. Here for 4 days congregate medical teachers and clinical investigators of the American medical scene: physician-professors, their colleagues, and subordinates on down through the various levels to the freshest and most enthusiastic neophytes in medical science and clinical investigation. These are the "Spring Meetings."

The parent organization of this gathering is the Association of American Physicians. Founded 75 years ago by Sir William Osler and a small group of medical teachers, the Association has set a high standard of excellence for medical practice and medical science. But youth is ever impatient with its elders. In 1913 a junior society was formed to permit the presentation and discussion of clinical research at a scientific level more advanced than that indulged in by the Association. Thus was born the American Society for Clinical Investigation. Election to either or both of these societies has become a highly coveted honor, for which the competition has become increasingly keen over the years. In 1942 history repeated itself. At the urging of Henry Christian, late professor of medicine at Harvard, a still younger group of physician-investigators founded the American Federation for Clinical Research. This new society by its unrestricted membership has greatly broadened the opportunity of able young clinical investigators to present their work—work that is quite as excellent as that of their elders.

This cold cataloging of organizations, however, gives little hint of the stirring and delightful potpourri of new ideas and old friends that is the essence of these 4 days. The formal meetings are held in Haddon Hall or (in the past) in the Steel Pier Theater, and the opening presidential address in each organization is always a star occasion with its offering of wisdom and penetrating analysis. The scientific sessions each year become more stimulating as one's interests broaden or more frustrating as the accelerating rate of basic science leaves one floundering in a particular bay of personal ignorance. But the informal meetings are the ones that count the most; these are held in rooms, over drinks, and across memorable repasts of raw oysters and broiled lobsters that are being conducted to their predestined goal. And on the boardwalk hospital-bound workers bask in the sunlight, breathe in the brisk salt sea winds, and discuss the intellectual fare offered during these 4 days. Of what does this fare consist?

In two special articles in this issue of the *Annals,* Feinstein, Koss, and Austin present a detailed analysis of the scientific material submitted to the "Spring Meetings" of these three national organizations over the past 13 years. At first glance the importance of this survey to nonacademic physicians may be queried; the members and attenders of these meetings are only a small segment of the medical profession. Yet, because those who attend the "Spring Meetings" constitute the major portion of clinical investigators and medical educators in this country, the influence of the scientific content of these meetings ultimately will be felt by every practitioner of medicine throughout the land.

What are Drs. Feinstein, Koss, and Austin telling us about today's clinical research that will influence so strongly tomorrow's practice? In the main, their analysis shows that medical research in this country has not only grown tremendously in volume over the past 1½ decades but has also moved in the direction of a greater proportion of nonclinical projects. The proportion of "clinical" research projects—that is, those that contain human material, are disease oriented, or are "people centered"—has diminished, whereas the proportion of those that contain nonhuman material and are not disease oriented has increased. It is true that the program of the Association of American Physicians has contained more "clinical" subject matter than the other

two societies, but even here the "clinical" content has decreased.

Such a trend, of course, should surprise no one. It has not been confined to these three societies; it can be found in the program and publications of other national and regional medical organizations. The program of the 34th Annual Session of the American College of Physicians in 1953 contained no "nonclinical" titles; in that of the 1965 Golden Anniversary Session of the ACP 10 percent of the papers were in the "nonhuman, nondisease" category. This trend indicates that the so-called "basic" sciences are being used increasingly to gather knowledge that in the future may contribute to the understanding of disease processes and thus to the care of patients. Today's insights into the mechanism of deoxyribonucleic acid and ribonucleic acid in bacteria may lead to tomorrow's diagnosis and treatment of the patient with genetic disease or viral infection. That such "nonhuman, nondisease" projects are reported by, and to, physicians indicates a belief in their ultimate relevance to medical care; otherwise such projects would be reported to scientific organizations of a nonmedical nature.

But the trend does bear directly on certain problems that beset American medicine. The changing character of medical research and medical knowledge has serious implications for undergraduate medical education, for continuing education of the practicing physician, and for the future organization of medical care. Let us consider the effect on undergraduate medical education. At the present time the medical schools are under great pressure to produce more young doctors to meet the medical needs of a population that is both growing in size and demanding better medical service. The accelerating expansion in volume of ever more complex medical techniques and knowledge is making harder the task of the medical schools to meet these increasing demands. An earlier decision will be forced on the profession: whether to increase more rapidly the number of medical graduates and thereby dilute the quality of their medical education, whether to train two types of doctors—scientists and practicing clinicians—thereby producing a real dichotomy in the profession (1, 2), or whether to complement the supply of scientifically trained physicians by the development of a corps of especially trained medical service assistants to relieve doctors and nurses of many of their less difficult tasks (3, 4).

The effect of accelerating medical science on postgraduate medical education is likewise profound. Each year it becomes more difficult for the practicing physician to keep up, even in part, with the new knowledge that can improve his skill in diagnosis and treatment. The need to learn from the medical literature, postgraduate courses, and other programs for continuing medical education becomes more imperative. Physicians share with most other scholars and professional men this problem of coping with an expanding body of knowledge. This has recently been underscored by the report to the American Medical Association of the Millis Commission on *The Graduate Education of Physicians* (5), and lies back of the efforts on the part of the ACP to help its members to evaluate and fill the needs for continuing medical education.

The implications of this trend towards basic science in medical research for nationwide medical care are protean and beyond the scope of this editorial. Clearly, it will push the practice of medicine in the direction of more complex technology; and this, in turn, means reorientation of private practice in the direction of comprehensive health care through group and hospital practice. Even if the medical schools are able to turn out greater numbers of scientifically well-trained young physicians, they will be attracted to the areas of greatest need for family practice only if the organization of medical service is reorganized to accommodate the new technology. Meanwhile the public and the government, both of whom have been supporting generously the expanded programs of medical research, are demanding that the results of the programs be translated much more rapidly into medical care for the people.

Indeed, the university medical schools are under great pressure to move in several directions. One, as indicated above, is to move in the direction of providing more clinical service for their communities (and so threatening each medical school's function as a university institution for acquiring new knowledge). Another is to move in the direction of establishing institutes and laboratories for basic research within the major clinical departments but completely divorced from the department's clinical activities. Some currently independent branches of science, such as botany and inorganic chemistry, appear to have had their origin in such a medical school development. But for medicine as a healing profession such a development poses great dangers. In his recent presidential address last spring before the American Society for Clinical Investigation, Dr. Donald Seldin (6) presented a cogent analysis of these pressures on, and dangers to, a university department of medicine. He warned against separa-

tion of the academic clinician from research and separation of the researcher from clinical problems. The basic investigator has to remember that in a medical school "basic" research is research that is relevant to the problems of sick people. As Seldin puts it:

The elaboration of physiologic laws pertinent to clinical medicine has come increasingly to depend on an appreciation and mastery of elaborate and highly technical tools and theories of biochemistry and biophysics. But so long as the aim is to elucidate issues pertinent to a clinical discipline, the value of the investigation is a function of the insight it provides in the clinical domain. The claim is sometimes advanced, however, that the theories of clinical medicine can in principle always be reduced to more fundamental disciplines. . . . Attempts to reduce all problems to a very basic level may lead to investigations of a type which, whatever their technical sophistication, may be irrelevant from the point of view of clinical physiology and trivial from the point of view of basic biochemistry. . . . In the second place, excessive reductionist emphasis may be doomed to failure because it is by no means certain that physiologic laws can, even in principle, be uniformly reduced to a more fundamental level. In physics it appears impossible to reduce electromagnetic theory to mechanics. Similarly, in clinical physiology it may always be necessary to retain concepts and assert relations within and among organ systems that are neither defined in or derived from basic biochemistry. . . . It is essential, for this reason as well as for others, to cultivate clinical investigation as a basic research activity of practicing clinicians and teachers.

The relevance of these trends in the "Spring Meetings" to the practicing physician lies in the influence they will have in the kind and quality of teaching to which tomorrow's young graduates are being exposed. The task of the medical educator is to decide how much of the almost infinite range of basic science is relevant to the present and future training of the embryo clinician. "How much?" is the question, not "whether any?" Sir George Pickering (7), in his Harveian Oration before the Royal College of Physicians of London, has underscored the indivisibility of science and practice in medicine. The physician may not be able always to function as scientist, but his lack of exact knowledge at any moment is at the same time being overcome by advances in the sciences of chemistry, physics, and biology, and Pickering believes that "for the future of humanity the objectives of the two roles, however difficult they may be to combine in an individual and at a point of time, are ultimately one and the same."

So they should be. And that is why clinical and nonclinical subjects alike are wafted on the salt sea breezes down the boardwalk in Atlantic City at the time of the "Spring Meetings."

J. Russell Elkinton, MD

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PILONIDAL DISEASE

A LOGICAL APPROACH

Richard J. Miller MD, Stephen Mucha MD,† Clinton Lowery MD,† and William C. Turville MD,‡*
Medical Corps, United States Navy. *Postgrad Med 41(4):382–385, April, 1967.*

Pilonidal lesions of the intergluteal area can be managed on an outpatient basis. Treatment consists of obtaining a clean granulating wound and, more important, promoting healing in a warm, moist area of the body which, because of its anatomic location and configuration, lends itself to the accumulation of various foreign bodies, particularly hair. The importance of cleanliness in the intergluteal area is stressed as the basis of preventing recurrence of pilonidal disease.

Pilonidal disease has always been a significant problem in the military service. Although this rather trivial complaint is mentioned only slightly if at all in medical schools, it causes a great deal of discomfort and morbidity. Statistics concerning this disease are convincing. During World War II, from 1942 to 1945, when it was extremely important to have combat-ready men, 77,637 men—the equivalent of five Army divisions—were admitted to Army hospitals for pilonidal disease. In addition, pilonidal disease was found incidentally in 9,000 men admitted for other reasons. The average hospital stay was 43.6 days. No other disease came close to matching this record. Pilonidal disease is still an important problem despite the many informative publications that have appeared about it.

In 1961 there was an average daily census of 20 patients with pilonidal disease on the surgical wards of the United States Naval Hospital, Camp Lejeune, North Carolina. Our survey of the situation agreed with Hardaway's observation that the initial results seemed good after meticulous preoperative preparation and operation; yet large numbers of patients continued to occupy beds in the surgical wards for prolonged periods. This delayed recovery represented a great loss of man-days to the Navy and Marine Corps.

*Commander; † Lieutenant Commander; ‡ Captain, Medical Corps, United States Navy. Dr. Turville was Chief of the Surgical Service United States Naval Hospital, Camp Lejeune, North Carolina, where this paper originated.

The views and opinions expressed herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

The rationale of treatment had been based on a congenital theory of origin. Treatment consisted of wide-block excision of tissue followed by various technics ranging from healing by second intention to rather complicated closures and flaps. However, none of the methods consistently assured rapid healing or prevented recurrences.

History and Pathogenesis

Herbert Mayo published the first case report of pilonidal disease in 1833. Hodges in 1880 proposed the congenital theory of origin, which was almost universally accepted. Some connection with the primitive neural canal was alleged. Pathologists reported an absence of epithelial lining, but this finding was explained on the basis that suppuration had destroyed the lining cells.

The greatest advance in successful treatment of this disease came when several people in varied locations began to wonder what was really wrong and to challenge the congenital theory. Patey and Scharff noted discrepancies between cysts in adults and rare cysts and sinuses in children. True congenital dermal sinuses connected with the meninges were found almost exclusively in children and at varied sites. No sacrococcygeal sinuses were found in babies. These authors later reported hair-containing sinuses in the webs of two barbers' hands. The lesions were excised and found to be identical pathologically to pilonidal cysts. However, the hairs contained in the cysts were of different sizes, shapes and colors. Obviously they had been acquired from numerous persons. Other authors reported similar lesions in the axilla and the umbilicus; some of the cysts were from sheep's wool.

It was observed that a hair placed in a skin cleft that was almost constantly in motion could erode through the skin and form a sinus tract. The hair acted as a foreign body, causing a persistent reaction resulting in the formation of a chronic foreign body sinus.

