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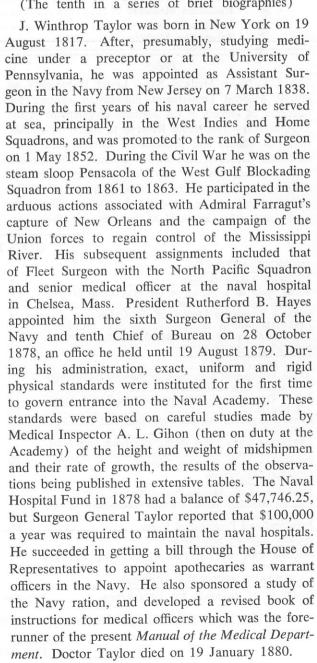
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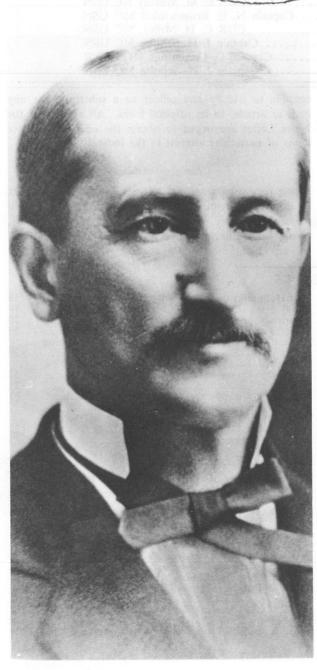
No. 8

U.S. ADDRY

Surgeons General of the Past

(The tenth in a series of brief biographies)





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

### CORONARY ARTERY DISEASE

### PHYSIOLOGICAL ASPECTS AND SURGICAL THERAPY

Circulation 35(1): 1-2, January 1967, "by permission of the American Heart Association, Inc."

#### **EDITORIAL**

Recent issues of *Modern Concepts of Cardiovas*cular Disease have featured two presentations on coronary artery disease.<sup>1,2</sup> The first, by Elliott and Gorlin, is a provocative, correlative study of the clinical, electrocardiographic, metabolic (lactate production), and cineangiographic findings in 100 patients exhibiting significant coronary disease.<sup>1</sup> Several facts of clinical importance deserve emphasis:

- 1. When pain occurs nocturnally, postprandially, or spontaneously at rest without inciting cause, when it radiates to two or more sites (neck, arms, back, and so forth), and when it has been present for more than 3 years, significant stenosis (>50%) of two, frequently three, major coronary vessels can be predicted with confidence.
- 2. Master's stress tests in *the* 26 patients whose resting electrocardiograms were normal disclosed negative electrocardiographic results in 10 patients (10% of the entire group), five of whom developed anginal pain; the remaining five patients (5%) exhibited neither pain nor electrocardiographic alterations. This finding, as well as the traditional variability of the anginal syndrome itself, may be related to the integrity of subendocardial collateral blood flow and to the various dynamic factors which modify it.<sup>3</sup>

Of considerable interest is the emergence of a fascinating new syndrome, not yet completely defined nor explained, consisting of a classic history of angina pectoris in the presence of normal selective cine coronary angiograms, normal metabolic studies, and negative Master's tests. One may in-

quire whether classic angina may exist in the presence of only small vessel disease not disclosed by present angiographic techniques, or whether it possesses a different (that is, transient coronary artery spasm) or even varied genesis in individual patients. These techniques, while unquestionably useful for the delineation of the larger coronary arteries, fail to display the smaller vessels. The demonstration of varying degrees of arterial stenosis may not mean necessarily that coronary flow itself is diminished or that perfusion to a specific area of cardiac muscle is critically deficient. Nevertheless, studies using selective coronary vein sampling for evaluating lactate production have tended to correlate well with ischemic areas corresponding to obstructed coronary arteries.

