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Medical News Letter

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Surgeons General of the Past

(The twenty-second in a series of brief biographies)

Perceval Sherer Rossiter was born in Shepardstown, West Virginia on 30 November 1874, and received his medical degree from the University of Maryland in 1895. He served in the Army in Cuba and the Philippines until 1902, being appointed Assistant Surgeon in the Navy 20 January 1903. After studying Naval and Tropical Medicine at the Naval Medical School he was ordered to Honolulu, served at the Naval Academy for 2 years and then at the Naval Station in Tutuila, Samoa until 1910. Doctor Rossiter next had duty in the Independence at Mare Island and at the naval hospital in Puget Sound. Following duty afloat on the California and the San Diego in the Pacific Station, he had shore duty as Senior Medical Officer and Medical Inspector from 1916–1917 at the San Francisco Naval Training Station. In October 1918 he was sent to Base Hospital No. 2 in Europe, and later was Medical Officer of the Cap Finisterre (of the Transport Force) and of the Idaho, a unit of Battleship Squadron 4, Pacific Fleet. From 1920 to 1922 he was Medical Officer of the Second Advanced Base Force, Marines in San Diego. For 3 years he was Medical Member of the U.S. Naval Mission to Brazil. Captain Rossiter was next Executive Officer at the Naval Medical Supply Depot in Brooklyn, N.Y. and also at the Chelsea Naval Hospital. He became the Brooklyn hospital's Medical Officer in Command, and assumed the same responsibility at the Washington Naval Hospital until his appointment as Surgeon General in March 1933. Rear Admiral Rossiter served until December 1938, when he retired. He was the first Surgeon General to accompany the U.S. Fleet on extensive maneuvers, and was President of the Association of Military Surgeons 1937–1938. His death occurred 20 December 1957 in Santa Barbara, California.

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Policy

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

THE RETINAL DISEASE OF RUBELLA

Alex E. Krill MD, Chicago, Arch Ophthal 77(4):445–449, April 1967.

An Australian physician, Aileen Mitchell, was the first to note fundus changes in a child born with rubella. In his initial report before the Ophthalmological Society of Australia in 1941, Gregg did not mention this observation. Several years later, however, while reviewing his notes of case reports collected for this original paper, he cites the following fundus description by Dr. Mitchell from a child with a left-sided monocular cataract: "The fundus of the right eye appeared pale, and some scattered irregular spots of pigment were observed."

Rubella retinitis is now recognized as one of the three most frequent ocular abnormalities in a child with congenital rubella. The exact incidence is uncertain since eyegrounds are sometimes not visualized because of dense congenital cataracts. Reported frequencies are: 16 out of 120 cases, 17 out of 38 cases, 15 out of 29 cases, 50 out of 82 cases, ten out of 27 cases, and six out of 17 cases.

The appearance of the retina is fairly similar in most cases. Widespread pigment deposits, usually of greatest density in the macula, are the typical finding. In some cases the deposits are found only in the macula and in some only in the periphery. The deposits may be restricted to one eye or to one or two sectors of both eyes.

The pigment is typically described as mottled or blotchy. In the macula it is likely to form clumps and may cause a loss of the foveal reflex. In the periphery it is more likely to appear dust-like or stippled. The pigment deposits have also been described as measly, powdery, fine, sprinkled, and peppery. Gregg has given the most colorful description of rubella retinitis: "It was like a piece of coarse Scotch tweed used for a sports coat over which pepper had been thrown." In a few cases the pigment was said to have a spicule-like form similar to that found in retinitis pigmentosa. In most cases it appears to be of uniform depth beneath the retinal vessels. (In one case deposits were found above the retina vessels.)

Cases are reported with pale optic nerves but the retinal vessels are always normal. Rare changes which have been described in one or more cases include punched out areas, diffuse yellow (along with pigment) spots, moth-eaten-like changes, slightly atrophic or prominent choroidal vasculature, an "abiotrophy of the Sorsby type," a fundus-flavimaculatus-like retinopathy, and optic neuritis.

The retinitis causes minimal or no effect on retinal function. Visual acuity, visual fields, dark adaptation, color vision, and electroretinography in patients with retinitis, (and no other ocular complications caused by rubella) have been normal or close to normal. It appears that there is no change in visual function over a period of time.

A retinal abnormality causing severe loss of visual acuity may occur in rubella as a result of other ocular changes. A dense cataract at or shortly after birth may result in faulty macular development. On the other hand, a small cataract present at birth may allow "normal" macular development. But it may later undergo progressive opacification resulting in a deep-seated amblyopia. It is also possible that optic atrophy may occur secondary to a congenital glaucoma. None of these retinal abnormalities will cause any change in the standard electroretinogram (ERG). It is obvious that a normal ERG does not necessarily imply good visual prognosis after cataract surgery in rubella. In fact, since none of the secondary retinal changes causing abnormal vision affect the ERG, there is little value to this test in a child with known rubellar cataracts. One could argue that a markedly abnormal ERG definitely implies a poor prognosis.

Two pathological reports confirm the insignificance of pigmentary retinopathy in most rubella cases. The changes were limited to the pigment epithelium and consisted of abnormal distributions of pigment in this layer. (Pigment was collected

From the Eye Research Laboratories, The University of Chicago, Chicago.

Read before the Section on Ophthalmology at the 115th annual convention of the American Medical Association, June 29, 1966.

Reprint requests to the Eye Research Laboratories, University of Chicago, 950 E 59th St., Chicago 60637 (Dr. Krill).

in masses at certain areas and was absent in other areas.) No abnormalities in the rest of the retina or choroid were found. The occasional occurrence of more severe retinal involvement is suggested in two other histological reports. In one report, small retinal ganglion cells and "poorly developed rods and cones" were noted. In another, retinal dysplasia and rosettes were found.

The observation of a pigmentary retinopathy in the newborn or young infant, should always bring up the possibility of rubella etiology, even if there is no history of this disease in the first trimester of pregnancy. The mild nature of rubella in the pregnant mother may prevent its recognition. The association of cataracts and/or microphthalmia with the retinopathy suggests rubella. Deafness and certain systemic abnormalities (particularly cardiac) are other findings which suggest a rubella etiology.

Another condition which may produce a retinopathy similar to rubella in the newborn or young infant is a congenital tapetoretinal degeneration. In fact, in our experience this is the most common cause of pigmentary retinopathy in the first year of life. Leber originally described this condition as amaurosis congenita; later, other workers described, under different names, what appears to be the same disease. Children with congenital tapetoretinal degenerations may also have cataracts. However, a unique finding for this group is the occasional presence of keratoconus or keratoglobus. Defective development of all the receptor elements is suspected to be the cause of amaurosis congenita; therefore, it is not surprising that in this disease there is severe visual impairment resulting from the retinal abnormality. In fact, only a minimal response at best is obtained from the ERG of an affected child. This test easily distinguishes a case of amaurosis congenita from rubella retinitis.

The eyegrounds of an infant with a certain type of syphilitic chorioretinitis may resemble rubella retinitis. The "salt and pepper" fundus characterized by Sidler-Huguenin as type 1 has fine pigment deposits scattered throughout the eyegrounds. Frequently, these deposits are only seen in the peripheral retina but they may be seen in the posterior retina. The pigment dots are often intermingled with yellowish-red spots. The optic nerve is normal in the milder cases but may be atrophic in more severe cases. The retinal vessels are usually normal, but in severe cases they may be attenuated and even accompanied by white lines. Such vascular changes are not seen in rubella. Serologies are of prime importance in the diagnosis of syphilis. Visual functions are usually normal, but may be markedly abnormal in severe cases. In one case only a small negative response was detected with the ERG.

Only rarely, it seems, do other viral infections contracted during the first trimester of pregnancy cause ocular abnormalities in the newborn similar to those produced by rubella. These viral infections include morbilli, varicella, and influenza. There is not enough information to be sure of the severity of the retinitis in these cases.

Radiation during the first trimester of pregnancy may also cause a pigmentary retinopathy in the newborn. As with rubella, cataracts and microphthalmia can also occur. In a recent report changes were described in 45 newborns thought to be produced by irradiation. Ocular malformations occurred in 50 percent of these cases. Apparently the retinopathy has little effect on visual function. The ERG has been studied in some of these cases and found to be either normal or subnormal.

It is of interest to note that two diverse causes of an embryopathy in the newborn—a virus infection or irradiation during the first trimester of pregnancy—produce only minimal damage to the retina. Perhaps any insult to the embryo in the first trimester will cause only minimal damage to the retina. The stage of embryonic development may affect susceptibility. It is noteworthy that the 3-month-old embryonic retina consists of only two portions, the inner and outer neuroblastic layers. Differentiation into the various layers of the retina begins during the fourth month of pregnancy.

Retinopathies which occur later in childhood may resemble rubella retinitis. An early retinal degeneration or a postinfectious retinopathy are the two considerations. Usually a virus has been cited as an infectious cause and of the viruses morbilli is by far the most common. Other viruses cited include variola, vaccinia, epidemic parotitis, encephalitis and Bechet's disease (of questionable virus etiology). Rubella contracted in childhood may produce a retinitis similar to that found in cases of congenital rubella. Rarely, other types of infectious agents produce a retinopathy resembling rubella retinitis. These include typhoid fever, diphtheria, scarlatina, and typhus.

Differentiation of these diseases from rubella retinitis is usually easy. In early retinal degenera-

tions night blindness is a prominent symptom. The ERG is markedly abnormal, in most cases producing either a minimal or no response. Visual fields, dark adaptation, and sometimes acuity may be abnormal. With an infectious retinopathy, the child is normal at birth and there is usually an abrupt loss of vision in the course of convalescence from some childhood disease. The fundus picture at this stage may resemble that of a central retinal arterial occlusion or spasm. Although this fundus appearance is only transient, there is usually permanent impairment of retinal function. Acuity, visual fields and dark adaptation are usually abnormal and an ERG may show extinguished or minimal response. Eventually these children develop a pigmentary retinopathy similar to that of rubella. They usually do not have associated ocular abnormalities such as cataracts and microphthalmia.

Report of a Case

The following case report illustrates many of the features of rubella retinitis. The patient is a 13½-year-old deaf girl. She has never had any ocular complaints but was referred to the University of Chicago for retinal function evaluation because of a diffuse pigmentary retinopathy. She has been deaf since birth. No other abnormalities have been found. The mother had rubella during the first trimester of pregnancy. Ocular examination revealed corrected visual acuity of about 20/20 in both eyes. Reading vision was four point in both eyes. The remainder of the examination was normal except for the fundi, which revealed a diffuse distribution of pigment clumps, of greatest concentration and size in the macular area. In the periphery the pigment was rather dot-like in appearance. The retinal vessels and optic nerve were normal. Retinal function evaluation revealed normal color vision (pseudoisochromatic plates, Nagel anomaloscope, and Farnsworth-Munsell 100 Hue Test), normal visual fields, normal ERG and a normal electroculogram (EOG).

This case illustrates the typical appearance of pigmentation in rubella retinitis. The lack of any abnormality on retinal function is typical, although a few cases have shown a mild abnormality on the ERG. Of particular interest is the finding of a normal EOG. The identity of all the layers which contribute to the EOG is uncertain, but undoubtedly a large portion of this potential originates from the pigment epithelium. Since the abnormality in rubella retinitis has been shown to be in the pigment epithelium, the normal EOG implies that the histological abnormality is strictly one of pigment distribution and not of pigment epithelial cell function. The finding of normal retinal function in a 13-year-old patient with congenital rubella retinitis is further evidence of the stationary nature of this disease.

Summary

In general, retinitis exhibits high incidence in children with congenital rubella. The retinitis usually consists of stable wide spread pigmentary deposits of greatest size and concentration in the macular region. These changes produce little or no effect on visual function.

Retinal changes may occur as the consequence of other congenital ocular abnormalities in rubella, such as cataract or glaucoma. These retinal abnormalities produce a loss of visual acuity which may be irreversible.

This work was supported in part by National Institutes of Health, Public Health Service, grants NB–3358 and FR–55.

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

(The article about retinal disease of rubella is one of seven which were presented at a Rubella Symposium read before the Section on Ophthalmology at the 115th Annual Convention of the American Medical Association, Chicago, June 29, 1966. All of the articles appear in the Archives of Ophthalmology, Vol. 77, No. 4, April 1967—Editor.)

CHRONIC LYMPHOCYTIC LEUKEMIA: NEW CONCEPTS AND MANAGEMENT

George A. Hyman MD, New York, New York, Clin Med 74(7):17–20, July 1967.*

Patients with chronic lymphocytic leukemia should not be treated until symptoms warrant it, and then treatment should be cautiously administered with frequent checks. Awareness of possible complications prolongs survival and gives a more comfortable life.

The etiology of the leukemias in man is unknown. Chronic lymphocytic leukemia (CLL), however, differs from chronic myeloid leukemia and acute leukemia in several respects. CLL runs a more benign course; when death occurs, it is often the result of complications of the disease, such as infection, rather than of the disease itself. CLL, unlike chronic myeloid or acute leukemia, is not radiation induced. Thus, there was no increase in the incidence of CLL in survivors of the Hiroshima atomic blast although there was an increase in other forms of leukemia and in myeloid metaplasia five to six years later in people who were near the blast's epicenter. The British have also noted an increased incidence of chronic myeloid and acute leukemia in patients who have undergone excessive diagnostic radiography of truncal areas or radiotherapy for Marie-Strümpell arthritis. Again, there was no evidence of an increase in CLL. Finally, although viruses have been implicated in the etiology of acute leukemia and chronic myeloid leukemia in rodents, there is no clear proof of their importance in CLL.