A logical explanation of the sequence of events began to unfold. At puberty the intergluteal hair thickens and become stiff. During adolescence the intergluteal area is subjected to repeated trauma. Perspiration and poor local hygiene allow sebaceous material, desquamated epithelial cells, hair, bits of toilet tissue and lint, and even fecal material to accumulate in the intergluteal cleft. The skin becomes macerated and soft, and the foreign bodies, especially the hair, enter through the skin. A foreign-body reaction occurs that can progress to infection and deep abscess formation. Epithelium can easily grow down along the tracts. Hair follicles are rarely seen; in fact, the hairs in the sinus can be pulled out and are free at both ends. The hair is "sticking in," not "sticking out."

Thus, a pilonidal sinus is an acquired chronic foreign body sinus, and a pilonidal cyst is a foreign body granuloma at the end of one or more sinus tracts.

Treatment

If one accepts this theory of pathogenesis, it would seem that a simple operative procedure preserving normal tissue would suffice. This had proved true in the past, but failures continued until the emphasis was shifted to the basic principles of wound healing. The key to successful treatment lay in careful postoperative care and long-term preventive medicine.

Abramson, surgical consultant at Walter Reed Army Hospital, Washington, D.C., described in detail a procedure wherein patients with pilonidal disease were treated in the surgical outpatient clinic, thereby allowing them to remain on light duty and reduce lost man-days. The results were reported to be excellent. We decided to adopt this plan with a few changes and innovations. We omitted marsupialization and added cautery with the intention of eliminating the chronic granulomatous tissue that much faster and producing a clean granulating wound that much sooner. Our modified plan is as follows:

Day of operation—The patient is placed in proper position on the proctologic examination table. The intergluteal area is properly shaved and the skin prepared with povidone-iodine (BETADINE ®). Local field block anesthesia is achieved with a 1 percent solution of lidocaine (XYLOCAINE ® hydrochloride) without epinephrine. All sinus tracts are opened with a scalpel, and the accumulations of hair and other debris and grumous tissue are removed, either by wiping with gauze or, if necessary, plucking with forceps. Hemostasis is achieved by compression, and the wound is packed open with iodoform gauze. A pressure dressing is applied.

Second postoperative day—The pack is removed, usually with very little bleeding, and the remaining granulomatous tissue and sac wall are cauterized with phenol and alcohol. The wound is repacked with iodoform gauze, and a pressure dressing is applied.

Fourth postoperative day—The pack is removed, usually revealing a clean granulating wound. The wound is cleaned with hydrogen peroxide and a light dressing is applied.

The individual doctor can modify this operative procedure according to his own ideas and convictions. The only object of the procedure is to obtain a clean granulating wound as quickly as possible. Success or failure depends on the care of the healing wound, especially during the following two to three weeks. Meticulous postoperative care is essential. Many wounds heal naturally, but because of its location this particular wound needs attention and care to heal properly. The same clean granulating wound on a patient's arm or abdomen would probably heal quite rapidly. In fact, according to Joseph and Gifford, barbers often treat pilonidal sinuses in their hands by pulling out the hairs and allowing the sinuses to heal spontaneously. The intergluteal cleft, however, is a dirty area and a perfect receptacle for contaminants already mentioned, in addition to being warm and moist from perspiration.

Our plan for postoperative care required the patients to take sitz baths twice daily. Once each day they were to report to their local dispensary, where a corpsman cleaned the wound with cotton applicators soaked in hydrogen peroxide, removed all accumulated debris, and kept the area shaved. The patients were seen once a week in the surgical clinic until the wound was fully epithelialized.

Results

From November 1961 to May 1964 we treated 362 patients with pilonidal disease. The only patients admitted to the hospital were those having deep abscesses with signs of systemic infection. They received the same treatment as outpatients but remained in the hospital for an average of two to three days after incision and drainage. The average healing time was three to four weeks.

Three percent of the patients had recurrences during this period. These recurrences invariably fell into two groups: (1) small tracts that had been overlooked initially, and (2) bridging of skin and

formation of pockets, which invariably indicated that the patient had neglected to have the area examined for several days. Delayed healing was usually due to incomplete or poor follow-up care or failure to follow the strict regimen as prescribed. In many of the neglected cases we could see the various stages in the formation of a new foreign body granuloma and secondary infection.

Prevention

The prevention of new sinus formation is, of course, of the utmost importance. By following the patients and observing the wound in different stages of repair, we knew that the wound could heal completely. In fact, most of the long-term recurrences were actually new lesions adjacent to or in the healed area.

The conditions at the Marine amphibious base on which our hospital is located were highly conducive to the development of pilonidal disease. Here were young men in a hot moist climate, undergoing the rigors of military training, bouncing about in vehicles, slouching instead of sitting, and going on field exercises during which hygiene is minimal. Conditions were ideal for the accumulation of hair, perspiration, sebaceous material, and desquamated epithelial cells in the intergluteal cleft. In addition, when these men did wash, more often than not they took showers and the water flowed over the exposed surfaces of the body but did not reach the intergluteal cleft.

We instructed all patients to use soap and water daily in the intergluteal region and stressed the importance of removing accumulated debris and hair. We instructed them to keep the area clean and dry and urged them to sit rather than slouch.

Discussion

During the period of this study we eliminated pilonidal disease as an inpatient hospital problem. The Walter Reed Hospital group emphasized that in civilian practice treatment of this disorder can be an office procedure. We agree with this practice as long as the physician has a proctologic examination table so that the patient can be placed in the proper position to expose the operative field. If hospitalization is desired, it need not exceed two or three days. The physician can see the patient every second day at his office until the wound becomes clean and granulating and once or twice a week thereafter until the wound is completely healed. Someone other than the patient should clean the wound daily at home, using hydrogen peroxide. We noted a remarkable difference in cleanliness of wounds and in healing time between married patients who went home every day and single patients who lived in barracks. At first we attributed the difference to the availability of tubs at home for sitz baths, but we soon realized that it was the meticulous care of the wives that accounted for the difference. We had told these patients to return promptly if they noticed hair or debris covered by a film of tissue, making it more difficult to remove. This seldom happened if the wounds were cleaned daily.

Summary

We have presented what we believe to be a simple, logical approach to intergluteal pilonidal disease. Results of our approach, which was based on the findings and experiences of others, have been gratifying. We believe that the regimen described can be adapted successfully to civilian practice.

(The omitted references may be seen in the original article.)

PULMONARY LESIONS ASSOCIATED WITH OXYGEN THERAPY AND ARTIFICIAL VENTILATION*

Gerald Nash MD, John B. Blennerhassett MB, Ch.B, MRACP, and Henning Pontoppidan MD Boston,
New Eng J Med 276(7):368–374, February 16, 1967.

Clinicians concerned with the care of patients requiring mechanical artificial ventilation have been impressed by the occasional development of gradually progressive deterioration of pulmonary function, apparently unrelated to the disease that necessitated the respiratory assistance. These patients have increasing reduction in pulmonary compliance and vital capacity, with consequent hypoxia, are difficult to wean from the ventilator and often die of pulmonary insufficiency. Many have had no respiratory or cardiac disease before the use of the ventilator. Clinicians have referred to this symptom complex as the "respirator lung syndrome." At autopsy in such cases the unusual gross and microscopical appearance of the lungs has raised the question whether the changes are related to a factor or factors inherent in the use of the mechanical ventilator. This study was undertaken to determine whether there is such a clinicopathological entity and, if so, to characterize it and assess the role of clinical and therapeutic variables in its pathogenesis.

Materials and Methods

The study group was composed of 70 patients who were examined post mortem after prolonged artificial ventilation with a mechanical ventilator in the Respiratory Unit of the Massachusetts General Hospital. Although many patients elsewhere in the hospital have received similar treatment those from the Respiratory Unit were chosen for study because more detailed information was available concerning their management. The control group consisted of 70 patients who were examined at autopsy consecutively during approximately the same period as the study group but were never treated with a mechanical ventilator. The 2 groups were comparable in age, sex and underlying diseases. The inherent factor of selection was responsible for certain differences: more cases of postoperative cardiac surgery were included in the study group (17 in the study group and 1 in the control group); there were fewer cases of cancer (7:16), acute myocardial infarction (0:11), bronchopneumonia (22:34) and emphysema (12:18) in the study group.

Combined lung weights and descriptions of the gross appearance of the lungs were obtained from the autopsy records. Before the weights were known it was decided to divide them arbitrarily into 4 groups for easier consideration: 600 to 1000 gm. (high-normal range); 1001 to 1400 gm. (definitely abnormal, but found in a variety of conditions); 1401 to 1800 gm. (more abnormal, but similarly found in many diseases); and over 1800 gm. (unusually heavy lungs found infrequently in the general autopsy population).

In the routine study of lungs at autopsy in this hospital one lung is dissected fresh, and the other is fixed in the inflated state by formalin instillation into the bronchus. Slides from both the study and the control groups were reviewed independently of details of the clinical background of the patient. Clinical, physiologic and therapeutic data from the records of the Respiratory Unit were compiled separately. The combined clinical and pathological information for each case in the study group was then coded on a punch card.

The study group was divided into 4 treatment groups on the basis of a roughly ascending order of duration of treatment with the ventilator and with various concentrations of oxygen, as shown in Table 1.

The patients in Groups 1 and 2 received treatment with oxygen at concentrations between 21 and 90 percent exclusively, with the possible exception of higher inspired concentrations for a few hours before death; patients in Groups 3 and 4 often had received treatment with lower inspired concentrations of oxygen for varying periods as well as concentrations between 90 and 100 percent for the periods stated.

* From the Departments of Pathology, Harvard Medical School, and the James Homer Wright Laboratories of the Massachusetts General Hospital, and from the Anesthesia Laboratories and Respiratory Unit of the Harvard Medical School at the Massachusetts General Hospital.

Table 1. DURATION OF TREATMENT AND OXYGEN CONCENTRATIONS.

Treatment Group	Time on Ventilator	Approximate Oxygen Concentration *
	days	%
1	10 or less	21-90
2	>10	21-90
3	10 or less	90-100
4	>10	90-100

* Most patients were ventilated with pressure-limited ventilators (Bennett PRIA and Bird Mark VII), always in association with mainline humidification. With use of ventilator "air-mix" & with oxygen at 6-8 liters/min. operating mainline humidifier, inspired oxygen concentration is 93% with standard deviation of 6.3%. With compressed air at 6-8 liters/min. operating the nebulizer, oxygen concentration is 61%, with standard deviation of 4.9%. Remainder of patients were ventilated with a volume-limited (Engström) ventilator. With this machine inspired oxygen can be varied between 21 & 100% with considerable accuracy.

Results

Comparison of Pulmonary Pathological Findings in Study and Control Groups

A wide range of gross and microscopical abnormality was encountered since both groups included patients with survivals ranging from twenty-four hours to many weeks. The average combined lung weight of the study group was 1697 gm., and that of the control group was 1176 gm. This difference is statistically significant (p less than 0.001).* Figure 1 shows the distribution of the combined lung, weights of the study and control groups; 32 patients in the study group (45.7 percent) and only 7 patients in the control group (10 percent) had combined lung weights greater than 1800 gm. This difference also has statistical significance (p less than 0.02).† In the patients in the study group lungs weighing over 1800 gm. tended to be deeply congested, inelastic, noncrepitant and of markedly increased consistence, retaining their shape without collapse. The appearance of the cut surface was usually that of a hemorrhagic, "beefy" consolidation throughout, and only a small amount of fluid exudate could be scraped from the surface. In a few cases there was grayish-pink solidification with no demonstrable exudate, suggesting fibrous organization. Conversely, in the control-group lungs of this weight the gross appearance was typical of either "watery" pulmonary edema or extensive nodular and confluent bronchopneumonia.