The development of coronary arteriography and improvements in surgical technique have given impetus to and permitted a more direct surgical approach to the therapy of ischemic heart disease, a field admirably summarized by Sabiston.2 Endarterectomy is suggested after medical management has failed for those patients who exhibit proximal arterial lesions of short length but good distal arteries and are under 50 years of age. The demonstration that implants of the internal mammary artery into the anterior wall of the left ventricular myocardium remain patent (63 to 85% of patients 4, 5), anastomose with coronary vessels, and apparently increase blood supply to ischemic muscle has led to a resurgence of interest in Vineberg's and other revascularization procedures. The mortality is acceptable and amelioration of pain has been achieved in the majority. Limited experience utilizing an autogenous saphenous vein graft from artery to myocardium has been reported. In our clinic, results have been dis-

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appointing due to failure of vein graft patency. Data on the volume of blood flow through endarterectomized vessels or through implants obviously are of critical importance but are not yet available. Indirect estimates of flow utilizing Kr curves and lactate changes, before and after revascularization, suggest increased blood flow through such implants.5 The normal, resting, beating heart utilizes 0.08 to 0.1 ml of oxygen per gram of left ventricular muscle per minute; this requires a coronary flow of 105 to 135 ml/min for an average normal subject. The question remains unresolved whether such surgical procedures actually provide a sufficient increase in the delivery of oxygen flow to the myocardium to justify surgery. It is evident that one must know which coronary artery is involved and precisely what area of heart muscle is ischemic before surgery is attempted. The cardinal indication for consideration of an implantation procedure is uncontrolled angina. An impending or healing myocardial infarction is an obvious contraindication. Disease of all three coronary vessels and rise in end-diastolic pressure above 14 mm Hg predicate a high operative mortality (82%).

A priori, long-standing, and conventional ideas regarding coronary artery disease are undergoing

constant modification as new data become available. New advances in the treatment of coronary disease certainly are applied best against a rational background of understanding the patient and the precise nature of his problem. At present surgery seems indicated for only a small percentage of patients suffering from ischemic heart disease. Caution is needed in the application of new drugs (for example beta adrenergic receptor blockers). Knowledge of the pharmacological background of the drug and careful patient selection is mandatory, for while such drugs may be effective in the relief of anginal pain, they can precipitate heart failure, shock, and death.

> Edward S. Orgain MD Henry D. McIntosh MD

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### LACTIC ACID AS A FACTOR IN THE PRODUCTION OF IRREVERSIBILITY IN OLIGOHAEMIC SHOCK

William Schumer MD\* Nature 212(5067):1210-1212, December 10, 1966.

Earlier investigations have revealed that with graded haemorrhage there is a decreased perfusion in peripheral tissues. This decreased perfusion produces the microcirculatory changes of pooling, sludging and absence of flow. These are indicative of microcirculatory irreversibility; that is, reinfusion of blood does not return the microcirculation to a normal state. There is a correlation between these microscopic changes and mortality. As the changes appear, the mortality increases. Microscopic irreversibility was found to occur when 50 percent of the total volume of blood of the animal had been removed. Shock is a state in which there is a peripheral vascular collapse or decreased perfusion

through non-vital tissues (skin, muscle and gastrointestinal tract) and therefore anoxia will have its greatest metabolic effect in these cells. There is an increased production of lactic acid secondary to this anoxia. Other investigations have found that vasoconstrictors (norepinephrine) used with only 30-40 percent of the total volume of blood bled produce depressed non-vital tissue perfusion, increased lactic acidosis and decreased survival rate. The use of vasodilators such as nitrates or phenoxybenzamine produces the opposite effect even when 55 percent of total volume of blood is removed. Vasodilators augment tissue perfusion, and thereby decrease the production of lactic acid, increase pH and the rates of survival. This has led us to propose the following mechanism for death in shock. In order to maintain