Chromosome studies of marrow and peripheral blood reveal another difference. The pathognomonic abnormal chromosome 21 is found in chronic myeloid leukemia. Abnormal, nondiagnostic, highly variable chromosomal abnormalities are found in more than one-half of the patients with acute leukemia. There does not seem to be any significantly consistent alteration in the chromosome pattern of the blood of patients with CLL, however.

These differences in regard to radiation induction and viral and chromosome studies suggest a basic difference in the pathogenesis of CLL as compared to the other leukemias discussed.

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History of Therapy

Progress in the understanding and management of the leukemias in general and CLL in particular was very slow until the introduction of radiation therapy in the early 1900s. Until that time, emphasis was on descriptive morphology, classification, and natural history of these disorders. In 1927, potassium arsenite solution was introduced for therapy of the chronic leukemias, followed by radioactive phosphorus (P^{32}) in the 1940s. The introduction of nitrogen mustard therapy in 1946 opened the modern era of chemotherapy. Subsequently, urethane, busulfan (Myleran) and chlorambucil (Leukeran) have been used as neoplastic suppressants.

In the past 10 years, growing insight into the pathogenesis of CLL and improvement in chemotherapeutic agents have opened a new era, one in which amelioration of the chronic leukemic disorder occurs regularly and in which eventual cure or prevention may be anticipated. Indeed, there are several reports of patients with CLL and others with acute leukemia who are alive, without any evidence of disease, more than 10 years after the last therapy was administered.

Clinical Picture

Absolute lymphocytosis is a cardinal and usually the first abnormal finding in patients with CLL. Frequently discovered during routine peripheral blood counts, it may precede the clinical manifestations of the disease by many years. In fact, the diagnosis often cannot be made with certainty until the peripheral white count rises above 25,000, nodes enlarge, or an adequate marrow aspirate shows a lymphocytosis of greater than 30 to 50%. A lymph node biopsy is not required to make the diagnosis.

Some helpful diagnostic features include hypogammaglobulinemia, which occurs early in more than 50% of the patients (a serum protein electrophoresis is suggested for patients with unexplained lymphocytosis); an abnormal "spike" in the protein pattern in the gamma globulin range, which occurs in 5 to 10% of the patients; normocytic anemia and thrombocytopenia; and hyperuricemia. In regard

to differentiating between benign lymphocytosis and CLL, a test has been suggested to separate normal from abnormal lymphocytes based upon the increased sensitivity of the CLL lymphocyte to prednisolone. This "prednisolone test" requires further evaluation. Another differential point is the failure of the lymphocyte in CLL to undergo the mitogenic change which occurs within the normal lymphocyte after exposure to phytohemagglutinin.

Survival and Function

Knowledge of factors leading to absolute lymphocytosis, the essential feature of CLL, provides some insight into the pathogenesis of this disorder. Current studies indicate that the lymphocyte is a long-lived cell which may return from the blood stream to the lymph channels two or more times. The *in vivo* life span of the normal lymphocyte may vary from 100 to 300 days or more, far longer than that of the granulocyte, although shorter lived lymphocytes also exist. The *in vitro* survival of the lymphocyte of CLL is increased four- to five-fold over the normal, and the increased life span correlates directly with the height of the white count, suggesting that a prolonged survival associated with a diminished removal rate is important in the lymphocytosis seen in this disorder.

Other data also indicate the increased resistance of the lymphocyte in CLL, in this instance to x-rays. Although the normal lymphocyte is extremely sensitive to radiotherapy in doses as small as 2 to 5 *r*, 29% of patients with CLL have lymphocytes resistant to radiation, some to more than 1000 *r*.

It has been postulated that the small lymphocyte is not a mature cell but rather a pluripotential one. Although six divisions are necessary for the parent reticular cell to become a small lymphocyte, this pathway may be reversible. The small lymphocyte has been described as a specialized form of the primitive mesenchymal cell, in a resting, relatively inactive state, and reduced to the smallest possible size for the purpose of easy mobilization and transport through the blood stream. Thus, some small lymphocytes may be hematopoietic stem cells, whereas others may already have been conditioned to develop along special lines.

Compared to normal lymphocytes, the CLL lymphocytes have numerous functional defects. They show decreased or absent type-specific antigenicity and, unlike the normal lymphocyte and the immature cells of other types of leukemia, they fail to undergo blastogenic or mitogenic growth in culture after the addition of phytohemagglutinin. Also, the lymphocyte of CLL does not change to a more primitive cell when exposed to antigens to which the individual has previously been challenged. This failure of an anamnestic response, like the hypogammaglobulinemia, is part of the known impairment of the immune mechanism which is seen in virtually all patients with CLL as the disease progresses. Some authors, however, feel that there is a range of ability of the lymphocyte of CLL to undergo mitosis with a wide range of competence in these cells varying from normal to extreme incompetence.

Complications of CLL

In patients with CLL, complications may lead to death more often than the disease itself. Unrelated disorders, which are common in the older age group in which CLL occurs, may be lethal. Anemia and thrombocytopenia, with fatal hemorrhagic manifestations, are seen in the late stage of CLL. Prolonged lymphocyte survival may contribute to bone marrow failure through progressive infiltration. The apparently impaired function of the lymphocyte, with failure to respond normally to antigenic stimuli, the decreased gamma globulin, and the diminished phagocytic capacity as the granulocytes decrease, lead to the repeated infections often associated with CLL. Septicemia is a common cause of death, and fatal fungal and disseminated viral disorders occur with increased frequency. Herpes zoster and generalized vaccina following vaccination have been reported in such patients; therefore, patients with CLL (or with congenital or other forms of acquired hypogammaglobulinemia) should not be immunized with live vaccine and, specifically, not with a live vaccinia vaccine as prophylaxis against smallpox. There is now available hyperimmune antivaccinia gamma globulin which can be helpful in reducing the risk of disseminated vaccinia in such patients.

The hazard of renal shutdown is ever present in these frequently hyperuricemic patients. Uric acid levels rise during therapy as a result of the destruction of large numbers of lymphocytes. If adequate provision has not been made for hydration with good urinary output and a falling blood uric acid and urea nitrogen level, ureteropelvic obstruction because of uric acid precipitation in a scanty, acid urine may lead to death from uremia.

Anemia, another complication, is usually normocytic and normochromic and is the result of a

combination of erythrocytic hypoplasia, increased erythrocyte destruction and, eventually, marrow replacement. In approximately 20% of the patients the increased hemolysis becomes acute. A dramatic fall in hemoglobin and a reticulocytosis take place associated with a positive Coombs' test. A coating globulin is present on the lymphocytes, as well as on the red cells, and results in agglutination and an earlier than normal removal of red cells by the spleen. If blood loss is a problem, a hypochromic anemia may supervene. In many instances, therefore, either infection, hemorrhage, congestive failure brought on by anemia and renal damage, or a combination of these events, rather than the leukemic process itself, leads to the death of the patient.

Survival Time

To evaluate the benefits of specific therapy in the patient with CLL, it is important to determine the mean survival time of such patients. In 1954, Tivey presented the first useful review of a large number of patients (685) with CLL. He pointed out that it was no longer possible to collect an adequate series of untreated patients. For patients treated by different forms of radiant energy, the median survival time from onset of symptoms was 2.77 years, and the median survival time from diagnosis was 1.7 years, slightly higher than that seen in patients with other forms of chronic leukemia. Another group of investigators, who treated groups of patients with P^{32}, found a survival time of 2.7 years from onset of symptoms in 50% of the patients. Tivey concluded that supportive measures, radiation therapy, and the administration of P^{32} improved the chances of survival in patients with CLL. By instituting titrated P^{32} therapy as soon as the diagnosis was made, one clinician reported achieving a median survival time of 5.1 years from onset and 3.75 years from diagnosis. A decade later, reporting on 212 patients treated by the titrated P^{32} method, the same investigator found that the predicted total survival time from onset of symptoms was now 8.16 years compared to the previously predicted survival time of 3.9 years, and that the mean survival time was now 6.5 years compared to 2.66 years as reported by Tivey. Furthermore, 13% of Osgood's group of patients survived more than 10 years after treatment was instituted. About the same time another pair of investigators reported a study of 125 patients treated with chemotherapy or radiant energy as soon as symptoms developed; median survival time for these patients was 4.0 years from onset and 3.25 years from diagnosis.

Despite these favorable figures, other authors claim that the differences between the results of therapy with titrated P^{32} and other agents, such as chlorambucil and triethylene (TEM), are not yet sufficient to favor any one method of treatment. Nevertheless, proper use of these modalities seems to prolong the life of the patient with CLL.

The majority of hematology clinics favor withholding therapy until symptoms require it rather than initiating treatment on the basis of a simple white blood cell elevation. Symptoms requiring treatment might be a fall in hemoglobin, increase in the size of lymph nodes or other masses with discomfort, or a white blood cell count of 100,000/cu. mm. or greater and rapidly increasing. However, patients with white blood cell counts of 200,000/cu. mm. have been seen who are comfortable, asymptomatic, and do not require therapy. In the Green (and Dixon) series, 13 of 25 living patients were untreated and have survived from 54 to 128 months. Of 97 patients who died, 22 were never treated, and only five of these died of CLL. This underlines the fact that, in this elderly population, causes other than the leukemic process or its complications may lead to the death of the patient.

Specific Therapeutic

When therapy is indicated, chlorambucil is the drug preferred by the author. It is administered orally in an average dose of 6 mg./day. Blood counts are made weekly. The initial course of therapy is concluded if there is an abrupt fall in white count; if, after a gradual fall in white count, a level of 20,000 is reached; if there is significant platelet depression; or if a serious hemoglobin fall ensues. After improvement in the hemogram has occurred, maintenance therapy of from 2 mg. twice weekly to 4 mg. daily should be instituted, depending on blood and platelet counts (made regularly every two to six weeks).

Another dose schedule is the initial administration of 0.1 mg./kg./day of chlorambucil in patients with marrow infiltration and 0.2 mg./kg./day in other patients. The dosage range required for control is considerable. Previous therapy plays an important role in determining appropriate dosage for each patient. Some patients are sensitive initially to as little as 100 mg. while others may require more than 1300 mg. of the drug for a good objective response.

Cyclophosphamide (Cytoxan) has been given orally in doses of 2.0 mg./kg./day for periods of from eight to 12 weeks. Wilkinson states that Uramustine is the treatment of choice for all chronic leukemias, including CLL, and recommends a daily oral dose of 1 to 3 mg. until control is achieved and then a weekly maintenance dose of 1 to 3 mg. Chlorambucil will achieve approximately a 65% significant remission rate compared to 52% for cyclophosphamide. The numbers of patients studied to date are too small to make the difference significant, however. Cyclophosphamide has a platelet-sparing effect, whereas chlorambucil often leads to thrombocytopenia. In some patients this may be persistent in spite of adjustment of dosage.

Non-specific Therapy

In patients in whom anemia becomes a serious problem, and especially if it is of the acute hemolytic variety, corticosteroids are most useful in management. Prednisone is generally given at 0.5 mg./kg./day in divided doses orally and tapered as control is achieved. Most often it must be continued at low doses (e.g., 10 mg./day) indefinitely and there seems to be a definite breakthrough level. When this occurs a return to higher doses is required. This agent also is useful in helping to prevent or control hemorrhagic manifestations in patients with significant thrombocytopenia. In patients with erythrocytic hypoplasia and severe anemia, one investigator has advocated the use of androgen, either Halotestin, 20 to 50 mg. orally daily, or testosterone enanthate, 400 to 1800 mg. weekly intramuscularly, for at least two months in association with corticosteroids. One-half of his patients responded with a significant rise in hemoglobin and in three of five, a significant rise in platelets. One-third of the patients also had a rise in lymphocyte counts which required additional therapy. The improvement lasted for 24 months or longer in some patients. Finally, antibiotics and blood transfusion have an important supportive role in CLL, but marrow transplantation has not been found to be of value.

Radiation Therapy

Radiation therapy, either in the form of P^{32}, total body spray, or splenic radiotherapy has proved useful in the management of patients with CLL. More recently, extracorporeal radiation, using an arteriovenous loop devised by Scribner for renal dialysis, has been tried. In one series, Thomas found four patients with CLL who had improvement in white cell counts for one to nine months; one of these patients had a relapse after 30 days, requiring chemotherapy, and two had only been followed for 30 days. Therapy apparently affects only circulating white cells (a small proportion of the total lymphocyte population) and must be continued for two to eight hours over a period of four weeks or more. This experimental therapy can be performed only in special institutions and does not improve the hemoglobin, platelet count, or physical findings. In fact, it has not yet been compared to simple radiotherapeutic management alone. Thus, in itself, it does not seem to be a major advance.

Conclusion

Patients with CLL should not be treated until symptoms warrant it. The agent used should be one with which the physician and institution have the most experience, whether it is Leukeran, Cytoxan, Uramustine, P^{32}, or radiant energy. The treatment should be cautiously administered with reasonably frequent checks on blood counts, platelet counts, and physical findings, and supportive therapy instituted where necessary. These measures, as well as an awareness of the possible complications of therapy and of the disease itself, will lead to prolongation of survival and a more comfortable life in the majority of patients with CLL.