The microscopical changes commonly encountered in any autopsy population, such as congestion,

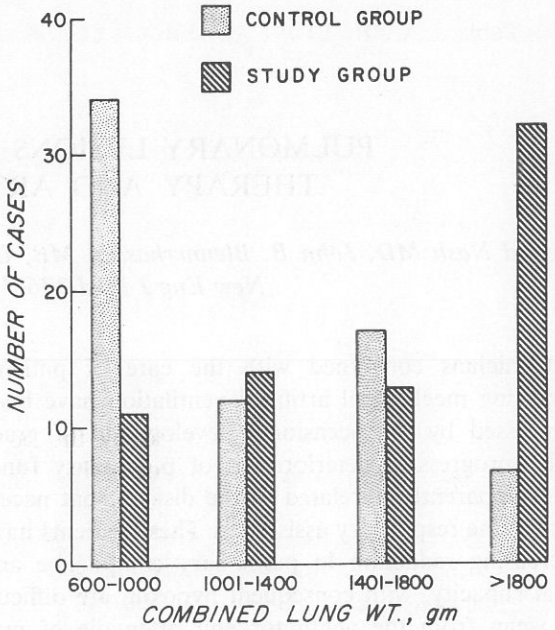

Figure 1. *Distribution of the Combined Lung Weights.*

edema, intra-alveolar macrophages, alveolar hemorrhage, pneumonia, emphysema, old scars and focal collagenous fibrosis, pulmonary emboli, foreign-body aspiration and anthracosis, were seen approximately as often in the control as in the study group. However, several unusual microscopical changes occurred with great frequency in the study group. These included a prominent intra-alveolar fibrin exudate, often associated with layering of fibrin on the walls of alveoli, alveolar ducts and respiratory bronchioles to form "hyaline membranes". Such fibrin membranes were found in 17 cases in the study group and in only 2 cases in the control group. In the 2 control cases the fibrin membranes were observed in areas of severe bronchopneumonia, whereas bronchopneumonia was not a feature in the 17 cases with hyaline membranes in the study group. Of these 17 patients 2 had associated uremia (12 percent), whereas in the entire study group there were 10 patients with uremia (14 percent); thus, there is no reason to attribute the development of hyaline membranes to uremia. There was also no association with radiation therapy, since none of the 17 patients with hyaline membranes had received it.

Another striking microscopical finding in many cases in the study group was marked thickening of alveolar and interlobular septa by a combination of edema and an extremely cellular fibroblastic proliferation, with the deposition of reticulin and a mod-

* T test.
† Chi-square.

Table 2. CORRELATION OF GROSS AND MICROSCOPICAL FINDINGS WITH THERAPY.

Treatment Group	No. of Cases	Weight >1800 Gm.	Fibrin Membranes	Interstitial Edema & Fibrosis	Alveolar-Cell Hyperplasia	Edema	Bronchopneumonia	Cardiorespiratory Disease
		%	%	%	%	%	%	%
1	17	35.3	17.8	5.9	17.6	35.3	35.3	41.2
2	13	23.1	15.4	23.1	23.1	38.4	30.8	38.5
3	31	48.4	29.0	38.8	19.4	58.1	32.2	42.0
4	9	88.9	33.3	77.8	55.6	44.5	22.2	44.5

erate amount of loose fibrillar collagen. This alteration was associated with only a mild-to-moderate component of lymphocytes, without evidence of infection. The histologic pattern was distinctive and did not resemble either organizing pneumonia or the dense collagenization of septa often seen in association with emphysema or postinfective scars. This severe interstitial edema and early fibrosis were present in 23 cases (33 percent) in the study group and in only 1 case in the control population. Again, there was no correlation with pneumonia, uremia or radiation therapy. Diffuse hyperplasia of the alveolar lining cells, with the formation of a cuboidal epithelial layer, was a further feature in 17 cases (24 percent) in the study group.

Special stains (including phosphotungstic acid and hematoxylin, Masson trichrome, silver impregnation reticulin stain and elastic-tissue stain) confirmed the impressions obtained from study of hematoxylin and eosin sections of the presence of fibrin, collagen and reticulin.

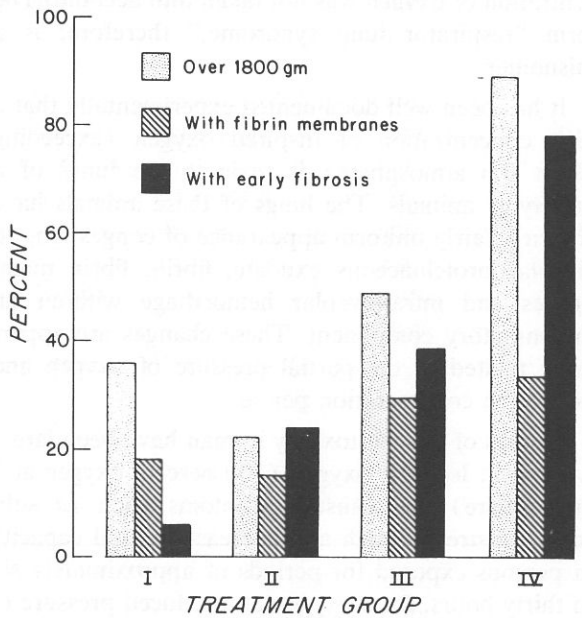

Figure 4. *Percent of Each Treatment Group with Combined Lung Weights over 1800 Gm., Fibrin Membranes and Early Fibrosis.*

Correlation of Pathological Findings with Treatment

Table 2 shows the distribution of the various pathological findings in the 4 treatment groups. The distribution of the lung weights, fibrin membranes and fibrosis in the treatment groups is represented graphically in Figure 4. Table 3 represents the same categories of pathologic alterations according to the duration of artificial ventilation regardless of the percentage of oxygen delivered.

From these tables it is evident that in treatment groups 1 through 4, there is a progressive increase in the percentage of "heavy lungs" (combined weight over 1800 gm.) and lungs showing interstitial edema and fibrosis. Statistical analysis indicates that the difference among the treatment groups is significant for both abnormalities (p less than 0.02)* and that the linear trend in the treatment groups is sufficient to explain most of the difference (residual chi-square value of p greater than 0.10).† If the oxygen concentration of inspired air is not taken into account there is no statistically significant correlation of any pathological finding with the duration of mechanical ventilation (Table 3). Of the 3 most striking findings (lung weights greater than 1800 gm., hyaline membranes and interstitial edema and fibrosis), 2 or more were present in 77 percent of Group 4 but in only 11.8 percent of Group 1, 15.4 percent of Group 2 and 19.5 percent of Group 3 (Table 4).

* Chi-square.
† Test for trend among proportions.

Table 3. CORRELATION OF GROSS AND MICROSCOPICAL FINDINGS WITH TIME ON RESPIRATOR.

Time on Respirator	No. of Cases	Weight >1800 Gm.	Fibrin Membranes	Interstitial Edema & Fibrosis *	Alveolar-Cell Hyperplasia *	Edema	Bronchopneumonia	Cardiorespiratory Disease
days		%	%	%	%	%	%	%
<10	48	43.8	25.0	27.1	18.8	50.0	33.3	41.7
>10	22	50.0	22.8	45.5	36.4	40.9	27.3	40.9

*P >0.05 (chi-square).

Table 4. FREQUENCY OF COMBINATIONS OF IMPORTANT PATHOLOGICAL FINDINGS.*

Group	None Present	1 Finding Only	2 Findings	All 3 Findings
	%	%	%	%
1	47.0	41.2	11.8	0
2	53.8	30.8	15.4	0
3	35.5	45.0	13.0	6.5
4	11.0	11.0	44.0	33.0

* 3 pathological findings considered: lung weights >1800 gm.; fibrin "hyaline" membranes; & interstitial fibrosis & edema.

The incidence of diffuse alveolar-lining-cell hyperplasia was greatest in Group 4, but there was not a progressive increase in this parameter from Groups 1 through 4 and the incidence is not statistically significant (p greater than 0.05).* Although in Groups 3 and 4 there was a greater percentage of cases in which fibrin membranes were found than in Groups 1 and 2, this difference also is not statistically significant (p greater than 0.05).* The incidence of edema, bronchopneumonia and pre-existing chronic cardiorespiratory disease was virtually the same among the treatment groups.

Discussion

In this study we have demonstrated that some patients who die after prolonged artificial ventilation exhibit characteristic pulmonary pathological changes. We have been impressed by the existence of 2 phases of the changes as observed microscopically: an exudative and a proliferative phase. The lungs in the exudative phase showed capillary congestion, an alveolar proteinaceous exudate, intra-alveolar hemorrhage and a fibrinous exudate. Prominent "hyaline" membranes lined the alveolar walls, alveolar ducts and respiratory bronchioles. Only a sparse chronic inflammatory component was present. The striking features of the lungs in the proliferative phase were marked alveolar and interlobular septal edema, fibroblastic proliferation with early fibrosis, prominent hyperplasia of the alveolar lining cells and a variable component of the alterations characteristic of the exudative phase. It is our impression that these 2 categories are stages of a progressive deterioration, with the exudative phase representing an earlier change that progresses, if survival is sufficiently prolonged, to the proliferative or fibrotic phase.

Although these distinctive changes were found in patients in all 4 treatment groups, there was a definite correlation with prolonged ventilator therapy utilizing high concentrations of inspired oxygen. There was no significant correlation of these changes with the duration of artificial ventilation when the concentration of oxygen was not taken into account. The term "respirator lung syndrome," therefore, is a misnomer.

It has been well documented experimentally that a high concentration of inspired oxygen (exceeding about 0.6 atmosphere) is toxic to the lungs of a variety of animals. The lungs of these animals have shown a fairly uniform appearance of congestion, an alveolar proteinaceous exudate, fibrin, fibrin membranes and intra-alveolar hemorrhage without an inflammatory component. These changes are apparently related to the partial pressure of oxygen and not to the concentration per se.

Studies of oxygen toxicity in man have been largely clinical. Isobaric oxygen (100 percent oxygen at 1 atmosphere) has caused symptoms such as substernal distress, cough and decrease in vital capacity in persons exposed for periods of approximately six to thirty hours. Pure oxygen at a reduced pressure of about 250 mm. of mercury has been breathed by normal male subjects for up to thirty days without producing pulmonary changes, and many observers have stated that man could probably tolerate oxygen

* Chi-square.

at partial pressures below 425 mm. of mercury (approximately 60 percent at 1 atmosphere) indefinitely without the development of symptoms of oxygen toxicity. However, more recent reports have described the development of symptoms of oxygen toxicity after prolonged exposure to oxygen tensions as low as 176 mm. of mercury.

For obvious reasons, the experimental exposure of human subjects to toxic levels of oxygen has not been carried to the stage of severe pulmonary damage, and the literature on the pathological changes that characterize pulmonary oxygen toxicity in man is perforce extremely sparse. Cederberg et al. described the post-mortem findings in a series of 150 patients who died in a respiratory unit. Pulmonary hyaline membranes were seen in 28 of the patients; in 14, these membranes could be ascribed to other causes. Of the remaining 14 patients, 11 had been treated with oxygen, and it was suggested that the duration of therapy was the important factor. On gross examination the lungs of these patients appeared abnormally large, firm and dark. The microscopical examination disclosed alveolar septal edema, and fibrous organization of the hyaline membranes was seen in 2 cases. In addition, Fuson and his associates have reported a case in which exposure to therapeutic hyperbaric oxygen may have produced pulmonary pathological changes similar to those seen in animals.

In the cases in the present series in which the exudative phase of the pulmonary lesion was found, the pathological picture closely resembled that observed in the lungs of laboratory animals dying with acute pulmonary oxygen toxicity and also that described in some of the cases reported by Cederberg et al. The progression of these changes to the proliferative fibrotic phase has no experimental counterpart, but changes that may be similar have been alluded to in previous clinical studies. In our opinion, these morphologic alterations provide an explanation for the marked deterioration in pulmonary function observed during life in most of these cases and may account in part for the difficulty in weaning such patients from artificial ventilation. In our study, as in others, both the oxygen concentration and the duration of exposure appeared to be important factors in the development of the pulmonary lesion. Although safety limits for the administration of oxygen in man have not yet been determined, the use of 90 to 100 percent oxygen for a prolonged period is probably hazardous. It should be emphasized that we have not established a definite cause-and-effect relation between the characteristic pathological appearance and any particular facet of the therapy. A post-mortem study of this sort does not take into account the fact that most patients treated in the Respiratory Unit at this hospital survive with adequate lung function, including many to whom 100 percent oxygen is given for a prolonged period in the treatment of respiratory failure. Moreover, in view of the severe and complicated pathologic states encountered and the multifaceted treatment invariably required in such cases, many etiologic factors could theoretically have been responsible for the pathological changes. The possible role of physical factors such as the pattern of ventilation and high airway pressure must be considered, as well as a multitude of biochemical changes associated with both the disease and the treatment. The role of all these factors cannot be analyzed in the context of this study.