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a normal flow of blood to vital organs, it is necessary to divert blood from the peripheral tissues. In diverting this blood there is a decreased perfusion to the cell which produces anoxia. Anoxia will produce anaerobic metabolism which will have as its end result the production of increased lactic acid. Lactic acid is a strong metabolic proton producer, and therefore decreases the pH to a point where it has its effect on the vital organ molecular and enzyme reactions. This production of metabolic acidaemia leads to death. Accordingly, if lactic acid were the promoter of the metabolic acidaemia, then giving the animal the concentration of lactic acid found in the irreversible shock state, 65 percent of the volume bled, should cause death with decreased pH. Investigations already quoted have shown that the lactic acid concentration found in the irreversible shock state is 7.99 mmoles/l. of body water. When lactic acid has been infused in normovolaemic dogs it has caused death in every case and produced microcirculatory changes of irreversibility as visualized in the omental microcirculation.

Twenty mongrel dogs of the same sex and of approximately the same weight were used in this investigation. The animals were anaesthetized with sodium pentobarbital (25 mg/kg). A No. 14 polyethylene catheter was placed in the right femoral artery for bleeding, and another in the right femoral vein for injection. A small, lateral flank incision was made from which the omentum was freed and tacked to a cork-bordered slide on the stage of a microscope. Light from a source beneath the stage was passed through a Zeiss C heat filter to prevent the omentum from drying. The omentum was kept moist by saline moistened packs. The microcirculation was microphotographed at magnifications of 150-640 times. The lower magnification was used for the general picture of arteriolar, venular and capillary anatomy, and the higher magnification for a study of sphincter function.

In the first part of the study the ten animals were given 8 mmoles of sodium lactate/l. of body water and the pH studies on the blood were carried out. In the second part of the study ten animals were given 8 mmoles of lactic acid/l. of body water. In the third part, ten animals were given 8 mmoles of 0.1 normal hydrochloric acid and pH measurements of the total blood were made. The infusion of lactic acid and sodium lactate was regulated at the rate of twenty drops a minute for 30 min and was injected into the catheter in the inferior vena-cava. The dosage was 0.3 mmoles/min.

Table 1. Survival Effect of Infusion of Lactic Acid in Non-bled Dogs

Laura V v. mush	No. of animals	Sur- vival	pH at	Micro- circulation signs of irrevers- ibility
Infusion of lactic acid (8 mmoles	10 s/1.	0	6·8±0·4	+
body water) Infusion of sodium lactate	10	10	7·36±0·	3 0
(8 mmoles/1. body water)				
Infusion of 0·1 normal hydro- chloric acid	10	0	7·0±0·2	+
(8 mmoles/l. body water)				

The above chart reveals the mortality, pH at the end of experiment, condition of microcirculation of dogs infused with metabolic proton donors such as hydrochloric and lactic acid in comparison with sodium lactate.

The results are presented in Table 1. All animals which received lactic acid or 0.1 normal hydrochloric acid in concentrations to 8 mmoles of body water succumbed. The photomicrographs reveal that the microcirculation is similar to that in an animal which has had 65 percent of its total volume of blood removed. There was increased sludging, pooling and retardation of flow as the lactic acid was infused. The five animals which were treated with sodium lactate in order to increase the lactate ion concentration survived. Minimal differences from the control animals were observed in experimental animals. It was evident that the hydrogen ion was the significant factor in the production of the irreversibility. The observed fall in pH was related to the amount of lactic acid infused.

The effect of pH on the production of cellular aggregation in the peripheral microcirculation has been investigated further by the injection at the same dosage of 0.1 normal hydrochloric acid and observation of the omental microcirculation. The same findings concerning cellular aggregation were noted with a different proton donor. In this laboratory and others it has been found that a buffer such as *tris* (2-amino-2-hydroxymethyl-1, 3 propanediol) or 5 percent sodium bicarbonate will protect the animal

against microscopic irreversibility produced by a large volume of haemorrhage (bleeding 55-65 percent of the blood volume of the animal) and produce an improved rate of survival.