A REVIEW OF THERAPEUTIC AND HEMOLYTIC EFFECTS OF DAPSONE

Richard L. DeGowin MD, Chicago, Arch Intern Med 120(2):242–248, August 1967.

Clinicians in the army and in civilian practice will probably use sulfone drugs with increasing frequency. After extensive use of sulfones for the past 25 years, dapsone (DDS), the parent sulfone, remains foremost in the therapy of leprosy throughout the world. Introduction of dapsone into der-

matologic practice in the United States followed reports describing the salutary effects of the sulfone on certain chronic skin diseases. Recently, the emergence of falciparum malaria resistant to chloroquine and other synthetic antimalarial drugs led to an evaluation of dapsone in the therapy of these refractory strains. Results of field trials have encouraged the US Army to add dapsone to their regimen for malaria prophylaxis.

A consideration of this effective but potentially toxic drug seems timely in view of its rapidly increasing use in civilian and military practice. Since extensive reviews of sulfones have appeared in the literature, this discussion deals with historical aspects briefly and emphasizes the results of recent research.

Therapy

Streptococcal Infections.—Synthesized in 1908 by Fromm and Whittmann, dapsone was tested for antibacterial activity in 1937 by Buttle and associates and by Fourneau and co-workers. The former found that dapsone was active in curing streptococcal infections in mice in doses about one hundredth of those required with sulfanilamide, but it was 25 times as toxic.

Because it was assumed that therapeutic dosages of the sulfones and sulfonamides should be comparable, patients with streptococcal infections were given dapsone in quantities that proved to be sufficient to cause severe anemia and cyanosis. Consequently, the drug was set aside, and less toxic compounds were sought by adding side chains to the parent dapsone.

Tuberculosis.—Enthusiasm for producing a presumably less toxic drug was heightened when the inhibitory action of dapsone against *Mycobacterium avium* in rabbits and of glucosulfone sodium (Promin, one of the new substituted derivatives) against *M tuberculosis* was reported in 1940. The tuberculostatic effect of sulfones in experimental animals gave great impetus to the development of chemotherapy against tuberculous infections. Although sputum reverted to normal in many patients receiving sulfones, the drugs only arrested the disease and did not eradicate it. Moreover, the sulfones were considered too toxic and, after the development of streptomycin after 1944, were soon abandoned as therapy for tuberculosis.

Leprosy.—No less exciting than the early studies with experimental tuberculosis was the discovery of the efficacy of glucosulfone against rat leprosy in 1940, and against *M leprae* in patients at the National Leprosorium in 1941, which inaugurated an era of hope. Indeed, Bushby was able to write in 1964, " . . . today, in the sulphone group of drugs, we have as effective remedies in the treatment of leprosy as those in the treatment of tuberculosis." The development of congeners of dapsone like sodium sulfoxone (Diasone), that could be given orally, obviated the inconvenience of parenteral injections required by the use of glucosulfone. The derivatives were expensive, however, and this was of some importance because of the high prevalence of leprosy in economically insecure areas of the world.

The parent sulfone was relatively inexpensive, and reconsideration of dapsone was prompted by information arising from at least two other quarters. Many years of pharmacological investigations demonstrated that ingested dapsone was almost completely absorbed, whereas most of the substituted derivatives underwent modification. Hydrolysis in the stomach split off the side chains that had been attached at such expense to release the active component dapsone which was then absorbed. In essence, the lower toxicity of the analogues simply reflected a reduced dose of active sulfone. Veterinarians had successfully used dapsone in the treatment of streptococcal mastitis in cattle since 1941. The results of the pharmacologic studies and the experience with animal therapy encouraged a trial of reduced doses of the drug in leprous patients in 1949. Since then, dapsone has probably been the most widely used sulfone.

Over the years, the maximum dose has been repeatedly lowered to minify toxic effects. Bushby recommends gradually increasing the dosage from 25 to 200 mg of dapsone twice a week for three months. He finds that the occurrence of side effects and untoward reactions are unlikely after the patient has been taking dapsone for more than six months. Although there have been recent reports of *M leprae* infections that were resistant to dapsone, the sulfones have saved thousands of patients from chronic illness and social ostracism.

Dermatitis Herpetiformis.—Although leprous patients respond to small doses of dapsone, larger doses have been required in the therapy of dermatitis herpetiformis. Regimens using 200 or 300 mg of dapsone daily have diminished the severe pruritus and produced remission in the lesions of dermatitis herpetiformis. The effectiveness of dap-

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sone in this nonbacterial dermatitis has evoked speculation that the sulfone may react with tissue polysaccharide in ameliorating the disease. Sulfones, administered in similar doses to those just mentioned, have been used with some success in the treatment of other skin diseases including pyoderma gangrenosum, subcorneal pustular dermatosis, and recalcitrant eczematiform eruptions.

Malaria.—It is necessary to retrace our steps to the pre-World War II era of sulfone investigation to follow the development of dapsone for use against chloroquine-resistant *Plasmodium falciparum*. Along with the studies in tuberculosis and leprosy, Coggeshall and co-workers reported in 1941 on the suppressive effect of glucosulfone in patients with falciparum infections; *P vivax* was less responsive than *P falciparum*. The authors concluded that glucosulfone and sulfadiazine, " . . . possess considerable activity against experimental and human malaria . . . , " but that, " . . . at present there are no reasons for giving the drugs in preference to quinine or [quinacrine hydrochloride] atabrine for the treatment of malaria, and they should be regarded only as important substitutes." Fortunately, quinacrine, chloroquine, and other antimalarial drugs served so admirably for the next 20 years that a malaria eradication program combining spraying of breeding places of mosquitoes and chemotherapy of infections held out the hope of eliminating one of the most prevalent infectious diseases in the world.

Fifteen years after Coggeshall's report, Leiker and others who treated leprosy with sulfones noted the absence of malaria in their patients, who continued to reside in a holoendemic area of malaria transmission. Results of later studies with dapsone in patients with *P falciparum* confirmed Coggeshall's earlier experience with glucosulfone. Dapsone, however, fell short of chloroquine and the other 4-aminoquinolines as a rapidly-acting blood schizontocidal drug in nonimmune persons. It was therefore not needed nor generally used until the discovery that certain strains of *P falciparum* from South America and Southeast Asia were resistant to chloroquine, hydroxychloroquine, amodiaquine, quinacrine, pyrimethamine, chloroguanide hydrochloride, cycloguanil pamoate, and in some cases even quinine. The implications of this discovery may be appreciated when one realizes that the number of US soldiers evacuated from Vietnam during 1965 because of malaria equaled the number evacuated for wounds.

The protective effect of a small daily dose of dapsone against a strain of *P falciparum* from Malaya, resistant to chloroquine and the other synthetic antimalarial drugs, was suppressive and did not inhibit exoerythrocytic schizogony. Concommitant administration of aminobenzoic acid vitiated the protective effect of dapsone, suggesting that the sulfone inhibited parasite-folate biosynthesis. That aminobenzoic acid did not simply diminish the blood levels by enhancing the excretion of dapsone is suggested by the failure of aminobenzoic acid to ameliorate sulfone-induced hemolysis in a man with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Field trials were carried out in Vietnam after it had been demonstrated that nonimmune persons were protected from resistant strains of *P falciparum* by a regimen combining 25 mg of dapsone daily with the standard weekly chloroquine-primaquine prophylaxis. The chloroquine-primaquine tablet was retained for its ability to prevent infections with *P vivax*. Results of extensive use of dapsone in the field are not yet available, but a reduction of at least 50% of recalcitrant malaria cases is hoped for.

Hemolysis.—A review of the literature, prompted by the prospect of prophylactic administration of dapsone to large numbers of healthy military personnel, quickly revealed a startling lack of specific information on the hemolytic effects of the parent sulfone compound. It was known that dapsone and its derivatives caused hemolysis in patients with leprosy or dermatitis herpetiformis. It remained unclear whether those inflammatory diseases predisposed to hemolysis or whether the patients reported to have had hemolysis had also inherited a biochemical defect of the erythrocytes (like G6PD-deficiency), which predisposed to hemolysis. Studies in which "primaquine-sensitive" erythrocytes were given by transfusion to normal persons demonstrated that sulfoxone was hemolytic to those enzyme-deficient cells. Sulfoxone caused hemolysis in a patient with leprosy who did not have G6PD-deficiency, but assays of the erythrocyte enzymes revealed diminished activity of glutathione reductase, an abnormality associated with drug-induced hemolysis.

There is at least one report of a healthy Indian volunteer who received 100 mg of dapsone daily for 19 days as "an experiment." The "half chromium time" of his labeled erythrocytes had not reached 50% of the initial radioactivity by the end of 22 days, but the "mean red-cell life span"

was interpreted as "reduced." Although the glutathione stability and G6PD activity of the erythrocytes from four patients were reported to be normal, the paper does not mention whether the Indian's erythrocytes were assayed for G6PD or glutathione stability.

Recent studies have demonstrated that dapsone is more hemolytic to G6PD-deficient erythrocytes than it is to normal erythrocytes, but therapeutic doses (200 to 300 mg daily) definitely produced hemolysis in normal young men. The severity of the hemolysis is directly related to the dose of dapsone. It is interesting that primaquine has a greater hemolytic effect in G6PD-deficient persons but causes less hemolysis in normal individuals than dapsone does. Addition of a daily dose of 25 mg of dapsone to the usual weekly chloroquine-primaquine prophylactic regimen gave complete protection against chloroquine-resistant *P falciparum* and did not cause appreciable shortening of erythrocyte life-span.

Firm conclusions about the level of sulfone in the blood required to produce hemolysis are precluded by the lack of specificity and sensitivity of the diazotization procedure used for assay. Short-term studies suggest that daily doses of dapsone of 100 mg or less in healthy normal persons and of 50 mg or less in healthy G6PD-deficient persons will not produce easily detectable hemolysis. Mean minimum levels of sulfone with these doses rarely exceed 0.5 mg/100 ml of blood. However, hemolysis induced by primaquine or sulfonamides in G6PD-deficient patients with infectious diseases is greatly accentuated; this is probably true for sulfone-induced hemolysis.

Presumably dapsone lyses G6PD-deficient erythrocytes by an oxidant action similar to that of primaquine. Certainly, the prelytic diminution of erythrocyte-reduced glutathione is similar. In marked contrast to the fall in glutathione seen in hemolysates of G6PD-deficient erythrocytes, glutathione increases in normal erythrocytes reaching a peak during the second week of dapsone administration. Hemolysis occurs in the presence of elevated erythrocyte glutathione levels. With continued administration of dapsone for another week, glutathione falls below baseline levels and an accelerated hemolysis ensues. Despite cessation of drug administration, glutathione failed to return to pretreatment levels for at least six weeks in one individual.

There was no apparent inhibition of the erythrocyte enzymes G6PD, 6-phosphogluconic dehydrogenase, glutathione reductase, and pyruvate kinase associated with the changes in glutathione; neither did glutathione stability and levels of oxidized glutathione in red blood cells change.

Body surface scanning of the liver and spleen revealed enhanced uptake of radioactive chromium (^{51}CR) by both organs during dapsone ingestion, suggesting that both intravascular hemolysis and sequestration of intact erythrocytes occurred. This coincides with the pattern of hemolysis seen in G6PD-deficient persons who receive primaquine.

Other Toxic Manifestations.—Methemoglobinemia and Heinz-body formation were common findings and have been reported before. The former seemed to be related to the dose of dapsone, but it is not known whether the drug's effect is on the methemoglobin reductase of the pentose phosphate pathway or on the diaphorase system in the anaerobic glycolytic pathway.

The significance of some manifestations of toxicity attributed to sulfone in the leprosy literature is difficult to assess because of the effects of the disease requiring therapy. For instance, exacerbation of leprous lesions (lepra reaction) may occur and is presumably analogous to the Herxheimer reaction. Another toxic reaction attributed to hypersensitivity to sulfone occurs infrequently in malnourished patients five to six weeks after beginning therapy. Referred to as the "sulfone syndrome," its manifestations include fever, malaise, exfoliative dermatitis, jaundice with liver necrosis, lymphadenopathy, methemoglobinemia, and anemia. Most patients have recovered after prompt cessation of therapy. Headaches and rare transient psychotic episodes are mentioned often enough in the literature to deserve attention but are difficult to assess.

Further Research

A number of partially answered questions persist. Can the reports of preferential distribution of dapsone to the skin and erythrocytes be confirmed? Is dapsone hemolytic in vitro, or must it be metabolized in vivo before it will lyse erythrocytes? A more specific and more sensitive assay for dapsone would be of great help for these studies. What is the significance of the sulfone-induced changes in glutathione levels in normal and in G6PD-deficient erythrocytes and their relation to subsequent hemolysis?

Conclusions

Undoubtedly, the use of dapsone will increase greatly in the near future. Its therapeutic and toxic effects have been briefly reviewed here in order to avert some of the mischances that have attended its use in the past. Therapeutic doses of dapsone produce a biochemical alteration in congenitally normal erythrocytes that is associated with hemolysis. Not only should continued research contribute to the rational use of dapsone, but it may also elucidate the relationship of reduced glutathione to the lysis of normal erythrocytes, in vivo.

Margot Doyle, Frances Skozen, and Elmer L. DeGowin MD, aided in the preparation of the manuscript.