Many patients, particularly those who died within the last two years, were given a high concentration of inspired oxygen to ensure a safe level of arterial oxygen tension and saturation in the face of very severe lung disease. However, some patients who died between four and five years ago had been treated with pressure-limited ventilators, which deliver approximately 90 percent oxygen unless a compressed-air source is used in combination with oxygen, and were undoubtedly subjected to unnecessarily high levels of inspired oxygen for prolonged periods. It is possible that the pulmonary changes observed in those cases were a direct result of this treatment. The current practice in the Respiratory Unit of this hospital, prompted by this study, is to measure the inspired oxygen concentration with a Pauling paramagnetic analyzer and to provide a concentration that results in an arterial oxygen tension of 80 to 120 mm. of mercury, sufficient to give a 95 to 99 percent saturation of arterial blood. This treatment often entails the use of a high concentration of inspired oxygen, including 100 percent oxygen. It should be emphasized that such therapy is not withheld for fear of possible toxic effects on the lungs or other organs. However, the inspired oxygen concentration is reduced as soon as arterial-blood gas measurements show that a reduction can safely be accomplished.

Summary and Conclusions

A study of 70 patients who died after prolonged artificial ventilation revealed a common denominator of characteristic pulmonary changes in many of them. Grossly, the lungs appeared heavy, "beefy" and edematous; microscopically, there seemed to be 2 phases, which merged and were not distinct. An early exudative phase was characterized by congestion,

alveolar edema, intra-alveolar hemorrhage and a fibrin exudate, with the formation of prominent hyaline membranes without an associated inflammatory component. A late proliferative phase was characterized by marked alveolar and interlobular septal edema and fibroblastic proliferation, with early fibrosis and prominent hyperplasia of the alveolar lining cells. These morphologic changes were unrelated to the duration of the artificial ventilation per se, but they were correlated with the prolonged use of the ventilator delivering a high concentration of inspired oxygen. However, a definite cause-and-effect relation has not been established by this study. Optimal treatment demands that patients receive an inspired oxygen concentration sufficient to ensure normal or nearly normal arterial oxygen tension. Such therapy should not be withheld for fear of possible toxic effects on the lungs or other organs, but the inspired oxygen concentration should be monitored and reduced as soon as arterial-blood gas measurements show that the reduction can be accomplished safely.

We are indebted to Theodore Colton, Sc.D., of the Department of Preventive Medicine, Harvard Medical School, for advice on methods of statistical analysis.

(The omitted figures and references may be seen in the original article.)

[In the same issue of the *New England Journal of Medicine,* Dr. John H. Knowles discusses this same problem at some length and suggests the term "oxygen alveolopathy" (Lung-surfactant-deficit syndrome). Case Records of the Massachusetts General Hospital, Case 7–1967, Vol. 476, pgs. 401–411, Feb 16,1967. Also, in the same issue, pages 357–368, W. H. Northway, Jr., MD, R. C. Rosan, MD, and D. Y. Porter, MD (Stanford University School of Medicine) report a study of Pulmonary Disease Following Respirator Therapy of Hyaline-Membrane Disease —Editor.]

CURRENT THERAPY OF BACTERIAL PNEUMONIAS

Marvin Turck MD, Med Clin N Amer 51(2):541–548, March 1967.*

Specific therapy for bacterial pneumonia depends upon identification of the etiologic agent causing the infection. The pneumococcus remains the major cause of bacterial pneumonia and appropriate chemotherapy often may be initiated on the basis of the typical clinical picture. However, since the drug of choice for the treatment of pneumococcal infection, penicillin G, may not be effective in pneumonia caused by other bacteria, it is essential to be keenly aware of situations in which one of the less common bacterial species is encountered. These include infections occurring in hospitals, in patients receiving antibiotics, in neonates, and in elderly patients, many of whom have debilitating diseases as well. In addition, pneumonia complicating influenza, pregnancy, rheumatic heart disease, pneumonia in the alcoholics, and pulmonary infections complicating hematologic disorders such as lymphoma, leukemia, and agranulocytosis may be associated with unusual microorganisms.

Although knowledge of the background in which the infection occurs provides important clinical clues to help differentiate pneumococcal pneumonia from the pneumonias caused by other microorganisms, for the most part early diagonsis and correct antimicrobial therapy are contingent upon Gram staining and culturing of an appropriately collected sputum specimen. It is important that the specimen be representative of bronchial secretions rather than saliva and, at times, tracheal catheterization or transtracheal aspiration may be necessary to obtain an adequate specimen. Pneumococci can be identified by their classical appearance in the form of gram-positive encapsulated diplococci often within leukocytes. In addition, blood cultures should be drawn but treatment need not be withheld until the results are reported. If cultures subsequently fail to substantiate the impression of the smear and the patient's response to treatment is poor, the antibiotic can be changed.

Pneumococcal Pneumonia

Penicillin G still remains the most dependable drug for treating pneumococcal infections, and there

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are no strains of D. pneumoniae which are resistant to penicillin. The usual dosage for infections of moderate severity is 600,000 to 1,200,000 units of penicillin G per day (375 to 750 mg.), given intramuscularly. Treatment should be continued for five to seven days or until the patient has been afebrile for 72 hours. Actually, this quantity of drug is probably excessive for the majority of patients with pneumococcal pneumonia and there is little reason to give larger amounts. When pneumococcal pneumonia does not respond to penicillin, it is not related to the drug's inability to eradicate the organism but is due to associated illnesses, such as pulmonary malignancy or failure to drain a pyogenic focus such as an empyema. In uncomplicated pneumococcal pneumonia neither "massive" doses nor frequent injections at short intervals offer any therapeutic advantage. The practice of giving superfluous amounts of penicillin is not only of no clinical value, but also may be harmful. The frequency of superinfections occurring in hospitalized patients has been directly proportional to the dosage of penicillin. No superinfections occurred among patients receiving daily parenteral doses of 2.4 million units or less, while almost 30 percent of patients receiving 10 to 20 million units daily acquired superinfections.

In pneumococcal pneumonia, subjective improvement usually occurs within 48 to 72 hours after the institution of antimicrobial treatment, and frequently is accompanied by a decline in temperature. However, a delayed response to treatment is not unusual in patients with multiple lobe involvement, in alcoholics, in elderly and very young patients, in those with pre-existent pulmonary disease, and in patients with a specific pyogenic complication of pneumococcal infection such as empyema, arthritis, meningitis, pericarditis, or endocarditis. Persistence of a low-grade fever is not unusual and improvement in x-ray and physical findings may also lag behind clinical improvement for several days or even weeks. Moreover, a secondary rise in temperature, following initial defervescence, may indicate a superinfection or drug fever due to penicillin. In addition, sterile pleural effusions, which are much more common than empyema, often are associated with persistent fever which subsides once the fluid has resolved or has been removed by thoracentesis.

Although penicillin is the drug of choice in pneumococcal infections, it should not be administered to patients with suspected hypersensitivity to penicillin or to one of its semisynthetic congeners. Fortunately, there are a number of alternative antimicrobials which are effective, including tetracycline, chloramphenicol, erythromycin, lincomycin, and cephalothin. In most instances, erythromycin in daily dosage of 250 mg. orally every six hours is an excellent alternative to penicillin. A limiting factor with erythromycin, however, is the lack of a suitable injectable preparation which is free from severe discomfort and irritation. The parenteral preparation of lincomycin appears to be tolerated well, and is an acceptable substitute.

Cephalothin, a bactericidal antibiotic effective against all strains of D. pneumoniae in vitro, is available only for parenteral administration but, like erythromycin, is associated with considerable pain and soft tissue reaction. In addition, although cephalothin usually may be given to penicillin-sensitive patients without adverse reaction, two patients who were presumably sensitive to penicillin had anaphylactic reactions to cephalothin following their initial exposure to this drug. In the past, one of the tetracyclines also has provided adequate therapy for pneumococcal pneumonia in patients hypersensitive to penicillin. However, recent reports of treatment failures because of tetracycline-resistant pneumococci dictate that this agent not be used. On the other hand, there have been no clinical isolates of pneumococci which are resistant to erythromycin, lincomycin, cephalothin, or chloramphenicol. The risk of bone marrow depression and irreversible aplastic anemia occasionally associated with chloramphenicol, however, is unwarranted in pneumococcal pneumonia when other, equally efficacious agents are available.

Staphylococcal Pneumonia

Staphylococcal pneumonia frequently occurs in the hospital setting, often in debilitated patients or in those convalescing from surgical procedures. In general, this infection is more severe than pneumococcal pneumonia and convalescence may be prolonged. Empyema is a common complication and requires early recognition and drainage to prevent bronchopleural fistula, residual abscess and cyst formation, and healing by fibrosis. Staphylococcal pneumonia may also present with multiple lung abscesses secondary to dissemination of organisms via the blood stream. This form of staphylococcal infection also tends to occur within hospitals and is associated with infected "cut-downs" or is prevalent in narcotic addicts. It may also follow staphylococcal infection elsewhere in the body, as in bone, soft tissue, or kidney. Bacteremia is not common in primary staphylococcal pneumonia and may be a clue

that the focus of infection is elsewhere. Staphylococcal pneumonia may also occur as a complication of viral influenza, and in this situation the course often is fulminating and is characterized by dyspnea, profound cyanosis, cough, fever, and bloody sputum. In epidemics of influenzal disease, this infection occurs most often in patients with chronic lung disease, valvular heart disease, or in pregnant women.

Although patients continue to die from staphylococcal pneumonia despite treatment with antibiotics to which the microorganism is susceptible in vitro, the prognosis has improved during the past five to seven years. This is related, in part, to the changing ecology of staphylococcal disease. For example, epidemics of staphylococcal infection with "epidemiologically virulent" strains, such as 80/81, are much less frequent causes of hospital associated sepsis. In addition, vaccination of highly susceptible patients against influenza may have had a favorable influence on this epidemiologic pattern.

Most likely, of equal importance in making headway in staphylococcal pneumonia has been the availability of potent penicillinase-resistant penicillins. The first of these agents was methicillin, 2, 6-dimethoxyphenyl penicillin. This drug is inactivated by gastric acid and must be administered parenterally. For practical purposes, all clinical isolates of pathogenic staphylococci are inhibited by methicillin, and nowadays it is mandatory that this drug or an acceptable congener be used as initial therapy in all staphylococcal infections, as well as in other severe gram-positive coccal infections in which the etiology is not entirely clear. Although methicillin is only about one-fiftieth as active as penicillin G against nonpenicillinase-producing staphylococci and Diplococcus pneumoniae in vitro, the antibacterial activity in serum achieved with recommended dosages of methicillin is sufficiently high against these common coccal organisms to insure their eradication. For these reasons there is little indication for the use of penicillin G along with methicillin until the susceptibility of a given strain is known. Once culture and sensitivity tests have shown, however, that the organism is susceptible to penicillin G, methicillin may be discontinued and penicillin G should be given. Methicillin should not be used in infections *known* to be susceptible to penicillin G, primarily because it is far more expensive.

The theoretical possibility of producing strains resistant to methicillin has not presented a clinical problem. If the patient can take drugs by mouth, one of the penicillinase-resistant penicillins that possess greater stability in gastric acid, such as cloxacillin, may be substituted. The usual dose of cloxacillin is 500 mg. every six hours, preferably given in the fasting state.

As is the case with penicillin G, the new penicillins are relatively nontoxic even when given in larger doses. Superinfections, however, may be more frequent among patients treated with the newer penicillins than was the case with penicillin G. This may be related, in part, to the higher dosage of the new penicillins and also to the use of these drugs in more severely ill and debilitated patients. The new penicillins may also provoke hypersensitivity reactions in patients sensitive to penicillin G. Although there are numerous patients with alleged hypersensitivity to penicillin who have subsequently been challenged with one of its newer semisynthetic derivatives without incident, this practice is not recommended.