Recent studies of the omentum, ileum and muscle have shown that large intracellular "pools" of lactic acid are produced with increased haemorrhage. When the blood volume is returned to normal there is an increased serum lactic acid and acidosis as a result partly of the excretion of the intracellular lactic acid into the replenished vascular volume.

In clinical work, banked blood augments the increase in acidity after infusion because blood preserved with ACD (acid-trisodium citrate-dextrose solution) has a pH of 6.8.

From the foregoing it can be stated that the increase in H<sup>+</sup> ion produced by anaerobic metabolites may be the prime factor in producing refractoriness to return of volume. Lactic acid is the most common and earliest of the proton donors produced in anaerobic metabolism, and therefore the lactic acid infusion and subsequent death of all the animals with a microcirculatory picture of irreversible shock are

significant. The marked increase in intracellular and extracellular lactic acid does have a physiological effect in the vascular smooth muscle. Investigations have revealed that lactic acid in low concentrations acts as a vasoconstrictor, while at high concentration it produces vasodilatation. These physiological activities on smooth muscle mimic what occurs in situations in which there is only a low volume of blood. The constrictions at first, and the refractory vasodilatation in the terminal stages of shock, are consistent with the concentration of lactic acid found in the cell and serum. These observations further modify the therapy of shock by suggesting a monitoring of the pH of the serum as the blood volume is reinfused and the buffering of excess hydrogen by adequate buffer solution (5 percent sodium bicarbonate).

This work was supported by research grants from the U.S. Public Health Service, National Institutes of Health.

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

### PRIMARY ULCERATIVE DISEASE OF THE COLON

William A. Hawk MD\* and Rupert B. Turnbull, Jr. MD,\*\* Division of Pathology and Department of General Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio. Gastroenterology 51(5): 802-805, November 1966.

Primary ulcerative disease of the colon is comprised of at least two principal and well described entities, chronic ulcerative colitis and regional enteritis (Crohn's disease) of the colon. A review of 151 surgically treated cases of primary ulcerative disease of the colon disclosed important similarities and dissimilarities between the two conditions and some of these form the basis of the report.

#### Material and Methods

This report is concerned with a review of surgical material collected from 1950 to 1955. In this study, no attempt was made to select cases on the basis of clinical history, appearance at operation, radiological findings, or pathological features. A total of

151 patients comprises the series, for most of whom there are current follow-up records.

The descriptions of the gross operative specimens and the histological preparations of each case were reviewed without knowledge of the clinical history, the radiological findings, or the appearance at operation. Tentative diagnostic classification of the disorder in each case was then made. The pathological findings were then correlated with the clinical features and grouped on the basis of the following classification.

Primary Ulcerative Disease of the Colon

- I. Chronic ulcerative colitis
- II. Regional enteritis (Crohn's disease)
  - A. Granulomatous
  - B. Nongranulomatous
  - III. Unclassified ulcerative disease

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This investigation was supported by the John M. Wilson and Noah Butkin Fund for research in ulcerative colitis.

### Analysis of Material

Of the 151 patients, 87 were classified as Crohn's disease compared to 28 who had chronic ulcerative colitis; 16 patients were considered to have an unclassified form of ulcerative disease of the colon. Most of the patients in this series represent the severest late forms of the disorders, and patients not having shown satisfactory response to prolonged medical management. This series of cases does not include any of the approximately 300 patients with primary ulcerative disease treated on our medical services during the same time period, and more of whom, on clinical grounds, appear to have chronic ulcerative colitis.

The sex incidence in these various disorders shows an almost equal distribution between males and females. Age ranges for each of these categories were, likewise, quite similar and of the magnitude of 9 to 75 years.