Generic and Trade Names of Drugs

Dapsone—*Avlosulfon.*
Quinacrine hydrochloride—*Atabrine Hydrochloride, Palusan.*
Chloroquine—*Aralen.*
Hydroxychloroquine sulfate—*Plaquenil Sulfate.*
Amodiaquine hydrochloride—*Camoquine Hydrochloride.*
Pyrimethamine—*Daraprim.*

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

NEW CONCEPTS IN CHEMOTHERAPY OF ADVANCED GASTROINTESTINAL CANCER

Richard A. Oberfield MD and Robert D. Sullivan MD, Department of Internal Medicine, Lahey Clin Found Bull 16(2):197–205, 1967.

Cancer continues to be one of our most challenging problems. Cancer of the gastrointestinal tract accounts for the largest number of newly diagnosed cases in both sexes and is the commonest cause of death from neoplastic disease. In 1966, of the estimated 300,000 deaths attributed to cancer in the United States, approximately 73,000 were from cancer of the colon and rectum and 21,000 from cancer of the stomach.

Fifty percent of patients with colorectal cancer will die of progressive disease despite our surgical and radiotherapeutic advances. Five-year survival rates are 0 to 5 percent for primary and secondary carcinomas of the liver, gallbladder, bile ducts, and pancreas, and 7 to 14 percent for cancer of the stomach. Recent data indicate improved five-year survivals of 29.8 percent for cancer of the ampulla and 35.7 percent for cancer of the distal bile ducts.

If we assume an ever-increasing population susceptible to gastrointestinal cancer combined with a limited cure rate by surgical and x-ray therapy, then there remains a large reservoir of patients requiring other therapeutic measures. It is these patients with advanced cancer of the gastrointestinal tract that is inoperable and not suitable for x-ray therapy who have been considered candidates for chemotherapy.

Despite the many attempts to arrest tumor growth by systemic administration of cancericidal agents, the objective remission rates vary from 10 to 30 percent. Hence, new approaches are urgently required for the treatment of advanced solid tumors.

Principles of Therapy

One of the major limitations of previous chemotherapeutic programs has been the short duration of treatment. Solid tumors have "doubling times" in excess of several months. Considerable evidence exists that the stage of the mitotic cycle may influence the response to chemotherapeutic agents. Since antimetabolites such as methotrexate inhibit cells primarily during the period of deoxyribonucleic acid synthesis, it would seem desirable to continue treatment with these agents for at least the average doubling time of cancer cells. We have previously elaborated the rationale for this therapy based on experimental data of solid tumor growth curves and the pharmacologic effects of antimetabolites. Prolonged and continuous infusions of antimetabolites systemically (orally or parenterally) have favorably altered the dose-toxicity response.

TABLE 1

Effective Chemotherapeutic Agents in Gastrointestinal Cancer

Drug	Method of Administration	Dosage
Methotrexate (Mtx)	24-hour intravenous infusion	5 mg./24 hours (7-12 days)*
Methotrexate (Mtx)	Divided daily oral dosage	1.25 mg. four times a day
Cytoxan	24-hour intravenous infusion	8 mg./kg./24 hours for five days
	Divided daily oral dosage	50 mg. four times a day
5-Fluorouracil (FU)	Rapid intravenous	15 mg./kg./day for five days; 7.5 mg./kg. a day on alternate days (5-9 doses)*
5-Fluoro-2′-deoxyuridine (FUDR)	24-hour intravenous infusion	0.75 mg./kg./day (5-9 days)*

*Or until moderate systemic toxicity develops.

Another important concept in treatment of solid tumors is that studies with cancericidal agents in blood and tumor tissue have shown that the highest concentration is obtained when the drug is given by continuous arterial infusion. Primary and secondary cancers of the liver are commonly considered not susceptible of any practical form of cancer chemotherapy. When given by systemic routes, any agent capable of destroying tumor tissue within the liver usually produces such profound toxicity on normal tissues as to preclude any effective response. In approximately 60 percent of such advanced cases, we have effectively employed continued arterial infusion of antimetabolites through the use of a permanent Teflon catheter inserted into the hepatic artery at laparotomy. Prolonged infusion with the patient ambulatory is maintained by a portable chronometric pump developed by Watkins of our group.

Methods of Treatment

Although fluorinated pyrimidines, 5-fluorouracil (FU) and 5-fluoro-2′-deoxyuridine (FUDR), given by rapid intravenous administration have been established as occasionally effective palliative agents for the treatment of gastrointestinal cancer, we will emphasize the methods and drugs currently employed in our patients.

Systemic Administration of Folic Acid Analogue (Table 1)

A daily dose of 5 mg. of methotrexate (Mtx), either orally in divided doses or by continuous intravenous infusion, is administered. The latter method is employed for hospitalized patients; 5 mg. is placed in 1,000 cc. of 5 percent dextrose in water each 24 hours. Daily white blood cell counts and biweekly hemoglobin and platelet counts are obtained. As soon as hematologic or gastrointestinal toxicity develops, the infusion is discontinued. For ambulatory patients or patients initially given intravenous therapy and then maintained on oral therapy, the oral dose is 1.25 mg. four times a day. A white blood cell count is obtained twice a week and a hemoglobin, hematocrit, and platelet count once a week. This maintenance dose is continued until signs of toxicity develop (that is, oral lesions or a fall in white blood cell count to levels below 4,500 cells per cubic centimeter) at which time treatment is discontinued or modified until signs of toxicity abate. Intermittent courses of oral methotrexate are given as long as improvement continues. Some patients have been given such therapy as long as two years.

TABLE 2

Hepatic Artery Infusion Cancer Chemotherapy and Effective Drug Dose Schedules

Drug	Dosage
5-Fluorouracil (FU)	5.0-7.5 mg./kg./24 hours
5-Fluoro-2′-deoxyuridine (FUDR)	0.1-0.3 mg./kg./24 hours
Methotrexate (Mtx)	5 mg./24 hours
Methotrexate and	50 mg./24 hours
Leucovorin (antidote, intramuscularly)	6 mg./6 hours

Patients selected for the above schedule should fulfill the following criteria: disseminated disease in which surgery or radiation is precluded as definitive therapy; minimal expected survival is one month or more; progressive tumor growth is associated with disability requiring palliation; and a cooperative patient whose course can be followed closely by a physician familiar with the drug regimen.

Regional Ambulatory Infusion of Antimetabolites (Table 2)

This form of chemotherapy employs a portable pump weighing about 12 ounces, driven by a clock mechanism, and carried or worn by the patient. The pump is connected to a Teflon catheter inserted into the hepatic artery supplying the hepatic tumor. It delivers approximately 5 cc. of fluid per 24 hours (the amount that contains the daily dose of the cancericidal drug) from a plastic bag having a capacity of 20 to 25 cc. (four to five days of infusion). In approximately four days the patient replaces this with another drug-containing plastic bag. Patients are instructed in the correct manner of replacement. Treatment consists of continuous infusion for four to six weeks until maximum local antimetabolic effects are evident and clinical improvement is noted. When chemical hepatitis or local toxic effect develops the drug-containing bags are replaced with bags containing sterile water. Courses of treatment are alternated with periods of water infusion.

Patients who are considered candidates for the above treatment are those with primary carcinoma of the liver, gallbladder, and bile ducts, and metastatic carcinoma of the liver from cancer of the gastrointestinal tract or from a distant primary site when the primary tumor is controlled or not producing symptoms.

The rationale of treatment, techniques of catheter insertion, methods of maintenance of high-volume and low-volume infusion, drug dose schedules, and results of treatment of patients with regionally-confined gastrointestinal cancer have previously been reported.

Illustrative Case Reports

Case 1. Epidermoid Carcinoma of Esophagus. A 75-year-old woman was seen at the Lahey Clinic in August 1965 because of weight loss of 25 pounds and dysphagia of ten months' duration. When initially seen she was subsisting on baby foods. Radiologic examination of the upper gastrointestinal tract revealed extensive infiltrating carcinoma, measuring 16 cm. in length, involving the distal third of the esophagus. Endoscopy and biopsy revealed epidermoid carcinoma, grade 3. Radiotherapy (cobalt 60) was begun elsewhere and between August 9 and September 17, 1965, she received 5,000 R. to the esophagus. The dysphagia was dramatically improved, and the patient was able to take a full diet. Radiologic examination of the upper gastrointestinal tract on August 28, 1965, showed that the lumen was considerably larger, although the mucosal irregularities consistent with carcinoma persisted.

The patient returned in April 1966 because of weight loss, weakness, and dysphagia. Radiologic study showed progressive carcinoma of the distal third of the esophagus. She was hospitalized and received a course of methotrexate in orally-divided doses of 1.25 mg. four times a day for seven and a half days, for a total dose of 37.5 mg. After she had recovered from hematologic and gastrointestinal toxicity, an x-ray series showed improvement in that the degree of irregularity was less marked and the esophagus expanded satisfactorily.

The patient felt better, dysphagia disappeared, she was able to take a full diet, and gained 3 pounds while in the hospital. Clinical improvement was maintained until September 1966 when she returned because of dysphagia and was readmitted for another course of therapy.

Comment. This case illustrates the palliation resulting from a single course of methotrexate administered in orally-divided doses for a condition usually considered beyond medical therapy.

Recently we reported that methotrexate has produced clinical responses in seven of 17 patients with colorectal adenocarcinoma, four of 11 with carcinoma of the stomach, and one of 11 with carcinoma of the pancreas and bile ducts.

Case 2. Adenocarcinoma of the Pancreas. The patient was a 69-year-old man in whom a diagnosis of nonresectable cancer of the head of the pancreas was made at laparotomy in January 1965. By April 1965 jaundice, severe pruritus, weight loss of 40 pounds, and pain in the region of the liver were noted. The liver extended 8 cm. below the right costal margin. Liver function tests gave abnormal results (Fig. 3). Oral administration of methotrexate was begun in May 1965 in the dose of 1.25 mg. four times a day. Over the next few weeks the pain and jaundice subsided and the

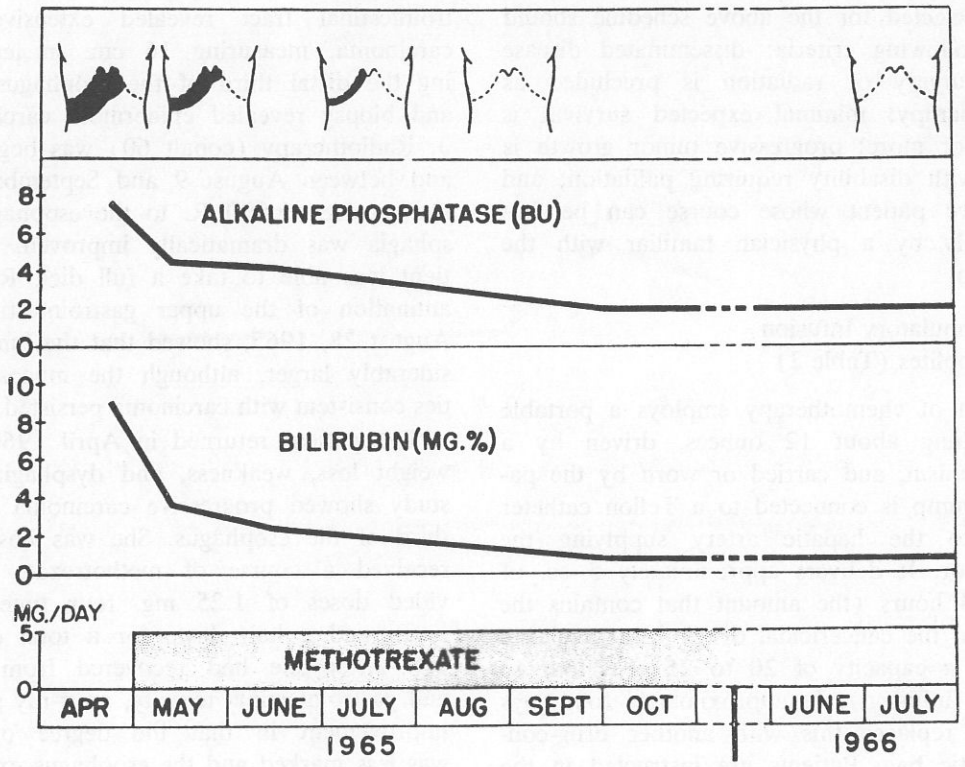

Fig. 3 (Case 2). Adenocarcinoma of the Pancreas. Summary of treatment.

liver became impalpable. Methotrexate has been given orally for maintenance to date, 24 months after therapy was begun. The patient is clinically well and has a normal performance status.

Comment. Methotrexate administered orally in divided doses resulted in significant objective improvement. There was complete abatement of symptoms, pruritus and jaundice improved, liver size was reduced to normal, and liver function tests returned to normal levels. This case illustrates the effectiveness of oral administration of methotrexate.

Case 3. Islet Cell Carcinoma. A 56-year-old man was first seen at the Lahey Clinic in August 1965 for consideration of hepatic artery infusion therapy for metastatic islet cell carcinoma involving the liver. On March 30, 1965, at another hospital, he was operated on for a functioning islet cell carcinoma of the body and tail of the pancreas with metastasis to the liver. Tumor nodules were scattered throughout both lobes of the liver. Resection of the spleen and the body and tail of the pancreas was performed in addition to a liver biopsy. The primary tumor involved the body and tail of the pancreas, and extended into the hilum of the spleen. Postoperatively he was given hydrocortisone. Subsequently he gained 30 pounds, presumably as a result of excessive caloric intake necessary to prevent episodes of syncope. These episodes had become progressively more severe.