Suitable alternatives for treatment of patients with staphylococcal pneumonia are available and include cephalothin, vancomycin and lincomycin. Virtually all staphylococci are sensitive to 5μg./ml. or less of vancomycin and to 2μg./ml. or less of cephalothin. Vancomycin must be infused intravenously over a period of 30 minutes in 1-gram doses, every 12 hours, diluted in 100 ml. of 5 percent dextrose in water. This dose should be reduced in the presence of renal insufficiency. Cephalothin may be administered intramuscularly or intravenously and has no significant toxicity. The recommended dose of cephalothin for serious infections is 1 gram every four hours. More recently lincomycin also has been demonstrated to be an effective antistaphylococcal drug, and 95.2 percent of 1,055 hospital staphylococcal isolates were susceptible to lincomycin while only 43.1 percent were inhibited by erythromycin. However, because an occasional strain may be resistant to lincomycin, it should not be used in the treatment of staphylococcal pneumonia prior to the results of sensitivity tests.

Klebsiella (Friedländer)
Pneumonia

Klebsiella infections of the lung present a difficult problem in therapy and their mortality rate is high despite seemingly adequate antimicrobial treatment. In part, at least, the poor prognosis is related to the fact that this encapsulated, gram-negative rod tends to attack chronically ill, debilitated patients and alcoholics. Patients with this type of infection often fail to develop leukocytosis and may, in fact,

have severe leukopenia. Leukopenia, however, is in no way diagnostic of Friedländer infection and also occurs commonly in alcoholic patients with pneumococcal pneumonia. It is important to recognize Friedländer infection early because tissue necrosis occurs rapidly, resulting in multiple abscesses with cyst formation. Bacteremia and empyema are also common. In addition, it is important to recognize Klebsiella pneumoniae promptly because the organism does not respond to penicillin. They are sensitive to a number of antibiotics in vitro but their susceptibility is not predictable. Kanamycin, chloramphenicol, and tetracycline are all active against the majority of isolates and one of these agents administered intramuscularly or intravenously should be given when the diagnosis of Friedländer's pneumonia is suspected. Some investigators have advocated combined antimicrobial treatment for Klebsiella infection.

More recently, cephalothin has been evaluated in the treatment of this infection. When Klebsiella are separated from members of the Aerobacter, Hafnia and Serratia groups, nomotile K. pneumoniae is frequently sensitive to 10μg./ml. or less of cephalothin, while the motile Aerobacter aerogenes is resistant to this concentration and often is not susceptible to concentrations as high as 50 or 100μg./ml. Therefore, cephalothin should be used in infections caused by Klebsiella-Aerobacter if the organisms are sensitive in vitro. The activity of this drug against staphylococci and other gram-positive organisms is an added advantage.

Pneumonia Due to Other Gram-Negative Organisms

Other gram-negative bacilli occasionally cause pneumonia, but more frequently are isolated from the sputum of hospitalized patients merely because the patient has been exposed to antibiotics. For example, during penicillin treatment of pneumococcal pneumonia, a predominance of Hemophilus influenzae may be isolated from the sputum. This represents the survival and overgrowth of one of the endogenous "normal flora" after suppression of more sensitive organisms. Bacteriologic superinfections of this nature only rarely are accompanied by clinical disease, and these patients need to be treated only if they have recurrent fever, purulent sputum, or show a new or extending infiltrate on chest x-ray. However, in children and occasionally in adults, especially those with chronic bronchitis, emphysema, or bronchiectasis, H. influenzae may be a causative pathogen in pulmonary infections. This small gram-negative rod is generally susceptible in vitro to one of the tetracyclines which can be administered in dosages of 2 grams per day or 25 mg./kg. in children. More recently, ampicillin has also been shown to be highly effective in the treatment of H. influenzae infections.

Nearly every gram-negative enteric bacillus has been incriminated at one time or another in causing lobar or bronchopneumonia. However, the epidemiology of these infections has not been defined and there is usually no typical clinical picture. Proper diagnosis depends on the isolation of the predominant organisms from a carefully collected sputum and must include as well evaluation of the clinical setting in which the organisms are recovered. Sensitivity tests may be extremely important because of the variable susceptibility of these strains. Most enteric organisms, including E. coli, Klebsiella-Aerobacter, and strains of Proteus are sensitive to kanamycin. As is the case with Friedländer's infection, many of the patients with gram-negative enteric pneumonias are severely debilitated and the mortality is high despite apparently effective antimicrobial therapy.

Pneumonias Simulating Bacterial Infection

Several viral and rickettsial organisms, as well as parasites and fungi, may produce a clinical and roentgenographic picture similar to bacterial infection of the lung. Often it is difficult to establish the precise etiology, and diagnosis is frequently inferential. Recent studies indicate that many cases of "viral pneumonias" are not viral pneumonia at all, and are caused by a pleuropneumonia-like organism, Mycoplasma pneumoniae, formerly termed the Eaton agent; Mycoplasma pneumonia responds to antimicrobial treatment and both tetracycline or erythromycin are effective. However, because M. pneumoniae lacks a rigid cell wall, it is not inhibited by penicillin. Any of the rickettsial illnesses can be associated with pneumonitis, but Q fever characteristically is accompanied by an infiltrate. This infection also responds to tetracyclines or to chloramphenicol, as does psittacosis, a "viral" disease which also is capable of causing pneumonia.

The influenza viruses as well as several types of adenoviruses also have been implicated in pneumonias. Antibiotics are not useful in combating these infections unless there is a clear-cut secondary bacterial invasion.

Principles of Therapy and Prevention of Complications

Although specific antimicrobial therapy has greatly reduced the morbidity and mortality from bacterial pneumonia, patients continue to die from this infection. Most of the fatalities are at the extremes of life or occur in debilitated patients with concomitant disease. However, in others, recovery is prolonged or treatment is ineffective because of failure to adhere to sound medical-surgical principles. For example, failure to aspirate a pleural effusion or to drain an empyema early in the course of an illness may result in prolonged convalescence and on occasion may necessitate decortication of the pleura. Small amounts of sterile fluid do not necessarily need repeated aspirations and frequently are resorbed spontaneously. On the other hand, with larger volumes, repeated thoracenteses or surgical drainage with a tube is necessary. Proteolytic enzymes to help liquefy the exudate also may be helpful.

At times, there is a long delay in initiation of appropriate chemotherapy. This delay often occurs because some patients do not come to the hospital until they are moribund. However, in many instances there is an excessive interval prior to institution of treatment because of prolonged waits in the emergency room or in the x-ray corridors. Possibly, failure to establish adequate antibacterial levels in the blood and tissues early in the course of pneumonia may account for the increased frequency of bacteremia and some of the excess mortality. The emphasis on early therapy in pneumococcal pneumonia, if the outcome is to be successful, may however be a gross oversimplification. Results of recent studies in 529 patients with pneumococcal pneumonia and bacteremia suggested that the outcome of this illness was established very early and was probably independent of prompt antimicrobial treatment. In fact, it was felt by the authors that any further decrease in mortality in pneumococcal pneumonia may depend upon immunization of susceptibles by means of common type specific polysaccharide vaccines rather than by earlier treatment with existing or new antibiotics. This approach is not unique and has been practiced in the past in institutional and military outbreaks of pneumococcal infection. However, large-scale immunization of a civilian population has not been employed for the prevention of pneumococcal pneumonia. Even this approach may not provide an answer, and most important of all may be improvement of the human substrate in which pneumonia occurs.

(The references may be seen in the original article.)

MEDICAL ABSTRACTS

THE PROGNOSTIC SIGNIFICANCE OF PROTEINURIA IN YOUNG COLLEGE STUDENTS

John I. Levitt MD, (From the Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota.) Ann Intern Med 66:683–696, April 1967.

Here is another report on the prognostic significance of proteinuria in young people (See U.S. Navy Medical News Letter 49:6–12, March 24, 1967), this one with perhaps a more optimistic outlook. One hundred eighty-five former University of Minnesota students whose urine demonstrated definite proteinuria on admission physical examination at the Student Health Service were surveyed after an interval of between 37 and 45 years. One hundred thirty-eight were alive, 45 had died, 6 of renal disease, and 2 were not traced. Little or no correlation was found between the duration or the maximal amount of recorded proteinuria and subsequent mortality rates. Characteristics most closely associated with a high mortality rate were: clinical diagnosis of renal disease (mortality rate 43 percent), a frequency of proteinuria in excess of 80 percent (mortality rate 57 percent). All six who had died of renal disease had both. The mortality rate was only 14 percent in those with less than an 80 percent frequency of proteinuria and 20 percent in those not classified clinically as having renal disease (that is, in those whose diagnosis was orthostatic proteinuria or no renal disease). Neither of these mortality figures differed significantly from the mortality rate of 16 percent expected to occur in a group of healthy insurees followed over a similar period of time. In none of those in the subgroups who had died was death due to renal disease.

The author concludes that intermittent proteinuria in a young adult, in the absence of other evidence of renal disease, is a benign condition that does not predispose to future renal insufficiency, but if the proteinuria is always or nearly always present, the prognosis is poor and the chances of renal death high.

JUXTACORTICAL OSTEOSARCOMA, DIAGNOSIS, DIFFERENTIAL DIAGNOSIS, TREATMENT, AND AN ANALYSIS OF EIGHTY CASES

R. O. Van Der Heul MD and J. R. Von Ronnen MD, (From The Netherlands Cancer Institute, Amsterdam, The Netherlands, and the Department of Radiology, University Hospital, Leiden, The Netherlands.) J Bone Joint Surg (Amer) 49–A:415–439, April 1967.

This tumor of bone, described by Geschickter and Copeland in 1951 and called parosteal osteoma by them has subsequently been named by other authors as juxtacortical osteogenic sarcoma (Jaffe and Selin); parosteal osteogenic sarcoma (Dwinnell, Dahlin, and Ghormley); ossifying parosteal sarcoma (Scaglietti and Calandriello); parosteal and periosteal ossifying fibrosarcoma (van der Heul). The authors have studied the relation of this tumor to intraosseous osteosarcoma and have reevaluated the treatment of 64 cases collected from the literature and 16 cases from the archives of the Netherlands Committee on Bone Tumors. They have concluded that juxtacortical osteosarcoma should be considered a distinctive entity and then recommend the following scheme for treatment:

"For primary tumors that are not too large, have a low-grade histological malignancy, and are separated from the neighboring cortex, as seen on roentgenograms, local removal seems justified. But this holds true only when complete removal is technically feasible, the tumor being removed *en bloc* together with a layer of covering soft tissues and the regional cortex, along a surface larger than the surface of contact with the growth. If invasion of the shaft is suspected or demonstrated, segmental resec-

tion of the regional shaft should be undertaken instead of removal of the underlying cortex.

"When extension of the primary tumor precludes local removal (large growths and obvious malignancy) or there is a recurrence, amputation or disarticulation (depending on the site of the tumor) should be performed whenever possible."

INFLUENCE OF HYPERBARIC OXYGEN ON THE SURVIVAL OF SPLIT SKIN GRAFTS

D. J. Perrins MB FRCS, (From Research Registrar Burns Unit, Queen Mary's Hospital, Roehampton, London.) Lancet 1:868–871, April 22, 1967.

An investigation of the effect of exposure to 100 percent oxygen at two atmospheres absolute on the survival of split skin grafts is recorded. The grafted regions were exposed in a Vicker's clinical transparent pressure chamber for two hours on the evening of operation and after that for two hours in the morning and evening for three days. A significant improvement over the controls was obtained. There was an increase in survival of 29 percent of the surface area of the grafts; a high proportion of complete "takes" occurred, (64 percent of the treated cases as opposed to 17 percent of the controls).

INFECTIOUS COMPLICATIONS OF CHEMOTHERAPY IN A PROTECTED ENVIRONMENT

A. A. Levitan MD and Seymour Perry MD, (From the Medicine Branch National Cancer Institute, National Institutes of Health.) New Eng J Med 276: 881–886, April 20, 1967.

This article reports further experience with the patient isolater system in the treatment of cancer with chemotherapeutic agents at the National Cancer Institute (See Patient Protection in Cancer Chemotherapy, U.S. Navy Medical News Letter 48:4–7, November 18, 1966). Eleven patients have undergone prophylactic reduction in body flora and chemotherapy in this enclosure over a period of 405 days. Sixty-five percent of this time was spent with granulocyte counts of less than 1,000, and 47 percent with counts of less than 500. Cultures of patients' stools were sterile 56 percent of the time, those of the nose and skin 70 percent and those of the throat one percent of the time. There were 109 days in which patients' temperatures exceeded 100.4° F (38° C). Systemic antibiotics were administered on 66 days. Infection was documented on 30 days. Seventy-two percent of all febrile episodes were not associated with documented infection. Infections observed were: one pseudomonas septicemia, one multiple pulmonary abscesses, one urinary-tract infection due to proteus species, and one cellulitis. Organisms responsible for infection had all been recovered from various body sites before the infectious episode. The development of significant resistant bacterial strains as a consequence of the intestinal antibiotic regimen did not occur. Gammaglobulin levels remained normal throughout the course of therapy and no relation to fever or infection could be established.