In chronic ulcerative colitis, the terminal ileum immediately proximal to the ileocecal valve was affected in direct continuity in 10.5% of cases. This retrograde extension of disease was seldom longer than 10.0 cm in length. However, in regional enteritis (Crohn's disease) ileal involvement was noted in 47% and was usually more extensive than 10.0 cm. In several patients almost the entire ileum revealed serosal inflammation at the initial operation, and in many the ileal disease was segmental, a feature not noted in patients with chronic ulcerative colitis.

In this series of patients, involvement of the rectum occurred in 43 of 48 patients who had chronic ulcerative colitis, in 72 of 87 patients with regional enteritis or Crohn's disease, and in 15 of 16 cases of the unclassified colitis. Such a high incidence of rectal mucosal disease is to be expected in chronic ulcerative colitis by virtue of the nature of the disease originating in the rectum and spreading proximally. The high incidence of rectal involvement in the regional enteritis group is at variance with that in other published reports and might perhaps be explained on the basis of the stage of the disease being treated.

Fistulas were frequent in association with regional enteritis and with unclassified colitis, but in patients with chronic ulcerative colitis, no spontaneously occurring abdominal or internal fistulas were seen. Six abdominal and 21 anorectal fistulas occurred in the group of patients with regional enteritis, and the abdominal or internal fistulas were between the colon and the small bowel, the colon and the bladder, and the colon and the skin.

Strictures of the colon and rectum occurred in association with both the granulomatous and nongranulomatous forms of regional enteritis. In 9 patients with regional enteritis significant, partially obstructing strictures of the colon or rectum developed, and an additional 12 patients had significant narrowings of the large bowel wall consequent upon mural fibrosis. Although 6 patients with long-standing chronic ulcerative colitis developed rectal strictures, these strictures were of a different pathological and clinical character. They were due to submucosal fibrosis in contrast to the transmural fibrosis observed in regional enteritis and clinically were easily lysed by the examining finger.

The forerunners of the perforations, the fistulous tracts, and the stenoses in patients with regional enteritis are the peculiar fissures or penetrating cracks which extend from the mucosa deep into the bowel wall, frequently to the subserosal tissues. These fissures have been emphasized by Lockhart-Mummery and Morson. Fissures were not present in patients with chronic ulcerative colitis, even when the disease was complicated by toxic dilation or perforation of the colon. Fissuring occurred in 30% of patients with regional enteritis.

The concept of a nongranulomatous form of regional enteritis of the colon is not new, since it is well recognized that this disorder may occur in the small intestine without granulomas. In the present series, 45% of the specimens did not contain granulomas. Noncaseating sarcoid-like granulomas may be present in great perfusion or in great sparsity. In the early material, it was not possible to perform a scrupulous search for granulomas by means of numerous sections so that the number of cases of nongranulomatous regional enteritis was increased. Our more recent material contains fewer nongranulomatous forms. However, it should be emphasized that the nongranulomatous forms exhibited pathological features that in every other respect were entirely similar to those of the granulomatous type. Of special interest was the occurrence of granulomas in the operative specimens from 48 patients classified as having granulomatous regional enteritis. In 30 cases, granulomas were found in all resected specimens. Thirteen had granulomas in the first resected specimen and none in subsequent specimens, and in 5 patients granulomas were found in the second or third specimens but not in the first. The fact that granulomas could not be identified in each operative specimen is further evidence that regional enteritis may not always be granulomatous. Toxic dilation of the colon occurred as a complication of regional enteritis in 14 of 87 patients (16%) and occurred with the same alarming suddenness as seen with ulcerative colitis. This complication occurred with the more acute forms of Crohn's disease, probably because the degree of fibrosis that would inhibit dilation of the bowel had not yet developed. Toxic dilation of the colon occurred in 13 of the 48 patients with chronic ulcerative colitis.