On admission to the hospital for arterial infusion treatment, the patient had documented recurrent hypoglycemic episodes with fasting blood sugar levels in the range of 20 to 25 mg. per 100 ml., requiring continuous intravenous infusion of glucose. At operation on August 30, 1965, bilateral massive involvement of the liver by invasive tumor nodules was seen. A Teflon catheter was inserted into the hepatic artery. A portable pump was attached to the catheter, and the patient was given 20 mg. of FUDR per day through the pump. The hypoglycemic episodes disappeared, and on September 17, 1965, shortly before he was discharged, the fasting blood sugar level was 55 mg. per 100 ml. Since discharge and until the present time he has been maintained on intermittent courses of therapy and has continued to do well, the fasting blood sugar value being in the range of 90 to 100 mg. per 100 ml. after an 8 to 10 hour fast without any hypoglycemic episodes. The insulin

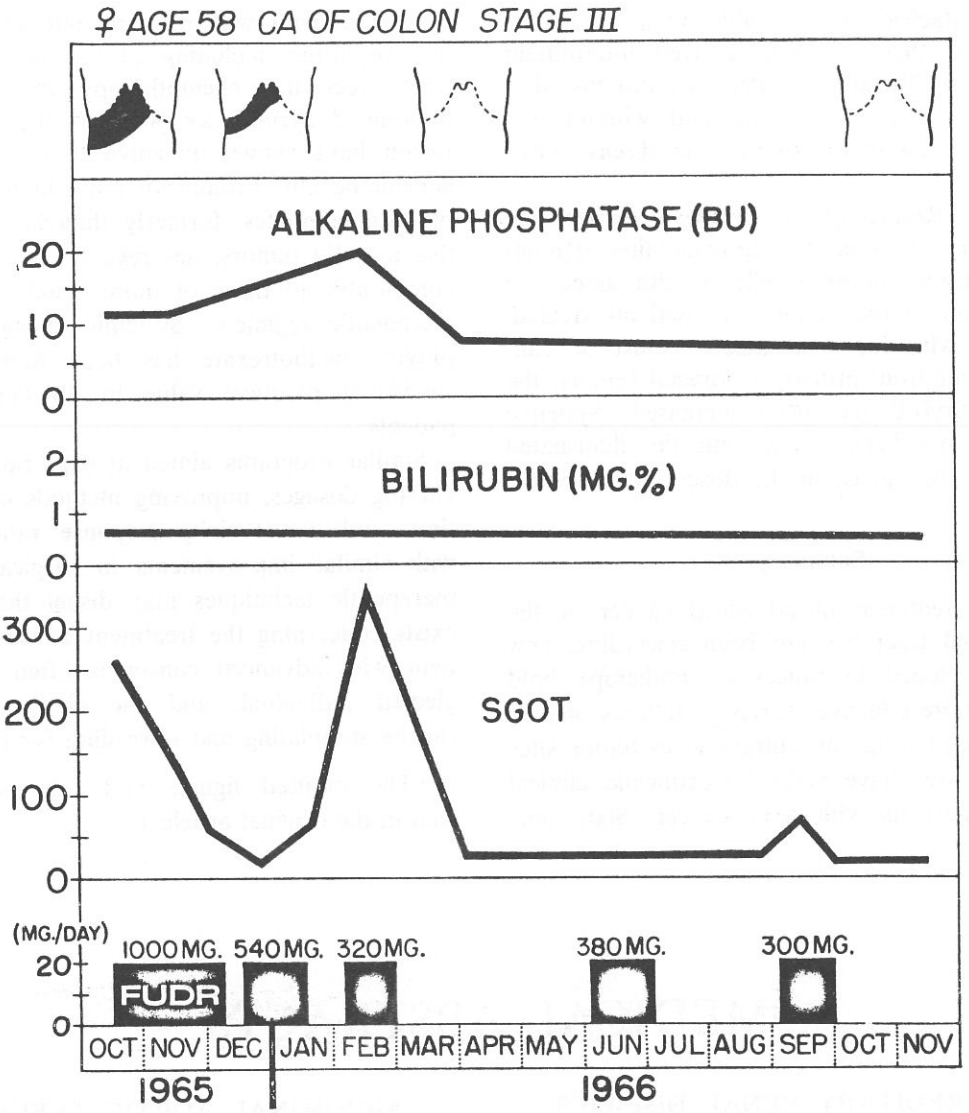

Fig. 4 (Case 4). Metastatic Adenocarcinoma of the Liver. Summary of treatment.

level measured by the immuno-assay method before operation was abnormal at 136 micro-units. Recently insulin levels were normal. At this date the patient continues to be well, 20 months after treatment was started.

Comment. This patient has received definite objective benefit from regional intra-arterial infusion chemotherapy for metastatic lesions of the liver from a functioning islet cell carcinoma. The objective response was measured by the response to fasting; the fasting blood sugar levels were greatly improved. This was confirmed by the level of insulin measured by the immuno-assay method. We have also treated patients with functioning carcinoid syndrome and have noted clinical responses to therapy, including reduction of abnormal urinary 5-hydroxyindoleacetic acid levels.

Case 4. Metastatic Adenocarcinoma of the Liver. A 58-year-old woman had an anterior resection of the colon for annular adenocarcinoma in January 1960, followed shortly by transverse colostomy because of leakage at the anastomotic site. She remained well until October 1965 when weight loss, weakness, and anorexia developed. Physical examination revealed enlargement of the liver which was palpable 11 cm. below the right costal margin. A few weeks later (October 18, 1965), laparotomy revealed numerous large nodules of carcinoma in the right hepatic lobe. A Teflon catheter was inserted into the hepatic

artery and attached to a portable pump containing FUDR. Since then she has received intermittent courses of FUDR and to date, 18 months after starting treatment, she is well and without evidence of progressive metastatic liver disease (Fig. 4).

Comment. Results of our studies in protracted hepatic artery infusion of antimetabolites demonstrate significant antitumor effects with associated clinical benefit in the majority of patients treated. In patients who have advanced metastatic cancer of the liver from primary colorectal tumors, the length of survival has been increased. Systemic toxicity has not been noted with the fluorinated pyrimidines when given in the doses recommended (Table 2).

Summary

Although treatment of advanced cancer of the gastrointestinal tract has not been rewarding, new concepts developed in cancer chemotherapy hold promise of more effective therapy. Methods of providing increased drug concentrations to tumor sites in selected cases have yielded worthwhile clinical benefit for patients with liver cancer. Sixty percent of patients with primary and secondary hepatic neoplasms, including carcinoma of the biliary tract, receiving chemotherapy in the form of fluorinated pyrimidines given by hepatic artery infusion have shown objective tumor response and clinical benefit. Prolonged and continuous infusion of antimetabolites, formerly thought to be ineffective in solid tumors, has resulted in clinical results comparable to those of more standardized chemotherapeutic regimens. Systemic chemotherapy employing methotrexate has been found to be of significant practical value in 30 percent of our patients.

Similar programs aimed at exploring new drugs, varying dosages, improving methods of administration, and dose-toxicity response ratios combined with similar improvements in surgical and radiotherapeutic techniques may dispel the gloom that exists concerning the treatment of cancer. The patient with advanced cancer is often a much neglected individual, and the challenge presented can be stimulating and rewarding for the physician.

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

MEDICAL ABSTRACTS

THE HEREDITARY RENAL DISEASES

Gerald T. Perkoff MD, New Eng J Med 277(2):79–85, July 13, 1967 (Part 1) and 277(3):129–137, July 20, 1967 (Part 2).

The number of diverse renal diseases now known to be hereditary has increased steadily from a few to 30 or more during the past two decades. At the same time, understanding of the pathogenesis of some of these disorders has increased. Growth in understanding has been variable, however, and has occurred mainly in the area of the physiology of several abnormalities of renal tubular function.

The purpose of this summary of what is known about hereditary diseases of the kidney is to make yet another attempt at their classification and to indicate what progress has been made and what areas might be fruitful for further study.

ABDOMINAL AORTIC ANEURYSMS

James D. Hardy MD FACS, Amer J Med Sci 254(2):221–235, Aug 1967.

A series of 84 consecutive unruptured abdominal aortic aneurysms resected with a 7% mortality rate is reviewed. The associated vascular and other lesions, operative technique, pre- and postoperative management, and complications are noted. The operative risk in the patient with an unruptured infrarenal abdominal aortic aneurysm who is otherwise in reasonably good health is quite low. Incomplete long term follow-up of the patients in this series indicates that subsequent problems related to the aortic prosthesis have been rare.

MALIGNANT TUMORS OF THE SMALL INTESTINE

C. J. McPeak MD, Amer J Surg 114(3):402–411, Sept 1967.

The twenty-five year experience in treatment of malignant tumors of the small intestine at Memorial Hospital is reviewed. In addition to giving the figures on incidence, symptoms, and cure rates, the study indicates the tendency for certain histologic types of tumor to occur in particular sections of the small intestine.

Anatomic characteristics of the vascular and lymphatic systems are considered as they relate to the surgical treatment of these tumors. Metastatic tumors to the small intestine from distant primary sites are discussed as a clinical entity.

Carcinoid tumors are reviewed as a surgical problem. The metabolic physiologic entity of metastatic carcinoid is discussed along with the methods of management of the carcinoid syndrome.

DIMETHYL SULFOXIDE (DMSO)— TOXICOLOGY, PHARMACOLOGY, AND CLINICAL EXPERIENCE

S. W. Jacob MD and D. C. Wood PhD, Amer J Surg 114(3):414–426, Sept 1967.

Clinical studies on dimethyl sulfoxide commenced in the United States in October 1963. A European symposium on DMSO was held in Berlin in July 1965. On November 11, 1965 clinical testing was halted by the Food and Drug Administration. In March 1966 a second international conference on the Biological Actions of DMSO was sponsored by the New York Academy of Sciences. In November 1966, a third international conference on DMSO was held in Vienna, Austria. This paper summarizes the current status under five categories: (1) animal toxicology, (2) side effects in man, (3) fate and metabolism, (4) primary pharmacology, and (5) clinical experience.

DENTAL SECTION

DENTAL OFFICER TRAINING

As the time approaches for the cut-off date (1 Dec 1967) when applications for training during FY 1969 *must be received in the Dental Division,* it is appropriate that comments relative to the over-all training program be made. Several points in the Dental Corps training program have created some questions which will be answered in this article.

Often the question has been raised as to the difference between the Graduate and Postgraduate Course in General Dentistry at the Naval Dental School, Bethesda, Maryland. The curriculum for the Graduate and Postgraduate Course in General Dentistry is identical. The difference is that the Graduate student competes academically in the Georgetown University Graduate School, to earn academic credits applicable to further graduate or specialty training. Postgraduate students are not enrolled in the Georgetown University Graduate School. Specialty courses conducted at the Naval Dental School are all Graduate Courses. The assumption is that an individual enrolled in a specialty course has aspirations for further study in that specialty. There is, however, no requirement that he continue if he elects to do otherwise. By the same token, there is no preclusion for an individual upon completion of the General Graduate Course to seek further training in a specialty.

Currently, graduate and postgraduate dental education is experiencing a period of considerable change, growth and expansion. The U.S. Naval Dental Corps has reacted to these gains; for exam-

	FY 1958	*FY 1968*
Graduate/Postgraduate level training (Residency type)	9	25
Dental Internship	18	32
Postdoctoral Fellowship Training	0	29
Graduate/Postgraduate Courses, Naval Dental School	24	32
Graduate long courses at civilian institutions	3	17
Total	54	135

ple, the graduate/postgraduate training program has increased by 150 percent in the past ten years.

In addition, there has been a comparable increase in outservice training and in the continuing education program of short postgraduate courses of instruction in civilian schools as well as at naval activities. In spite of the expanded program, it is regrettable that all applications for advanced training cannot be fulfilled and that some delays are encountered in awaiting assignment to the Naval Dental School. With the establishment of the Postdoctoral Fellowship Program and significant increases in the various other training programs, it is anticipated that advanced training opportunities will be more readily available and that specialty training, hopefully, can be offered earlier in the careers of naval dental officers.

The Bureau of Medicine and Surgery Dental Training Committee strives to distribute the training billets as equitably as is possible for the over-all welfare of the Naval Dental Corps. To correct a popular misconception that exists, it should be stated that the Graduate or Postgraduate Course at the Naval Dental School is not a prerequisite for promotion. The conscientious, capable, clinical operator stands an equal chance, all other factors being the same.

The objectives of the over-all educational program of the Naval Dental Corps include, primarily, the responsibility to raise the educational level of the entire corps from that which exists upon graduation from dental school. Secondly, it has the obligation of providing members of the Dental Corps with all the latest developments that may be applied to the clinical practice of dentistry. It has the third responsibility in providing accredited specialists to be made available for the various teaching programs conducted by the Naval Dental Corps and for consultation and treatment of challenging or unusual patients. A fourth is the obligation of providing the Dental Corps with a staff capable of conducting the various research programs related to the needs of the Navy.

In order to meet the changing requirements of evolutionary educational concepts and at the same time not compromise the primary mission of the Naval Dental Corps, it obviously places a great responsibility on the Training Committee.

All applicants for advanced courses of instruction are, therefore, urged to carefully consider their goals as related to the above philosophy prior to submitting requests for training. Applications should follow a carefully considered career plan of the individual officer that follows a realistic self-appraisal of his talents. For instance, those applying for long courses in civilian institutions should be cognizant of the fact that most graduate schools currently accept only applicants with a "B" or near "B" average earned in predental and dental school basic science courses.