The authors believe that patient isolater systems appear to have a definite role in cancer therapy. They were able to give larger amounts of antitumor therapy with a concomitant reduction in the incidence of infection when this type of patient protection was used.

BRONCHIAL ADENOMAS

J. N. Baldwin MD and O. F. Grimes MD FACS, (From the Department of Surgery, University of California School of Medicine, San Francisco.) Surg Gynec and Obstet 124:813–818, April 1967.

A series of 56 patients with respiratory tract adenomas who were seen at the University of California Medical Center, San Francisco and its affiliated hospitals (San Francisco General Hospital and the San Francisco Veterans Administration Hospital) is described in this report. The patients ranged from 17 to 81 years of age (mean 41 years). Symptoms appeared before the age of 40 in 36 (64 percent) which is in marked contrast to the usually later-appearing symptoms of carcinoma of the lung and 34 (60 percent) were females. Symptoms and signs, duration of symptoms, roentgenologic appearance, bronchoscopic findings, means of diagnosis, pathologic aspects, and treatment and follow-ups are discussed. In their summary, the authors state that because of diagnostic difficulties, a long period often exists between initial examination and precise diagnosis and treatment; tomography and bronchography must be utilized; bronchoscopic examination remains the single most accurate and direct method of definitive identification. They warn that piecemeal resection of bronchial adenomas through the bronchoscope is dangerous and temporary at best and emphasize that carefully planned, function-preserving surgical methods designed to remove the tumor through a thoracotomy will produce the best immediate and long term results.

EFFECT OF PHOSPHATE SUPPLEMENTS IN PATIENTS WITH FRACTURES

R. S. Goldsmith MD, C. F. Woodhouse MD, S. H. Ingbar MD, and David Segal MD, (From the Thorndike Memorial Laboratory, Second and Fourth (Harvard) Medical Services, Boston City Hospital and the Department of Medicine, Harvard Medical School and the Department of Orthopedic Surgery (Tufts), Boston City Hospital, Boston Massachusetts.) Lancet 1:688–690, April 1, 1967.

In this investigation, 24 patients with various fractures, femoral shaft, ankle, and Colles were given phosphate supplements (one gram of phosphorus daily) to their diets; 27 with fractures at the same sites did not receive these supplements. In the phosphate-treated patients with fractures of the femur and ankle, radiographically demonstrable demineralization and the time required for clinical union were signficantly reduced. No significant difference was noted in patients with Colles fractures. Phosphate supplementation gave rise to no complications. The authors comment that the shorter time to clinical union, and hence of immobilization with patients receiving phosphate probably contributed to the lesser degree of demineralization, although the additional phosphate may have had a direct effect in inhibiting demineralization and that the increase in callus six weeks after fracture in the phosphate-treated patients with femoral-shaft fractures suggests that phosphate supplementation may have increased the production of callus. The findings, say the authors must be considered preliminary; double-blind trials of phosphate or placebo are in progress.

DENTAL SECTION

AN ASSESSMENT OF METRONIDAZOLE IN THE TREATMENT OF ACUTE ULCERATIVE PSEUDOMEMBRANOUS GINGIVITIS (VINCENT'S DISEASE)

J. Fletcher and C. Plant, Oral Surg 22:729–736, December 1966.

Acute necrotizing ulcerative gingivitis was treated for two years in fifty patients with metronidazole ("Flagyl" by May and Baker, Ltd). The authors wished to study drug therapy that would provide prompt, safe relief of symptoms that required a minimum amount of patient cooperation and would eliminate the need for immediate emergency scheduling of dental office treatment.

The drug, Metronidazole, has been chiefly used in the oral treatment of infections caused by "Trichomonas vaginalis". The authors found the drug to also bring relief to some patients with Necrotizing Ulcerative Gingivitis. Treatment consisted of the prescription of 200 mg of metronidazole, three times a day for seven days. Thirty-nine patients completed the study. Thirty-seven patients reported complete or partial relief of symptoms within 2 days. Nearly all had marked relief of pain within 12 hours. All patients were symptom free and showed no ulcerations after 7 days of drug therapy. During the treatment period, there was a relative decrease in Borrelia and fusiform organisms, compared with the cocci and short rods. The authors did not know the mode of action of the drug and stated that routine periodontal therapy should be started after the acute symptoms have subsided. They conclude that metronidazole is a safe and effective oral agent for use in the treatment of the acute symptoms of Necrotizing Ulcerative Gingivitis.

An interesting table was presented of the relative incidence of local and predisposing factors presented by the patients. Ninety percent of the patients were between 15 and 30 years of age. Stress (28%) and inadequate diet (24%) were the most reported general factors; calculus (78%), smoking (54%) and poor oral hygiene (44%) were the most reported local factors.

(Abstracted by: CAPT P. F. Fedi DC USN.)

GINGIVAL CURETTAGE BY HAND AND ULTRASONIC INSTRUMENT: A HISTOLOGIC COMPARISON

A. D. Sanderson, J Periodont 37:17–28 July–August 1966.

The author made studies to determine the comparative histologic effect of the use of ultrasonic instru-

ments versus hand instrument curettage. Two hundred and four specimens were obtained from 34 separate patients. Each patient was curetted and two segments were biopsied, one immediately after curettage and one after a period of healing. Each segment biopsied included soft tissue walls from three adjacent pockets: one pocket was untreated and acted as a control; one pocket received hand curettage; and the third pocket received ultrasonic instrument curettage.

Specimens examined immediately after curettage were examined to determine the comparative effectiveness of hand and ultrasonic curettage in the removal of pocket epithelium.

Specimens taken at intervals from 2 to 18 days, were examined for degree of regeneration of crevicular epithelium and for the degree of inflammatory cell infiltration.

A significant difference in epithelial debridement was found between the two methods and complete removal of pocket epithelium was accomplished in more than 50 percent of the cases examined. The ultrasonic curettage appeared to be superior in the complete removal of the epithelium but the hand curettage tended to remove more connective tissue and to leave a smoother pocket wall.

Residual inflammatory cell infiltration was found after both procedures were performed. A relatively faster course of healing following ultrasonic curettage was apparent through the first 10 days of healing. The author felt that an optimum period of postcurettage healing was reached more rapidly following the use of ultrasonic curettage.

(Abstracted by: CAPT P. F. Fedi DC USN.)

PERSONNEL AND PROFESSIONAL NOTES

U.S. NAVAL DENTAL CORPS CONTINUING EDUCATION PROGRAM

The Continuing Education Courses presented at the Naval Dental School, National Naval Medical Center, Bethesda, Maryland, and those sponsored by Commandant, ELEVENTH Naval District at Naval Dental Technicians School, Naval Training Center, San Diego, California, are scheduled as follows during Fiscal Year 1968:

Naval Dental School, Bethesda, Maryland

Title	*Dates*
Preventive Dentistry	Sept 11-15, 1967
Occlusion	Sept 18-22, 1967
Complete Dentures	Sept 25-29, 1967
Fixed Partial Dentures	Oct 2-6, 1967
Operative Dentistry	Nov 27-Dec 1, 1967
Endodontics	Dec 4-8, 1967
Oral Pathology	Jan 8-12, 1968
Oral Surgery	Jan 15-19, 1968
Oral Roentgenology	Jan 22-26, 1968
Periodontics	Apr 22-26, 1968
Removable Partial Dentures	Apr 29-May 3, 1968

Naval Dental Technicians School, San Diego, Calif.

Title	*Dates*
Periodontics	Sept 11-15, 1967
Fixed Partial Dentures	Oct 16-20, 1967
Preventive Dentistry	Nov 13-17, 1967
Oral Diagnosis and Oral Roentgenology	Jan 15-19, 1968
Removable Partial Dentures	Feb 12-16, 1968
Operative Dentistry	Mar 11-15, 1968
Oral Surgery	Apr 15-19, 1968
Complete Dentures	May 13-17, 1968
Endodontics	June 3- 7, 1968

Quotas have been assigned to District and Staff Dental Officers for career dental officers. District Commandants have likewise been assigned quotas for inactive Naval Reserve Dental Officers (Ready Reserve).

For courses at the Naval Dental School, applications from career officers are to be submitted in accordance with current directives and in the format shown in ManMed art 6–130(e). The Professional Advisory Board will make recommendations on requests, and upon approval by the Surgeon General, applicants will be notified regarding final action. Those approved will be nominated for TAD or Authorization Orders, as appropriate. For courses at the Naval Dental Technician's School applications should be processed in a similar manner but directed to Commandant, ELEVENTH Naval District.

Requests from Reserve Dental Officers on active duty will be considered, on a space available basis, provided at least 6 months obligated service remains after the completion date of the course. Such re-

quests will be approved for Authorization Orders only.

The schedule of courses sponsored by the U.S. Army or the Armed Forces Institute of Pathology will be published in a later issue of the U.S. Navy Medical News Letter.

ACCELERATED CONUS DUTY

Due to the one-year tours of duty in South Vietnam areas, rotation of dental officer personnel has been accelerated. Although three and four year CONUS tours are desired for Lieutenant Commanders and Commanders respectively, it will continue to be necessary to reassign officers in those grades with two to three years in present shore tours.

CAPT John P. Arthur DC USN has relieved CAPT Victor J. Niiranen DC USN as Assistant Chief, Dental Division, Bureau of Medicine and Surgery.

CAPT Arthur served previously as Executive Officer, Naval Dental Clinic, Norfolk, Virginia.

CAPT Niiranen reports to his new assignment as Fleet and Force Dental Officer, COMSERVPAC with additional duty on Staff, CINCPACFLT.

CAPT Richard C. D'Vincent DC USN has reported to the Bureau of Medicine and Surgery to relieve CAPT George A. Besbekos DC USN as Head, Planning and Logistics Branch, Dental Division. CAPT D'Vincent was previously the Head, Extension Education Department, Naval Dental School. CAPT Besbekos reports to a new assignment at Naval Station, Roosevelt Roads, Puerto Rico.

NURSE CORPS SECTION

NAVY NURSE CORPS LUNCHEON IN NEW YORK CITY

During the recent National League for Nursing Convention held in New York City from 8-12 May 1967, Navy nurses sponsored a Nurse Corps luncheon to celebrate the fifty-ninth anniversary of their Corps. More than 200 persons attended including Nurse Corps officers, civilian nurses, and other guests. A proclamation from Governor Nelson A. Rockefeller declaring the week 8-12 May as Navy Nurse Corps Week in the State of New York was presented to CAPT Veronica M. Bulshefski NC USN by RADM Robert Granville Burke USN, Head of Naval Militia, New York. Among the many civilian guests were Dr. Lois Austin, President of the National League for Nursing, Miss Judith Whitaker, Executive Director, American Nurses Association, Mrs. Margaret L. Arnold, Vice Chairman, DACOWITS and Mr. Robert Beusse, Vice President, RKO General Broadcasting, Inc.

Left: CAPT Geraldine Houp NC USN, Chief, Nursing Service, U.S. Naval Hospital, St. Albans.

Right: CAPT Veronica M. Bulshefski NC USN, Director, Navy Nurse Corps.—Official U.S. Navy Photograph.

NURSE PROGRAMS OFFICERS MEET IN NEW YORK CITY

Twenty-three Nurse Programs Officers assigned to recruiting duty attended the National League for Nursing Convention in New York from 8-12 May 1967. During the week they also attended a Navy Recruiting Conference and a Public Information Seminar sponsored by WOR-AM-FM-TV division of RKO General Broadcasting Inc.

The purpose of the seminar was to provide a basic orientation to the Nurse Corps recruiting officers throughout the country on the use of the broadcast and print media. Many experts from these fields were participants in the program as speakers and panel session leaders. The meeting was held in the Board Room of RKO General Broadcasting Company. The Nurse Corps officers had the opportunity to meet with many representatives of the radio, TV stations, newspapers, advertising agencies, and information officers of the U.S. Armed Forces. Arlene Francis noted star of TV and radio was guest at the seminar luncheon.