"Postcolectomy ileitis," a nonspecific ulcerative process which occurs in the prestomal area of ileostomies of patients who have had colectomies, occurred in 17 of 87 patients with regional enteritis (20%) and in 3 of 48 patients with chronic ulcerative colitis (6%). Clinically, the complication has not appeared to be the result of ileostomy dysfunction. The occurrence of this disorder in patients who have ileal involvement at the time of colectomy suggests a relationship to the primary disease, but the characteristic gross and microscopic features of regional enteritis or of chronic ulcerative colitic are lacking.

The development of carcinoma as a late complication of chronic ulcerative colitis is well documented, and this occurrence is affirmed in the present series. Carcinoma occurred in 6 of 48 patients who had chronic ulcerative colitis, giving an incidence of 12.5%. All but one of the patients with chronic ulcerative colitis had a long history of disease, ranging from 7 to 25 years. In contrast to this incidence, cancer developed in only 1 patient with Crohn's disease, a 75-year-old man who had a carcinoma of the colon resected 4 months before the diagnosis of regional enteritis was established. A review of the operative specimens containing carcinoma did not reveal evidence of regional enteritis in that segment. Five of the 6 patients with cancer and ulcerative colitis are alive and well 5 to 11 years after definitive treatment. One patient has died of this disease 8 years after diagnosis. The patient with the carcinoma antecedent to his regional enteritis survived 5 years without evidence of recurrence and died of complications of the regional enteritis.

Of the 18 deaths that occurred in the entire series, 10 were in the chronic ulcerative colitis group and 7 in the regional enteritis group. There were more earlier postoperative deaths in the chronic ulcerative colitis group than in the regional enteritis group, principally from complications of the disease. These are listed in Table 1.

TABLE 1. CAUSES OF DEATH IN PRIMARY ULCERATIVE DISEASE OF THE COLON

and the control of th	No.	of cases
Chronic ulcerative colitis	wi)	militario
Postoperative		to bold
Peritonitis		2
Staphylococcal enteritis		2
Hemorrhagic necrosis of ileum		1
Remote		
Cardiac		2
Carcinoma of rectum		1
Intestinal obstruction		1
Gangrene, secondary to hernia		
repair		1
Crohn's disease		
Postoperative		
Following emergency surgery		
for obstruction		1
Remote		
Cardiac		2
Perforation of small intestine		2
Rupture of colon		1
Carcinoma of ovary		1

The 16 cases of unclassified colitis remain a challenge to precise classification. Five of these are probably regional enteritis, and 1 is probably chronic ulcerative colitis, but these cases are not sufficiently typical to warrant inclusion into specific groups.

### Summary

In summary, regional enteritis (Crohn's disease) appears to be a more common disorder of the large bowel than is chronic ulcerative colitis, as diagnosed in our specialized practice. Regional enteritis may be granulomatous or nongranulomatous, otherwise the two forms are entirely similar. Ileal involvement and postcolectomy ileitis were more common in Crohn's disease. Toxic dilation may be a complication of both ulcerative colitis and of regional enteritis. The development of carcinoma in patients with chronic ulcerative colitis remains a real threat and occurred in 12.5% of the patients. The carcinoma observed in the course of regional enteritis is considered coincidental.

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

Other recent articles on ulcerative and granulomatous colitis appear in *The Journal of The Mount Sinai Hospital*, New York, November-December issue, 1966, (vol 33 #6).—Editor

# LEUKOCYTE MITOSIS: SUPPRESSION IN VITRO ASSOCIATED WITH ACUTE INFECTIOUS HEPATITIS

Science 155(3758): 80-81, January 6, 1967, "Copyright 1967 by the American Association for the Advancement of Science."

Abstract. Inhibition of mitosis in vitro was observed in leukocytes from patients with acute infectious hepatitis. Similarly, in cultures of normal leukocytes, after the addition of small amounts of serum from patients with hepatitis, mitosis was suppressed. Although the incidence of mitosis became normal in leukocytes from convalescent patients, there were chromosomal abnormalities.