Early submission of applications to be received in the Bureau of Medicine and Surgery prior to the deadline of 1 December will allow for possible forwarding delays and give sufficient time for processing of records.

In conjunction with or immediately following submission of requests for assignment to any of the training programs, it is requested that transcripts of academic records earned during predental and dental school training be forwarded to this Bureau, Code 611, for review by the Dental Training Committee. Any charges incurred in the procurement of requested transcripts must be at the expense of the applicant.

Additionally, it is requested that a statement concerning motivation for requesting advanced training, consistent with known abilities, interests and career plans, be forwarded to this Bureau.

For additional information concerning dental officers training refer to MANMED art. 6–130. For changes in Dental Officer Service Training agreement and additional information concerning the Postdoctoral Fellowship Program refer to *U.S. Navy Medical News Letter*, Vol. 50, No. 3, of 11 August 1967.

GOOD ORAL HYGIENE— A STEP FORWARD

Editor's Note—In the process of implementing various programs, it often becomes a point of interest to know how the program is being carried on at other activities. It is with this thought in mind that the following article is published.

The efficacy of proper oral hygiene for the prevention of oral disease is universally accepted, yet programs in this direction often fall victim to the more immediate and demonstrable result of restorative dentistry. Thus the maxim "An ounce of prevention is worth a pound of cure" is oft-times shunted aside.

Aboard USS BOSTON the following program of mass and individual education has been found effective.

Initially each division was shown the film, "Oral Hygiene" (MN8952) followed by a question and answer period, and an explanation of the dental department's program.

Notes were frequently put in the Plan-of-the-Day which explained the rewards of proper oral hygiene, emphasized the values of fluoride toothpastes and proper toothbrushes, and clarified the misleading advertisements of some dental products.

In each divisional head a plastic-covered poster was placed which demonstrated by pictures the proper brushing method. A sign was put in the ship's store listing ADA recommended toothpastes.

The sales officer, meanwhile, had agreed to stock all approved fluoride toothpastes as well as limiting his toothbrush stock to those considered acceptable.

On an individual basis, all personnel reporting aboard were encouraged to exercise proper oral hygiene, and to report to dental as soon as possible for examination, evaluation, and treatment. Furthermore, each individual desiring routine dental care was required to show evidence of proper oral hygiene and was given additional instruction through the use of toothbrush and model. If considered necessary, the man was required to demonstrate orally with one of his own toothbrushes the proper strokes for brushing.

Each man aboard was provided a SnF_2 treatment yearly at which time he was again encouraged to brush properly, seek early treatment, and use fluoride toothpastes.

The entire program is carried out with the goal of encouraging the adoption of sound oral hygiene habits with proper aids, as opposed to forcing it upon the men. Thus criticism, sarcasm, etc., give way to education and encouragement.

The resultant upswing in patient attitude and oral hygiene has been evidenced (1) by a clinical demonstration of healthier supporting tissues—which of course lend themselves to speedier operative treatment as gingival bleeding is minimized—and (2) perhaps less objectively, by the tripling of toothbrush sales over the past two years, as well as a twofold increase in toothpaste buying, while the fluorides have leaped forward to command 72% of total dentifrice sales.—Submitted by: LCDR R. B. Maw, DC USN.

EQUIPMENT MODERNIZATION PROGRAM

The Equipment Modernization Program is now in its second year of implementation. The Dental Division is most anxious to hear of any complaints concerning the newly installed equipment. It is requested that these complaints be well documented and that they not be capricious or arbitrary due to personal likes or dislikes. Comments are also invited as to whether the person making the complaint feels that the problems incurred are due to basic shortcomings in equipment or are the result of faulty installation.

The Dental Division will review these complaints very critically and our Modernization Program will be altered accordingly if sufficient evidence presents itself to warrant such action. Direct all replies to the Bureau of Medicine and Surgery, Code 612.

NURSE CORPS SECTION

NURSING CARE OF THE ORTHOPEDIC PATIENT ON THE USS REPOSE AH–16

The USS REPOSE reported on station in Vietnam in mid-February 1966. As of 1 March 1967 she spent two-hundred and forty-two days on station.

Within the two-hundred and forty-two day period, the Orthopedic Service aboard the REPOSE had admitted over seven-hundred patients, either as direct admissions or transfers from other wards. This total does not include officer orthopedic patients or patients with orthopedic problems secondary to other major injuries, who were admitted to surgical wards. This figure includes only ad-

missions to the thirty-eight bed Orthopedic Ward and approximately two-thirds of these patients were returned to duty. Of the total admissions, two-hundred fifty-two patients requiring over sixty days convalescence were medically evacuated to the United States or Yokosuka, Japan.

During the thirteen months the REPOSE was in the Vietnam area, several hundred orthopedic surgical procedures were performed. Of special interest is the high number of fractured femurs and fairly low number of amputations. Thirty-two patients with fractured femurs were admitted, treated and evacuated to CONUS within an average of one to two weeks. Most of these patients received their fractures from high velocity missiles rather than shrapnel or fragmentation from mines, grenades and booby traps. Routine skeletal traction was applied until the time of wound closure after which a hip spica cast was applied to accommodate future evacuation.

Within the same amount of time, thirty-seven amputations were performed on twenty-five patients, several of whom were Vietnamese military and civilian personnel. The amputations consisted of:

Below the knee	6
Above the knee	2
Bilateral below the knee	6
Bilateral above the knee	2
Above the elbow	2
Below the elbow	2
Partial amputation of the hand	3
Triple amputations (both legs and arm)	2

As opposed to the etiology of fractured femurs, most of the amputations resulted from shrapnel and fragmentation wounds from booby traps, mortar, artillary, hand grenades and land mines, rather than from missiles. All amputees, except Vietnamese, were evacuated to CONUS. One of the primary reasons for the fairly low rate of amputations aboard the REPOSE was attributed to the immediate vascular surgery performed on patients with massive damage.

Early ambulation was hoped for in the amputee program, and attempted successfully in two instances. One eighteen-year-old below-the-knee amputee stood and walked twenty-four hours after surgery; one bilateral below-the-knee amputee took two steps the day following closure of both stumps. This procedure was later discontinued due to the early evacuation of most amputees to the rehabilitation center in Oakland, California. The shortage of bed space was also a deciding factor, thus most amputees were transferred from the ship as soon as their condition permitted.

The Orthopedic Service consists of a thirty-eight bed ward. Thirty-four of these are of the routine "bunk type" hospital beds found throughout the ship, with seventeen upper bunks and seventeen lower. The remaining four beds were fracture beds bolted to the deck at all four points of contact and equipped with Balken frame traction appliances. The beds were used primarily for patients with multiple wounds presenting nursing care problems in turning, feeding, and routine care. These four beds were the unique difference in the orthopedic ward and also the greatest single asset in caring for orthopedic patients aboard ship. There are only three other orthopedic beds located throughout the ship. One is on the Sick Officers Ward and two more on the Intensive Care Unit.

Because of the fracture beds and ingenuity of the orthopedic staff and ships crew, few problems were encountered in applying traction of any kind. Within the thirteen months, almost every kind of adult traction was used, Bucks, skeletal of both arms and legs, cervical and pelvic. Balanced suspension traction presented fewer problems than anticipated as a result of the perpetual motion of the ship. Due to the balance and gravity in this type of traction, no specific problems were encountered. Nor did the movement of the weights cause any difficulties or pain to the patients, other than increased apprehension during rough seas.

Because of the low bed capacity, especially with only seventeen bottom beds available, most of the patients in Buck's traction were placed in top beds. This was an ideal arrangement in many respects. The weights hung more freely and were out of the way. Since these patients were on strict bed rest while in traction there was no need for them to occupy lower beds. Utilizing the top bunks also solved many of the bed space problems. Most back strains, knee injuries, as well as post-operative hand cases were initially placed in top bunks. When the ward was at full capacity and extremely active many post-operative minor leg cases were transferred to upper bunks with assistance to remain there for the duration of bed rest.

The Orthopedic Ward also has an adjoining treatment room where debridements, first and sec-

ondary closures, and dressing changes are performed. This often served as a substitute operating room, making the ward more active at times when several minor surgical procedures a day were performed.

Two large ambulatory wards facilitated care of those patients who did not require treatment or medications. The Orthopedic Service made frequent use of these wards. At times as many as thirty to fifty ambulatory patients were managed here, thereby vacating beds urgently needed for incoming casualties.

The Orthopedic Service consisted of one nurse who covered both Orthopedics and EENT on AM and PM duty, and one nurse who covered Orthopedics and four additional wards at night. An average of ten corpsmen were assigned to the ward, rotating eight hour shifts except when the two-section staffing plan was used. The medical staff consists of two Medical Officers, one Orthopedic Surgeon and one General Medical Officer. Since December of 1966 a Vascular Surgeon has also been assigned to the ward. The remainder of the orthopedic team consists of two cast room technicians, and two to three physical therapists whose departments are very active.

The type of orthopedic patients admitted to the REPOSE varied from the routine orthopedic diagnosis, derangement of knees, low back strain, various dislocations, torn meniscus, and fractures to traumatic wounds from shrapnel and fragmentation. Some patients had up to fifty small penetrating wounds on each extremity. Gun shot wounds were another common admission diagnosis and varied from single to multiple bullet wounds. From experience it was quickly learned that all casualties needed close inspection to determine the extent of wounds. Often a patient would be admitted with a diagnosis of a shrapnel wound but, after closer observation, other wounds would be discovered, often larger and much more serious than the initial diagnosis indicated. The more severe and fresh wounds were taken immediately from Triage to X-ray, then to the Recovery Room, where preoperative preparations were carried out. Then, from surgery, they were admitted to the ward in a stable, post-operative condition. However, many patients were admitted directly to the ward from Triage, especially when many casualties were arriving and the Recovery Room was busy. These patients were always tired, hungry and very dirty. Showers or bed baths were given as soon as possible after admission and all dressings removed. The latter was done by a doctor who then made the decision whether the patient needed soaks, drains, casts, other treatment or immediate surgery. If surgery was indicated, most of the preoperative preparations were done on the ward, such as drawing blood specimens, preoperative medications, antibiotics and tetanus toxoid, intravenous fluids and preparing the operative site. At the same time, postoperative patients would be returning to the ward from surgery. So, at these times, the ward became extremely active.

Although orthopedic nursing care and its problems were much the same as in any hospital, routine nursing care was made more difficult on the REPOSE because of the compactness of the wards and lack of space. Beds could only be approached from one side, thus making turning patients, changing linen, taking vital signs, etc. more difficult. Supplies had to be ordered frequently, and in small amounts due to limited storage space. However, with the outstanding cooperation of the various hospital departments and easy availability, most supplies could be obtained rapidly.

In many instances, housekeeping and surgical appliances had to be improvised. Intravenous poles could not be used due to the ships movement; shower hooks and S-hooks were substituted. The ship-fitters shop was called upon, on occasions, to hand-tool braces, splints and other appliances, when supplies were low or not available on the ship.

Another nursing problem, although a very minor one, was the number of diets served on the ward. Due to the difficulty in ambulating on a ship with casts, splints and crutches, many more ward diets were served than would have been necessary under normal conditions.

Because most traumatic wounds were considered dirty and infected, these were left 'open' to be sutured approximately five days or more after injury, depending upon the extent of damage and contamination. Thus, drainage from wounds was a constant challenge to nursing care. At times a patient's linen was changed three or four times a shift, and dressings reinforced as frequently. 'Chux' or disposable pads were used in tremendous amounts and usually the supply aboard ship was depleted rapidly. Plaster casts were applied on patients with traumatic injuries only after primary or complete closures were performed. Most patients were immobilized with merely posterior splints and ace bandages.

Because a large portion of the traumatic admissions were due to multiple missile wounds, most patients had additional wounds requiring more extensive nursing care than on most orthopedic wards. A number of patients had shrapnel wounds of one or both eyes, requiring patches, facial fractures with wired jaws, chest tubes, tracheotomies, abdominal wounds requiring nasogastric tubes and often gavage. Thus, the ward became a combination of General Surgery, EENT, Urology and Medicine, as well as Orthopedics.

Routine nursing care consisted mainly of problem-solving techniques. Due to the fairly high rate of fat and pulmonary emboli with traumatic orthopedic patients, coughing and deep breathing were encouraged on all bed patients. Intermittant Positive Pressure Breathing was also used on many occasions. Patients were turned very frequently and only one decubitus ulcer developed in thirteen months. This was treated and cured in a few days. Increased fluids were a major factor in nursing care, to prevent and reduce elevated temperatures and alleviate the dehydration noted in patients admitted from the field. Wet dressings to the affected areas were ordered on many patients. The various solutions used were Neomycin, Bunnels, Acetic Acid, Burows and normal saline.

Physical therapy, as in most orthopedic services, is another major aspect of nursing care. Although we had two to three physical therapists who worked with patients, the ward personnel were responsible for encouraging, observing and assisting with these exercises.

Because of the unique function of the REPOSE, there were also many advantages in caring for patients on a ship rather than at a shore hospital. One, was the rapid turnover of patients. During inport periods the census would become very low due to discharges and medical evacuations. On several occasions, the ward could be closed for cleaning and restocking. This presented an ideal time to give classes and instruct the corpsmen in various areas of nursing.

Disciplinary problems were very few on the Orthopedic Service, as compared to military orthopedic wards in the United States and perhaps were due to rapid turnover of patients. There was never the long-term orthopedic patient who becomes bored and tired of hospitalization and presents constant administrative and disciplinary problems to the staff.