Left to right: LT Bobby G. Huskey NC USNR, Mr. Robert Beusse, Vice President WOR-AM-FM-TV, Mr. Hathaway Watson, President, RKO General Broadcasting, Inc. and LCDR Barbara Chaffin NC USN.—Official U.S. Navy Photograph.

FIFTY-NINTH ANNIVERSARY OF THE NAVY NURSE CORPS

CAPT Nellie Jane DeWitt NC USN (Ret), the Director of the Navy Nurse Corps from 1945-1950, joined the Fifty-ninth Anniversary Celebration of the Navy Nurse Corps at the Naval Hospital, National Naval Medical Center, Bethesda, Maryland on 20 May 1967. With CAPT DeWitt are CAPT Alice R. Reilly NC USN, Chief, Nursing Service, Naval Hospital, National Naval Medical Center, Bethesda, and CAPT Veronica M. Bulshefski NC USN, Director, Navy Nurse Corps.

—Official U.S. Navy Photograph.

PREVENTIVE MEDICINE SECTION

STUDIES ON THE ANTIMALARIAL EFFECTS OF CYCLOGUANIL PAMOATE (CI–501) IN MAN

Trop Dis Bull 63(10):1072, October 1966.

Three studies are reported on this long acting repository compound Camolar, a dihydrotriazine metabolite of chlorguanide (proguanil). A single dose of 350 mgm. base in a lipid vehicle, was given intramuscularly into the right buttock to those of the 22 healthy volunteers from Stateville Penitentiary, Illinois, not acting as control subjects. Excretion of the drug in the urine was found for at least 86 days. In studies 1 and 2 infection was sporozoite-induced by the bites of infected mosquitoes.

In study 1, protection against patent infection was shown with the Chesson strain of *Plasmodium vivax* in 2 subjects followed for 1 year when challenged 5 months after injection of CI–501. Challenge at 2½ months showed patent infection 11 months later in 1 subject—the other was lost to the experiment. Challenge at 9 months showed no protection in 1 of 2 subjects. These results confirm a suppressive effect of the drug but do not exclude the possibility of a causal prophylactic effect if challenge is performed early.

In study 2, 6 men were challenged 33 or 47 days after injection with 2 strains of *P. falciparum* from southeast Asia which are resistant to chloroquine and chlorguanide. The clinical course resembled that in control subjects. Using these strains the authors have also shown that oral chlorguanide (proguanil) given during the pre-erythrocytic phase of infection has no causal prophylactic effect.

In study 3, 3 men were tested for the therapeutic effect of CI–501 on trophozoite-induced infection with the strains of *P. falciparum* used in study 2. There was no effect, gametocytes appeared in 1–2 months after the injection of the drug, and this infection could be transmitted to further volunteers by mosquitoes. The infection in studies 2 and 3 were treated successfully with quinine.

It is concluded that CI–501 given by intramuscular injection in a lipid vehicle exerts a long term protective effect against at least some strains of malaria not resistant to chlorguanide and chloroquine.

IMMUNIZATION AGAINST RICKETTSIAL INFECTIONS WITH LIVING ATTENUATED VACCINES

P. Zdrodowski, et al., Trop Dis Bull 64(4):363, April 1967.

In a study of living rickettsial vaccines in the USSR, the E strain of *Rickettsia prowazeki* gave rise to febrile reactions in about 11% of persons vaccinated; about 0.9% had severe reactions, some of which were associated with a rash. A vaccine containing the living E strain and a soluble antigen obtained from the Breinl strain was studied in 1,610 subjects; this combined vaccine was well tolerated and produced a satisfactory serological response. An attenuated strain of *R. burneti* (strain M–44) was also well tolerated and immunogenically satisfactory.

The review includes a discussion of experimental work on avirulent vaccines obtained by treating rickettsiae (*R. prowazeki, R. mooseri, R. sibericus, R. burneti* and *R. orientalis*) with antibiotics.

ENTERIC VIRUSES AND BACTERIA IN DIARRHEA

Amer J Trop Med 16(2):178–185, March 1967.

The etiology of acute diarrhea was studied at Phoenix, Arizona, by the examination of fecal specimens from 438 children hospitalized because of diarrhea and from 318 comparable persons without diarrhea. Laboratory examinations revealed the following percentage of specimens with pathogens from patients and control subjects, respectively: Shigella 23.5 and 0, Salmonella 3.7 and 2.2, enteropathogenic *E. coli* (EEC) 30.6 and 6.9, adenovirus 2.5 and 0. Coxsackie virus 3.0 and 0.9, ECHO virus 11.9 and 4.4, and poliovirus 2.3 and 6.9. Poliovirus was probably of vaccine origin.

Shigella and EEC were associated, respectively, with diarrhea in about 15 and 37% of the infants under 1 year of age, who constituted about 78% of the cases. EEC was not recovered from persons over 2 years of age, but Shigella was relatively more prevalent among this group than among younger children.

Definitive data were not obtained on the etiologic significance of viruses. ECHO virus was isolated from patients at more than twice the rate as from control subjects.

LEUKEMIA

USDHEW PHS NCDC Morb & Mort Wkly Rpt 16(20):161–168, May 20, 1967.

Since the institution of the case-reporting program in 1966 to the National Communicable Disease Center, Atlanta, Georgia, there have been 3 instances of multiple cases of leukemia occurring among occupants of a single house at 3 different areas.

An 18-year-old man who moved into a 2nd floor apartment in North Kansas City, Missouri, in April 1964, developed acute lymphocytic leukemia in January 1966. A 28-year-old woman who lived on the 1st floor of the same building from June 1962 to June 1966 developed acute myelocytic leukemia in January 1967.

A 41-year-old man developed chronic myelocytic leukemia in February 1961, 13 months after moving out of a house in Prairie Village, Kansas. Another family moved into that house in January 1960 and lived there until October 1966. A 15-year-old girl in this family developed acute myelocytic leukemia in January 1967.

Finally, 1 member of the last 3 families that have lived in a small house in Douglas, Georgia, has developed acute leukemia. A 7-year-old boy became ill in July 1958, 13 months after his family moved out. A 36-year-old woman developed leukemia in March 1963 after living in the house for 6 years. In October 1964 another family moved into this house, and in December 1966 the boy (5 years old) in this family had the onset of leukemia.

Radiation levels in the apartment house in North Kansas City were studied and found to be normal. The house in Douglas will be investigated in a similar manner; also, prior occupants of the house will be traced in a search for other cases of neoplastic disease.

Table 1

THREE HOUSES WITH MULTIPLE LEUKEMIA CASES AMONG OCCUPANTS

House Location	Age *	Sex	Period Occupied the House	Date of Onset	Type of Leukemia
North Kansas City, Missouri	18	M	4/64– 6/66	1/66	Acute lymphocytic
	28	F	6/62– 6/66	1/67	Acute myelocytic
Prairie Village, Kansas	41	M	? – 1/60	2/61	Chronic myelocytic
	15	F	1/60–10/66	1/67	Acute myelocytic
Douglas, Georgia	7	M	4/57– 6/57	7/58	Acute lymphocytic
	36	F	6/57– 4/63	3/63	Acute lymphocytic
	5	M	10/64–present	12/66	Chronic myelocytic

*Age at diagnosis.

WORLDWIDE INCREASE IN CANCER MORTALITY AMONG MEN AT MIDLIFE

Statist Bull Metrop Life Insur Co 47:1–3, November 1966.

Death from cancer is an increasing hazard to middle-aged men in most of the Western world and in Japan. The impact of this disease can be measured not only in lives tragically shortened but also in social and economic losses. A considerable portion of all cancer deaths occurs among males at the prime ages of life, when men are most productive economically and bear the greatest responsibilities. In the United States in 1964, for example, somewhat over ⅓ of all cancer deaths among men were registered at ages 45–64.

The largest increases at these ages, amounting to 16%, were recorded in Italy and Portugal. France and nonwhite men in the United States showed the next highest increases, 13 and 12%, respectively. Only in Norway and Sweden was there no change or a very slight decline in mortality from this cause. In the other countries and among the white men of the United States, the increases ranged from 4 to 8%.

The reported mortality rate from all forms of cancer combined among men at ages 45–64 was highest during 1960–61 in the nonwhite male population of the United States, at 369.9 per 100,000.

England and Wales were next with a rate of 362.6, followed by France with 336.2. The lowest rate was observed in Sweden, at 205.8 per 100,000, followed closely by Israel's rate of 209.4 and Norway's 212.7. For white males in the United States the rate in 1960–61 was 278.0.

For cancer of the lung, the highest death rate, 169.5 per 100,000, was registered in England and Wales, and in Germany, second highest at 96.9. The nonwhite male population of the United States followed with a rate of 96.3. The lowest death rate for cancer of the lung was recorded in Japan, at 22.5 per 100,000 males in the age range considered. Portugal was almost as low with 23.3, followed in turn by Sweden and Norway with rates about 36 per 100,000.

For cancer of the stomach, the death rate reported from Japan, 157.0 per 100,000 was more than twice the next highest, 73.3 in Portugal. The lowest mortality rate from cancer of this site was 19.3 for the white male population of the United States at ages 45–64; however, the corresponding rate for nonwhite men was nearly 2½ times as high.

STUDIES ON TRYPANOSOMA CRUZI ISOLATED IN THE UNITED STATES

I. G. Kagan, et al., Trop Dis Bull 64(4):355–356, April 1967.

In the United States, 9 species of triatomids and 14 species of mammals have been found infected with *Trypanosoma cruzi*. Serologic studies for antibodies against *T. cruzi* in human beings are discussed. The epidemiology of *T. cruzi* infections in the United States differs from the classical pattern encountered in South America since infected insect hosts are found in trees and do not always defecate while feeding on the mammalian host. The infectivity and pathogenicity of "animal" strains of *T. cruzi* have been studied and are reviewed. Most strains are avirulent for mice. The cultural characteristics of several strains have been studied and the course of infection in mice examined. Differences among strains have been found. Immunologic studies have shown that avirulent North American strains of *T. cruzi* protect mice against a virulent lethal South American strain. Attempts to differentiate strains serologically by the indirect hemagglutination test were not successful. Experiments to demonstrate that an infection with *T. cruzi* suppressed the development of mammary cancers in mice indicate that statistically significant differences between infected and uninfected groups of female mice were obtained. The basis for the protective relationship was not determined. *T. cruzi* in the United States is found in animals in the southern part of the country. Whether or not clinical disease in man takes place has not been demonstrated.

ACCIDENTS AT THE HIGH SCHOOL AND COLLEGE AGES

Statist Bull Metrop Life Insur Co 47:6–8, November 1966.

Of all causes of death among adolescents and young adults, accidents take by far the greatest toll. In 1964, the latest year for which official figures are available, accidents were responsible for 62 percent of the deaths among males aged 15–24 and for 37 percent among females in the same age group. For both sexes combined, this was seven times the loss of life inflicted by cancer, next in importance as a cause of death at these ages. The 1964 death count from accidents included 17,190 young persons 15–24 years old—the high school and college ages. This is equivalent to an accident death rate of 59.2 per 100,000 adolescents and young adults.

The 1964 figures represent the third successive annual increase in the total number and rate of accidental fatalities among young people. Preliminary data point to still higher figures for 1965.

Accidents also play a major role in disability at these ages. Data from the National Health Survey show that each year about 7 million of these young people suffer nonfatal injuries serious enough to require medical attention or to result in at least one day of restricted activity. A fourth of them sustain their injuries in and about the home, and nearly as large a proportion are hurt in school buildings or on school premises. In addition, about a sixth are injured at work. Surprisingly, in view of their greater importance as the locale of fatalities, street and highway accidents—largely motor vehicle mishaps—account for only a seventh of the nonfatally injured.

Although motor vehicle accidents are thus responsible for only 14 percent of the nonfatally injured at ages 15–24, they cause 70 percent of the fatalities. Indeed, the recent upswing in accidental deaths among young people largely reflects the continued increase in motor vehicle accident fatalities; these rose from about 9,000 in 1961 to 10,000 the following year and climbed steadily to 13,000 in 1965, as estimated by the National Safety Council.