One advantage to ward nursing care on the REPOSE was the stability of the ward corpsmen. Corpsmen were assigned to the ship for twelve to thirteen months and usually worked in the same area during most of his time aboard ship. All Nursing Service Corpsmen rotated between the diet kitchens, and laundry, but then generally returned to the ward to which they had originally been assigned. This was an advantage in alleviating the problems of orienting and teaching new corpsmen every two to three months, and having a constant turnover of new and inexperienced corpsmen.

In summarizing, orthopedic nursing on board the REPOSE proved to be not much different from orthopedic nursing in any other Naval Hospital, except for unique problems that could be found only on a hospital ship and, the types of wounds treated could be found only during wartime.

Nursing on a Hospital Ship has proved to be many things; extremely discouraging and depressing at times, very active and demanding—perhaps more demanding professionally, than could be found in most nursing situations. But most of all it has been challenging, highly rewarding and satisfying, both personally and professionally. —Submitted by: LTJG Mary Taylor NC USN.

AEROSPACE MEDICINE SECTION

AEROSPACE MEDICINE RESIDENTS ATTEND SEMINAR AT SAFETY CENTER

A group of 12 residents in aerospace medicine from the Aerospace Medical Institute, Pensacola has just completed a three-day seminar at the Aviation Safety Center's Aero-Medical Department. They are CAPT Samuel A. Youngman, MC USN; CDR William R. Winter, MC USN; CDR Paul C. Gregg, MC USN; CDR Theodore J. Trumble, MC USN; CDR "J" Jerome Rinaldi, MC USN; LCDR Donald R. Hauler, MC USN; LCDR George W. Mathews, MC USN; LCDR William W. Simmons, MC USN; LCDR Clyde G. Jeffrey, MC USN; LCDR Robert D. Wasson, MC USN; MAJ Dudley R. Price, MC USA, and CAPT Burton H. Kaplan, MC USA.

On a tour of the Safety Center conducted by

LCDR George M. Stone, the group was briefed by CAPT R. E. Luehrs, head of the Aero-Medical Department, and the staffs of the Accident Investigation Department and the Aviation Operations Analysis Department.

A more detailed presentation of the work of the Aero-Medical Department included discussion of the Medical Officer's Report and projects in the Biomedical Sciences Division by Dr. Stone and LT C. C. Cole, aviation physiologist; briefing by CDR Walter Gable, aviation pathologist, head of the Aviation Pathology Division; briefing by LCDR F. J. Hill, head of the Biophysical and Survival Division; and briefing by Dr. Robert Alkov and Dr. Joseph Sgro, psychologists, on the work of the Behavioral Sciences Division.

Other topics covered in the seminar where the aero-medical problems in the SST, a training method for midair collision avoidance; underwater escape devices, the invasion of privacy issue in psychological testing of government employees; disorientation training in aircraft and plans to perform cockpit fatigue studies similar to the 1940–56 Cambridge Cockpit Studies.

Also attending the seminar was LT Aldo Juan Drasich, a flight surgeon from the Argentine Navy, who is spending a month in the Aero-Medical Department. Dr. Drasich recently completed the flight surgeon's six-month course at the Naval Aerospace Medical Institute.—Flight Surgeons News Letter 8–67, AeroMed Dpt. NAVAVN–SAFECEN.

NOTES FROM PERSONNEL

On 30 June 1967 there were 450 designated Flight Surgeon billets and on that date there were 482 Naval Flight Surgeons, including 44 graduates en route as replacements for Flight Surgeons being released.

To replace Flight Surgeons who departed the service on completion of obligated duty, those who resigned or retired, and those released to take up residency training in other specialties, 128 medical officers were graduated as Flight Surgeons and 1 as an Aviation Medical Examiner from the Naval Aerospace Medical Institute at the Naval Aerospace Medical Center, Pensacola, Florida, during the year. The Institute also graduated 6 officers of the Army Medical Corps, 2 Public Health Service officers assigned to duty with the U. S. Coast Guard, and 2 in the service of friendly foreign countries. The total number of Flight Surgeon/Naval Aviators on active duty as of 30 June 1967 was 16. One Flight Surgeon completed the full course leading to the designation of naval aviator in February 1967. Two Flight Surgeons are enrolled in the complete course leading to the designation of naval aviator, and one of these will be designated in September 1967.

The Aero-Medical Department, Naval Aviation Safety Center, Naval Air Station, Norfolk, Virginia, has been approved for an affiliated Resident. Because of previous experience of at least one tour as a fleet Flight Surgeon and because of graduate training in epidemiology and biostatistics in the Master of Public Health program he will be receptive to the training potential of the spectrum of crash investigation, accident prevention and the general aspects of Aviation Safety. This program consists of a six-month tour, and the Director of Training at the Naval Aerospace Medical Institute will receive monthly progress reports from the resident and a grading report from the supervisor, the Head, Aero-Medical Department. This program is offered during the first or final six-month period of the two-year residency at the Naval Aerospace Medical Institute.

The National Aeronautics and Space Administration, Manned Spacecraft Center, Houston, Texas, has offered the Navy a third year of residency training in Aerospace Medicine at the Center. It is planned to take advantage of this opportunity, but the Navy will be unable to provide a resident for this academic year as assignments have all been made. It is anticipated that a resident will be assigned to NASA for the 1968–69 academic year.

Increases in the Aviation Medicine manpower allowance were requested to compensate for the increased aviator input into the Naval Air Training Command. Nine additional Flight Surgeon billets were recommended to handle increased student workloads in the pipeline at the Basic Naval Aviation Officers School, Naval Air Station, Corpus Christi, Texas, Naval Auxiliary Air Station, Chase Field, Beeville, Texas, Naval Auxiliary Air Station, Kingsville, Texas, Naval Auxiliary Air Station, Meridian, Mississippi, and the Naval Auxiliary Air Station, Saufley Field, Florida.

In the future, Flight Surgeons being ordered to aircraft carriers and Senior Medical Officers ordered to extra-continental shore activities under the command of COMNAVAIRLANT and COMNAVAIRPAC will be assigned prior temporary duty at COMNAVAIRLANT and COMNAVAIRPAC for briefing for periods of not more than five days. In the past, Senior Medical Officers of

carriers were ordered for a two week period of indoctrination.

Approval has been received to order Flight Surgeons who have been serving in Vietnam and who are being assigned to a billet in the Southeastern United States, en route, to the Naval Aerospace Medical Institute for a one day debriefing. This project is intended to lead, ultimately, to standard and routine methods of obtaining information for research concerning the combat performance of naval and marine aviators and aviation personnel. In addition, this debriefing will be used to review the content of the current Flight Surgeon training course as this applies to the Flight Surgeon assignment with Marine squadrons. This policy will remain in effect until notification by the Institute that sufficient data have been collected.—AeroMed, BuMed.

ACTIVITIES OF THE AVIATION OPERATIONAL PSYCHOLOGY BRANCH

The primary responsibilities of the Aviation Operational Psychology Branch are (a) to recommend the assignment of experimental psychologists to appropriate operational billets, (b) supervision, logistic support, and monitoring of procedures used by activities authorized to administer the U. S. Navy and Marine Corps Aviation Selection Tests, and (c) the coordination of experimental research in the area of aviation psychology.

Aviation Selection Testing. The number of U.S. Navy and Marine Corps Aviation Selection Test answer sheets processed each month were as follows:

January	1,499
February	1,847
March	2,452
April	1,582
May	2,363
June	1,049
	10,792

Verified test results are entered on the Standard Form 88 as an official record. Jackets processed during this reporting period were as follows:

January	754
February	651
March	1,270
April	862
May	804
June	745
	5,086

The new test answer sheets for use with the Aviation Selection tests are now operational and all answer sheets are being scored by optical scoring equipment. This new procedure has completely eliminated the use of key punch operation in the preparation of the data cards.

New experimental question booklets of the Aviation Selection Tests have been prepared and the preliminary validation has begun. It is anticipated that the new test booklets will be available for use in January 1969.

There are presently twenty-seven authorized billets under the cognizance of the Aviation Operational Psychology Branch. Two of these billets are vacant at the present time. Four applications for commissioning in the Navy's Medical Service Corps have been approved and these new officers will fill these vacant billets as well as others which will occur in Fiscal Year 1968.

In Fiscal Year 1967 billet requests were received from six commands for twelve additional aviation experimental psychologists. The requests could not be fulfilled because of the non-availability of billets within the Medical Service Corps billet ceiling.

FLIGHT PHYSICAL EXAM OMISSIONS AND CHANGES

Numerous cases of failure to record sitting height and buttock-leg length on the SF 88, report of Medical Examination (Aviation) on applicants for student Naval Aviator and Naval Flight Officer have been received in the Bureau. These measurements are required to assign anthropometric codes. The requirement is established in MANMED 15–62(4)(a), change 34.

BUMED–52 letter of 8 August 1967 is a memorandum for all Naval Flight Surgeons concerning changes in visual standards for naval aviators. MANMED page change 39 of 7 July 1967 is discussed. All Flight Surgeons should take careful note of these changes in standards and of the guide lines set forth concerning the wearing of glasses during flight by Service Group I aviators.—AeroMed, BuMed.

AEROSPACE CREW EQUIPMENT LABORATORY CHANGES NAME AND COMMANDS

The veteran laboratory responsible for development and testing of aviation protective equipment, research in aviation and space survival and escape

systems and in numerous other vital areas relating to aerospace equipment has been redesignated the "Aerospace Crew Equipment Department of the Naval Air Development Center, Johnsville, Pennsylvania."

At present, the ACED will remain physically housed in its existing quarters at the Naval Air Engineering Center, Philadelphia, Pennsylvania, and the function of the department remains unchanged. The transfer of ACEL and two other Naval laboratories to NADC was done as part of a Navy program to realign research, development, test and evaluation functions for more effective systems management.

Mailing address will be:

Naval Air Development Center
Aerospace Crew Equipment Dept.
Johnsville, Warminister, Pa. 18974

Phones:

(215) HO-51000 ext. 3713/3705
Autovon: 243-3713/3705

SOUVENIRS PRESENTED TO MUSEUM

Dr. Harold J. Rickard, retired Navy Flight Surgeon and Head, Department of Aerospace Physiology, University of Southern California, presented some treasured mementos of his Naval Aviation career to the Pensacola Naval Aviation Museum on July 24.

The museum pieces are: two pairs of Navy Flight Surgeon wings, one of which is his own original design (subsequently modified to its present design); photographs of the original low pressure chamber of the School of Aviation Medicine; and the July 20, 1941 Sunday Edition of Pensacola News-Journal featuring "Flightless Flying Machine Being Used at Naval Air Station to Teach High-Altitude High-Speed Aerial Warfare to Young Pilots."

Dr. Rickard, a 25-year Navy veteran, retired in 1960 with the rank of Captain. An aviator before studying medicine, he helped train many aspiring Navy pilots at the Low Pressure Chamber of the School of Aviation Medicine, Pensacola.—NAVAEROSPMEDCEN *Capsule*, Volume 3, 15 Aug 1967.

CNO/BUMED AEROMEDICAL BIODATA TEAM CONTINUES STRESS STUDIES IN COMBAT

Further studies in combat were conducted during a trip to Vietnam by the team in July 1967. In order to increase the data base for carrier pilots, additional collections of blood, both pre- and post-flight were made from pilots flying off attack carriers operating in the Tonkin Gulf against the ever increasing anti-air defenses of North Vietnam. The team also extended its studies to aircrews before deployment and will follow those examined during combat upon their return to routine operational flying or into nonflying activity. For comparison purposes, a group of crewmen aboard a destroyer, also in the Tonkin Gulf, were similarly studied.

In order to extend the study of stresses and fatigue to helicopters during combat operations, the team examined 34 Marine Corps helicopter pilots and crewmen operating from Marble Mountain Air Base, Danang, R.V.N. in August 1967. In-flight electrocardiograms and voice transmissions utilizing a miniaturized package and onboard tape recorder developed by Mr. Jack Martin of the Naval Missile Center, Point Mugu, California, were taken during armed escort of medical evacuation missions and during insertion and extraction operations of ground troops into hostile territory and often under enemy fire. Post-flight blood samples were concurrently collected and the frozen plasma is to again be analyzed at AMRD, NADC, Johnsville. These data will be correlated with other parameters of stress, adaptation and response, and with the data bank accumulating from the continuing studies.

The search for new and better monitoring devices and parameters will continue. Preliminary indication is that in-flight monitoring is not as adaptable or useful in the combat and operational environments as it is in research, test and space flight. The results of ECG, respiration, etc. during a single or series of combat flights seems difficult to correlate with a pilot's "combat readiness." Continuous or frequent in-flight monitoring does not appear feasible within the present state of the art. However, other physiological functions suitable for in-flight monitoring may yet be found. Thus the continuing effort to improve in-flight monitoring techniques and equipment is amply justified.

The Flight Surgeon wishes to assure the highest peak of performance and capability of a combat pilot, but within the restraints imposed by the operational commitment. Pre- and post-flight monitoring of suitable physiological, biochemical or psychomotor parameters may best serve this purpose. It is hoped that the studies which the Aero-

medical Biodata Team is conducting in the combat environment may lead to the development of better stress monitoring methods. If a biochemical index can be developed, research efforts will be extended to devise laboratory equipment and techniques suitable for use near combat bases of operation.

Team members for the latest field trip were CAPT F. H. Austin, MC USN, (BUMED/CNO), and LTJG James H. Ashburn, MSC USN (Aviation Experimental Psychologist) and Mr. Jack Martin (Electronics Design Engineer) of the Missile Test Center, Point Mugu, California.—AeroMed, BuMed.

NAVY FLIGHT SURGEONS RECEIVE SPECIALTY BOARD CERTIFICATION

The following Flight Surgeons were among those physicians recently certified as Diplomats of the American Board of Preventive Medicine in Aerospace Medicine:

CAPT Martin G. Webb, Jr. MC USN
CDR Andrew W. Stevenson, Jr. MC USN
CDR Richard A. Millington, MC USN

Dr. Webb has been ordered to duty as Director of Training, Naval Aerospace Medical Institute, Naval Aerospace Medical Center, Pensacola, Florida. Dr. Stevenson is the Medical Officer aboard the USS Constellation (CVA–64) and Dr. Millington is the Medical Officer aboard the USS Enterprise (CVA(N)–65).—AeroMed, BuMed.

ARMY ACRONYM

You have undoubtedly seen PEARL in recent issues of the U. S. Army Aviation Digest. Technically, PEARL stands for Personal Equipment And Rescue/Survival Lowdown. More realistically, this young lady is eager to assist you with any and all problems associated with survival and personal equipment. Direct your inquiries and pearls to PEARL at USABAAR, Fort Rucker, Alabama. If you have no inquiries but a "pearl" of information that others would benefit from, PEARL would be pleased to hear from you and pass it on.—USABAAR–HF News Letter, July 1967.

NOTES FROM THE AEROSPACE PHYSIOLOGY TRAINING BRANCH

1. Aviation Physiology Officers.

(a) On 30 June 1967 there were thirty-five Aviation Physiologists on board. Rank structure was as follows:

3 Captains
4 Commanders
7 Lieutenant Commanders
7 Lieutenants
7 Lieutenants, Junior Grade
6 Ensigns
1 Chief Warrant Officer (W-4)

35 Total (24 USN 11 USNR)

One prospective Aviation Physiologist was recruited from civilian sources in April 1967, received a direct appointment to the rank of Lieutenant (jg) and was ordered to report to the Naval Aerospace Medical Institute, Naval Aerospace Medical Center, Pensacola, Florida for duty under instruction.

(b) Duty assignments of the thirty-five Aviation Physiologists as of 30 June 1967 were:

Training Units	24
Research, Development, Test and Evaluation Facilities	5
Bureau of Medicine and Surgery	1
Naval Air Systems Command	2
Naval Aviation Safety Center	1
National Aeronautics Space Administration, Houston, Texas	1
Under Instruction, University of Southern California	1
Total	35

(c) One Aviation Physiologist completed the requirements for the Master of Science Degree through part-time, out-service training. The degree was awarded on 11 June 1967 to LT David J. Horrigan, Jr., MSC USN attached to Aerospace Crew Equipment Department, NADC Johnsville, Pa.

(d) Twenty-seven Aviation Physiologists attended the 38th annual scientific meeting of the Aerospace Medical Association at Washington, D. C. 10–13 April 1967. Papers were presented by five of these officers.

(e) A committee of five Aviation Physiologists met at the Naval Air Station, Miramar, California 19–22 June 1967 to plan the agenda for the annual Aviation Physiology Symposium to be held at Miramar 31 October through 2 November 1967.

2. Aviation Physiology Technicians (NEC 8409). On 31 May 1967 there were 106 billets for avia-

tion physiology technicians with a total of 106 on board. Distribution was as follows:

	Allowance	*On Board*
CONUS	94	64
LANTFLT	8	13
PACFLT	4	29
	106	106

On 31 May 1966 the shortage of 8409's in CONUS was twenty-three. As expected, the manpower drain in Southeast Asia has made this picture worse. As indicated above, on 31 May 1967 the shortage of 8409's in CONUS was thirty.

There were four classes conducted for 8409's in Calendar Year 1966 with a total of thirty-one graduates, thirty Navy and one Army. Of the Navy graduates thirteen went to sea and seventeen were assigned to shore duty in EPDOCONUS.

3. Sub-project 43–03–19, submitted by this Code for development of programmed instruction capabilities utilizing automated multi-media teaching system equipment, was not approved for funding in FY 1967.

4. Aviation physiology training statistics for the Calendar Year 1966 are presented below:

Type Training	*Personnel Trained*
Low Pressure chamber (Sea level to 30,000 ft)	10247
Low Pressure chamber (Sea level to 43,000 ft)	16468
Full pressure suit (Sea level to 70,000 ft)	596
Ejection seat	12150
Night vision	19039
Flash Blindness	42
Water survival	6509
Total	65,051

The steady increase in the total number of personnel trained is indicated below:

CY 1964—60,678
CY 1965—63,047
CY 1966—65,051

5. Increases in the manpower allowance were requested to compensate for the increased aviator input into the Naval Air Training Command. Seven additional Aviation Physiologist billets and twenty-one additional enlisted billets were recommended to handle increased student workloads in the pipeline at the Naval Aviation Schools Command, Pensacola, Florida, the Naval Aerospace Medical Institute, Naval Aerospace Medical Center, Pensacola, Florida, and the Naval Air Station, Corpus Christi, Texas. Aviator input was 2,493 in 1965, 3,043 in 1966 and the projection for FY 1967 is 3,410.

6. A Flight Surgeon and a Flight Sergeant of the Royal New Zealand Air Force spent approximately five weeks visiting Naval Aviation Physiology Training Units during March, April and May 1967. The primary purpose of the visit was to observe training methods and to receive instruction in operation of the Rapid Decompression Altitude Training Chamber (Device 9A9). A chamber of this type was recently acquired by the Royal New Zealand Air Force.

7. A maintenance/operator training course on the 6EQ2 series ejection seat trainers and the 9A9 low pressure chambers was conducted at the Naval Air Station Miramar, California 26 April—2 May 1967. Twelve students attended the course. Attendees included three representatives from the Naval Training Device Center, five training devicemen from NAS Lemoore and NAS Miramar, two Marine Flight Equipment Specialists from MCAS El Toro, one Flight Surgeon and one Flight Sergeant from the Royal New Zealand Air Force. Similar courses will be conducted in other locations as required.

8. Full pressure suit training was given to twenty-five selected civilian employees of various companies of the aerospace industry who were engaged in contract work for the Department of Defense. This training is essential to the performance of contractor personnel in the testing of spacecraft and crew systems in the simulated void of outer space.

9. One of the inactive low pressure chambers (Device 9A1B Serial Number 2) at the Naval Air Station, Jacksonville, Florida has been offered to the Mexican Government under the terms of a Navy-to-Navy lease at no cost and for a period of five years. The Mexican Navy plans to sub-lease the chamber to the Director General of Civil Aeronautics of Mexico, who has requested a chamber for use in research and training by the Department of Aviation Medicine.

10. LT Donald E. Furry, MSC USN, Aviation Physiologist, has recently been elected to membership in the New York Academy of Sciences. He is Chief of the Laboratory of Aerospace Physiology, Environmental Stress Division, at the Naval Medical Research Institute, Bethesda, Maryland. LT Furry is currently working with the Aeromedical

Biodata Team in studying the problems of stress during combat carrier operations and is involved in several projects relating to radiation in hypobaric environments. LT Furry was recently assigned additional duty at the Bureau of Medicine and Surgery as an assistant in the Aerospace Physiology Training Branch and the Aerospace Physiology Systems Requirements Branch.

EDITOR'S SECTION

DRUGS AND OTHER FACTORS INTERFERING WITH RELIABILITY OF BLOOD CHEMISTRY DETERMINATIONS

The Medical Letter 9(15):59–60, July 28, 1967.

The unreliability of many clinical laboratories has been much discussed in recent years. There is less recognition of the physician's responsibility for misleading results of laboratory tests. The methods the physician uses in obtaining and handling specimens can affect the accuracy and reproducibility of test results. For some determinations, the timing of the collection of blood or other body fluids is important, since the chemical composition of body fluids may vary with exercise, food intake, emotions, and other factors. Drugs the patient is receiving may also alter components of the body fluids or affect the accuracy of chemical determinations. Dyes such as Sodium Sulfobromophthalein USP (BSP [Bromsulphalein]—Hynson, Westcott & Dunning) and Phenolsulfonphthalein USP (PSP) can interfere with colorimetric tests if the specimens for analysis are drawn after the dye is injected.

The factors within the control of the physician that are known to affect test results are far too numerous to be listed fully here. A few precautions will be discussed, however, and as examples of the kind of problems often encountered, some of the blood chemistry determinations that can be affected by drugs the patient is receiving will be noted. The reader is urged to refer to the publications cited on page 60 (The Medical Letter) for greater detail.

Timing of Specimen Collection—Glucose and lipid levels in specimens drawn after a meal may be high; lipemia may be great enough to interfere with colorimetric analyses. Exercise can affect glucose, lactic acid, and serum proteins. Emotional disturbances can affect hydrocortisone, glucose and cholesterol. In deciding when to take a specimen the physician will sometimes have to consider these factors.

Handling of Specimens—If unstable constituents (principally enzymes, serum proteins and glucose) are to be determined, the analysis is best done promptly after the specimen is obtained. If delay is unavoidable, the specimens should be either refrigerated or frozen. Many enzymes and proteins show significant deterioration within a few hours at room temperature but remain stable for several days at 4° C. Refrigeration may not always preserve stability, however; it was recently shown that some lactic dehydrogenase (LDH) isoenzymes which are elevated in patients with myocardial infarction and other diseases are stable at room temperature (20° to 25° C) but labile at 4° C (study cited by S. Winsten, in Standard Methods of Clinical Chemistry, Vol. 5, New York: Academic Press, 1965, p. 1). Serum or plasma for acid and alkaline phosphatase tests should be promptly frozen if the analysis is not to be done the same day. With serum proteins, however, freezing can cause denaturation and lead to erroneous results; preservation by refrigeration is therefore preferable if proteins are to be determined.

To prevent transfer between cells and serum in tests of enzymes such as LDH and serum glutamic oxalacetic transaminase (SGOT), or bilirubin, sulfobromophthalein or potassium, care should be taken to avoid hemolysis, and the cells should be promptly separated by centrifuge before refrigeration or freezing.

Enzymatic breakdown of glucose can be prevented by the addition of fluoride to the specimen. Fluoride can, however, interfere with enzymatic determinations of blood urea nitrogen (BUN), glu-

cose, and uric acid and methods which avoid such interference must be used (F. W. Fales, in Standard Methods of Clinical Chemistry, Vol. 4, New York: Academic Press, 1963, p. 101).

Drug Effects—Some drugs interfere chemically with clinical determinations, while others alter blood levels through their pharmacologic effects. Some of the more common drugs having such effects are tabulated below. (Interference by drugs with tests of thyroid function, such as PBI and T_3 uptake, will be discussed in a future issue of The Medical Letter.) For more complete information on factors affecting the accuracy of clinical determinations, see W. T. Caraway, in Standard Methods of Clinical Chemistry, Vol. 5, New York: Academic Press, 1965, p. 19; W. A. Wirth and R. L. Thompson, Amer. J. Clin. Path., 43:579, 1965.

Laboratory Test	Drugs Altering Concentrations of Substances in Blood	Drugs Causing Chemical Interference With Test
Amylase	Codeine, meperidine hydrochloride, morphine	
Bilirubin		Dextran
BUN (using Nessler's reagent)		Chloral hydrate, chlorobutanol
BUN	Triamterene (Dyrenium—SK&F)	
Chloride		Bromide
Cholesterol (using ferric chloride)		Bromide
Glucose (enzymatic method)		Ascorbic acid
Iron	Iron-dextran complex (Imferon—Lakeside)	
Phosphorus		Mannitol
SGOT	Oral contraceptives, clofibrate (Atromid-S—Ayerst)	
Uric acid (colorimetric)		Methyldopa (Aldomet—Merck), salicylates
Uric acid	Nitrogen mustards	

SPECTACLE LENS HARDENING REDUCES BREAKAGE

The Ophthalmic Service Unit of the Station Hospital, DaNang, Republic of Vietnam, has recently received its second lens heat treating machine. This will enable all spectacle lenses issued to combat personnel and others to be heat treated or "dress-hardened."

This toughening process introduces the lens into an electrically heated furnace maintained at a temperature of 1180° F. Heating time is set manually and is determined from a chart based on lens size and weight. The lens is automatically removed from the heating unit and is rapidly cooled by jets of air directed on the lens surfaces by nozzles. The "dress-hardened" lens should withstand an impact test of a 5/8 inch diameter steel ball dropped from a height of 50 inches. Stock lenses with minimum thickness of 2.0 mm are used. "Dress hardened" lenses do not meet Federal Specifications for industrial safety use and should not be substituted for eye protection in eye hazardous industrial occupations or areas.

Advantages of lens tempering are numerous. Besides reducing breakage, an enormous problem with combat troops, the type of break is modified. Sharp cutting edges of glass particles are minimized in the annealing process and along with glass "splinters" are greatly reduced, thereby decreasing the possibility of lacerations in and around the eye.

The Medical Officer of the Station Hospital is CAPT H. P. Mahin, MC USN; Optometry Officer is LCDR L. M. Roach, MSC USN. HMC J. A. Brock, USN is supervisor of the Optical Laboratory.—Submitted by CAPT H. P. Mahin, MC USN, Station Hospital, DaNang.

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