Mortality From Leading Types of Accidents at Ages 15–24, United States, 1962–63

	Average Annual Death Rate per 100,000 Population, at Ages		
	15–24	15–19	20–24
MALES			
Accidents—All Types	91.6	78.7	108.3
Motor vehicle	62.3	51.3	76.7
Traffic	61.6	50.8	75.8
Pedestrian	3.3	3.3	3.3
Nontraffic	0.7	0.5	0.9
Drowning *	8.4	10.2	6.2
Firearms	3.9	4.5	3.2
Water transport	1.9	1.5	2.5
Falls	1.9	1.5	2.4
FEMALES			
Accidents—All Types	21.4	21.5	21.3
Motor vehicle	16.6	16.9	16.2
Traffic	16.5	16.8	16.1
Pedestrian	0.9	1.0	0.7
Nontraffic	0.1	0.1	0.1
Fires and explosions	0.9	0.7	1.1
Drowning *	0.8	1.0	0.5
Poisoning by gases and vapors	0.6	0.7	0.6
Firearms	0.4	0.4	0.4
ACCIDENTAL DEATHS AS A PERCENT OF ALL DEATHS			
Males	62%	63%	60%
Females	35	40	30
MOTOR VEHICLE ACCIDENT DEATHS AS A PERCENT OF ALL ACCIDENTAL DEATHS			
Males	68	65	71
Females	78	79	76

*Exclusive of deaths in water transportation.
Source of basic data: Reports of the Division of Vital Statistics, National Center for Health Statistics.

As the accompanying table shows, motor vehicles were involved in 7 out of 10 accidental deaths among males at ages 15–24 during 1962–63. The proportion was a little higher, nearly 8 out of 10, for females, but their total accident mortality was less than a fourth that of males at these ages. The death rate from motor vehicle accidents among males was 3 times higher than that among females at ages 15–19 and nearly 5 times greater at 20–24. It is a striking fact that the death rate from such accidents among young men at ages 20–24 averaged 76.7 per 100,000 —higher than at any other period of life.

Other types of accidents also play a prominent, if lesser, role in fatal injuries among young people. Drownings (other than in water transportation) take about 1,100 lives annually among youths and young men 15–24 years of age, ranking second as a cause of accidental death in this group. At ages 15–19 the death rate from drowning among boys is higher than in any other age period; it was 10.2 per 100,000 in 1962–63, more than 10 times the rate for girls at these ages. Boat accident drownings in the age group 15–24 are responsible for an additional 250 fatalities each year among males, but only for very few among females.

Firearm accidents rank third as a cause of acci-

dental death among young males in the age groups under review. In 1962–63 such mishaps averaged 4.5 deaths per 100,000 at ages 15–19 and 3.2 at ages 20–24. Falls take about 250 lives annually among males 15–24 years of age.

Fires and explosions ranked second among accidental deaths of girls and young women, but accounted for only 4 percent of all their accident fatalities. Among males, fires and explosions represent only a minor threat to life compared with other causes, yet the death rate—1.1 per 100,000 at ages 15–19 and 2.3 at ages 20–24—was about twice that of females. Gas poisoning and firearm mishaps were among the lesser causes of accidental deaths among females.

Except for fatal motor vehicle accidents, whose continued rise has already been noted, there were substantial reductions in the death rates from most of the other major types of accidents shown in the table. Young men of 20–24 showed significantly lower mortality from water transport accidents and falls, although the reductions in these, as in other non-motor vehicle accidents, were smaller than the reductions registered for their juniors. Females at ages 14–24 benefited from a marked drop in fatalities due to fires and explosions.

KNOW YOUR WORLD

Did You Know?

That the most dangerous hours for automobile accidents are between 4:00 and 7:00 p.m., with Friday being the most dangerous day?

The ejection from the automobile accounts for 25% of serious and fatal injuries—use your seat belt. An Indiana study of 495 fatal accidents in 1954 revealed that 45% were experienced under 40 m.p.h.[1]

That a case of typhoid fever occurred in a 21-month-old child following exposure to a known typhoid carrier, the great-grandmother?

The typhoid carrier was the child's great-grandmother who had a colostomy performed for a carcinoma of the colon 3 years previously. It had been customary to observe strict precautions when the child made infrequent visits to his great-grandmother. However, on one visit 16 days prior to onset of his illness, the patient managed to enter a normally locked bathroom and was discovered chewing on the colostomy irrigation tube.

The great-grandmother was found to be a carrier in 1963, when another member of the same family contracted typhoid fever. The great-grandmother gave a history of having had typhoid fever in 1925.[2]

That in 460 female patients with typhoid fever, 37 (7.4%) proved to be carriers of *Salmonella typhi* after 2 years and an average of 3.7 years?

Patients, treated with chloramphenicol for typhoid fever, were dismissed from a hospital in Santiago, Chile. From 1960–1964, a study was made to determine rate of *Salmonella typhi* carriers among them. Two thousand were visited at home and nearly 2,000 fecal cultures were made in the index cases and their suspect contacts. Attention is invited to the associations: the ratio of carriers increases with age and depending on the length of time elapsed between the first symptoms and treatment; the ratio is significantly higher when there is a relapse; there is observable association between being a carrier and the presence of liver disorders.

The rate of typhoid fever among contacts exposed to a proved carrier was 5 times higher than among families in which no carrier was detected.[3]

That serum hepatitis in a 20-year-old woman occurred after taking methedrine, a stimulant similar to benzedrine, intravenously, at a party?

This was reported to the Utah State Health Department on 13 January 1967. The patient had never had a blood transfusion. Investigation of her contacts, revealed 16 persons who regularly or occasionally used drugs intravenously. Of this group, 10 had developed hepatitis within the 6 months before the investigation. All 16, ages 18–26, had attended a party between 27 October and 29 and used methedrine intravenously with the same needle and syringe.[4]

That a trachoma study in Tripoli, Libya, in 1,000 patients, using a new long-acting sulphonamide, RO 4–4393, has been investigated?

Percentage of recovery obtained with the smallest dose (20 mgm per kilogram) applied every 15 days

for 3 months did not differ from that obtained with higher dosages and more frequent application. Therefore, the author considered this therapeutic regimen to be suitable for mass antitrachoma campaigns.[5]

That 4 cases (with 2 hospitalizations) of leptospirosis in squirrel hunters with serologic evidence of *Leptospira australis* or *L. grippotyphosa* or both, occurred in New England?

From 9 fox squirrels caught, *Sciuris niger* was isolated from 1, in addition.

In patients with fever of undetermined origin diagnosis may be aided by adequate information concerning a patient's occupational and recreational exposure experience. Laboratory assistance is also a necessary adjunct to definitive diagnosis. As man gains more leisure time and participation in more recreational activities, he may become exposed to additional reservoirs of leptospirosis. The human cases above, and their association with a previously unreported animal host, further demonstrate the wide distribution of this infection in animals.[6]

That cirrhosis (of the liver) is now the 3rd cause of death among young and middle-aged individuals in urban areas?

Most cases occur in chronic alcoholics and are preceded by the fatty-liver stage. As little as 12 ounces of alcohol daily, over a period from 8 to 18 days, produced a reversible fatty liver in alcoholic volunteers whose diet was at least adequate.[7]

That a sharp rise in vivax infections and ¾ of the vivax malaria patients had their onset more than 30 days after their return from South Vietnam?

Six hundred seventy-eight cases of malaria were reported in the United States in 1966. All but 10 of the 722 cases preliminary reported through April 1967, occurred in military returnees.[8]

That the State of Maryland has become the first state to pass a law (1967) permitting physicians to treat minors with venereal disease privately without the consent of parents or guardians?

The law is aimed at encouraging teenagers to seek medical care.[9]

That, in Florida, 2 of the greatest pest mosquitoes, *Aedes sollicitans* and *Aedes taeniorhynchus,* usually breed in areas along the coast, marshes, swales and mangrove swamps, which may be flooded by rain or high tides (not normal tides) for a week or longer?

The most plentiful of any species, these two can fly up to 25 miles.[10]

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EDITOR'S SECTION

DR. GRAYBIEL RECEIVES SECOND LEGION OF MERIT AWARD

Dr. Ashton Graybiel, Naval Aerospace Medical Institute's Director of Research, received a Gold Star in lieu of the Second Legion of Merit Medal at change of command ceremonies at NAMI May 2. CAPT H. C. Hunley before turning over the command to CAPT J. W. Weaver said he would be remiss in his duties if he did not recognize Dr. Graybiel who has done more than anyone to make the Institute continue to grow and make progress. He presented the Gold Star and a citation signed by the Secretary of the Navy for the President of the United States. The citation reads: "For exceptionally meritorious service as Director of Research at the U.S. Naval Aerospace Medical Institute, Pensacola, Florida from 1 January 1960 to 30 June 1966. Through dedicated and energetic research, CAPT Graybiel has brought distinction to the United States Navy by his pioneering of studies in the field of vestibular physiology and is considered one of the foremost authorities in this field. Although relatively new, these studies have had a tremendous impact on aviation and space medicine. Having become an international authority in the field of cardiovascular physiology for which he is still noted, and then changing his field of interest to vestibular physiology

to acclaim an international reputation, requires an extremely intellectual, imaginative and devoted scientist. In the past six years, he has been honored by no less than eight awards for scientific and technical achievement in the field of medicine. CAPT Graybiel's extremely effective leadership, tireless energy and exceptional professional aptitude reflect great credit upon himself and the United States Naval Service."—Research Div, BuMed.

NAVAL MEDICAL SCHOOL REQUESTS PARASITE SAMPLES

Review of Naval Medical School teaching materials in parasitology reveals shortages of specimens of the following items.

Plasmodium ovale—thin smears
Taenia solium—proglottids & scolices
Metagonimus eggs
Opisthorchis eggs
Paragonimus westermani—or other species
Cysticerci of *Taenia solium*
Diphyllobothrium latum eggs
Schistosoma japonicum eggs
Ancylostoma duodenale—adults
Dientamoeba fragilis
Heterophyes heterophyes eggs
Echinostoma ilocanum eggs

Specimens will be most welcome and should be addressed to the Commanding Officer, Naval Medical School, National Naval Medical Center, Bethesda, Maryland 20014.

HELICOPTER SPRAYING FOR TICK CONTROL

On 25 and 26 May 1967, the Naval Medical Field Research Laboratory, Camp Lejeune, in cooperation with the Army Medical Equipment Research and Development Laboratory, Fort Totten, New York, and the Entomology Research Laboratory of the Department of Agriculture, Gainesville, Florida, applied an insecticide at four different rates of deposit to plots of up to 50 acres in size at Camp Lejeune for experimental tick control by helicopter.

The spraying equipment used had been developed by the Medical Equipment Research and Development Laboratory at Fort Totten, for mosquito control by helicopter and several units are now in operational use in the Republic of Vietnam for malaria control.

The tests reported on were:

(1) to determine the effectiveness of helicopter spraying against ticks, and

(2) to determine possible Navy-Marine Corps interest in the Army developed system.

The insecticide applied was fenthion, a relatively short-lived chemical (compared to DDT), at rates of 0.25 to 2.0 pounds of the technical material per acre. The higher rate of application gave complete control of ticks within 24 hours, and intermediate rates showed evidence of producing acceptable tick control within 48 or more hours after application. The Medical Equipment Research Development Laboratory, Fort Totten, spray equipment performed admirably, and recommendations for its acceptance by the Navy will be made, eliminating development time and cost for a comparable Navy system.—Public Affairs Office, BuMed.

MEASLES IMMUNIZATION CAMPAIGN

LCDR Stephen J. Kendra, MC USN, Head of the Communicable Disease Branch of the Preventive Medicine Division of the Bureau of Medicine and Surgery, Department of the Navy, participated in the Montgomery County (Maryland) Measles Immunization Campaign, conducted on 21 May 1967. This campaign was sponsored by the Medical Society of the State of Maryland, the Montgomery County Medical Society in cooperation with the Montgomery County Health Department.

LCDR Kendra administered Schwartz strain measles vaccine to 780 children, utilizing the jet injector apparatus. No difficulties were encountered. —Public Affairs Office, BuMed.

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