The effect of infectious hepatitis on the chromosomes of cells in human peripheral blood was studied during a recent epidemic of this disease, in which more than 100 cases were recognized. Many were symptomatic; others were discovered during a survey of tests for liver functions [primarily for serum glutamic oxalacetic transaminase (SGOT)]. Specimens of blood and serum were obtained from 16 patients, some of whom had been previously karyotyped. Additional samples were obtained from patients at the Massachusetts General, Boston City, and St. Elizabeth's Hospitals. Serums from eight patients with noninfectious hepatic disease and comparable abnormalities of liver function served as controls. Normal specimens were obtained from healthy students and employees in the same institutions.

The standard method of Moorhead *et al.* for culturing leukocytes and preparing chromosomes was used, with two modifications; eight drops of whole blood were added to the culture medium in place of the 1.0 ml of plasma, and the cells were exposed to colcemid for 2 hours instead of the 6 hours suggested by Moorhead. In every case all stained cells were studied. The percentage of leukocytes in metaphase was derived from a count of at least 200 cells.

The initial studies were performed with preparations of peripheral leukocytes obtained from patients with acute infectious hepatitis (hereafter referred to as the direct method). In another method (indirect) 0.1 ml of the serum to be tested was added to cultures of leukocytes obtained from healthy individ-

uals. Preparations to which no serum was added served as culture controls.

No metaphase figures, as judged by the direct method, were seen in specimens obtained from 12 patients with acute infectious hepatitis. Most of the leukocytes present were contracted and deeply stained or macerated. Chromatin clumping occurred in a few cells, but there was no other sign of mitosis. Eight to 20 percent of cells taken from patients before they developed hepatitis had metaphase figures. Thirteen to 20 percent of leukocytes from convalescent patients after liver function tests had become normal had metaphase figures. However, these chromosomes, showed an unusual sticky quality as well as multiple breaks, deletions, and additions.

Serums from nine patients with infectious hepatitis repeatedly inhibited the development of metaphase figures in normal leukocytes. The incidence of metaphase figures in these preparations ranged from 0 to 0.5 percent of the cells examined. In contrast, control cultures revealed 8 to 20 percent of the leukocytes in metaphase.

Using the indirect method, dilutions of four serums that inhibited leukocyte mitosis were tested. In each case, the serums diluted up to one part in 1,000 inhibited mitotic activity. Serums from normal, healthy individuals and eight patients with non-infectious hepatic disease did not suppress metaphase figures in leukocyte cultures; 12 to 20 percent of the leukocytes were in metaphase.

The blood and serum of patients with acute infectious hepatitis have a factor that inhibits leukocyte mitosis and mitosis of normal leukocytes in culture. The inhibition of leukocyte mitosis does not seem to be mediated by elevated concentrations of SGOT or bilirubin since mitotic suppression was not evident in cultures inoculated with serum from patients with other forms of liver disease. The inhibition of mitosis may be related to damage of leukocytes by the virus of hepatitis, which may multiply in the leukocytes with resultant cell injury or

interference with cell replication. Indeed, infectious hepatitis is characterized by viremia and by a prominent leukopenia during the late period of incubation and early acute illness.

These results do not provide definite evidence that mitotic suppression reflects the action of virus. Other, as yet undefined, factors may be responsible for these effects. Inhibition of leukocyte mitosis for which there has been no explanation has been frequently observed. Rubella virus has been associated with suppression of mitotic activity in several monolayer tissue cultures. Leukocytes from patients with Hodgkin's disease are affected similarly.

Chromosomes of leukocytes taken from patients with hepatitis during convalescence had an increased

incidence of breaks, stickiness, and abnormal numbers (deletions or additions) that were not present previously. Similar changes have been seen in association with other viral infections. Chromosome breaks have been reported in association with acute infectious hepatitis. Suppression of mitosis and aneuploidy have not been observed. The appearance of chromosomal aberrations following hepatitis is of interest in light of recent observations suggesting an epidemiologic association of hepatitis and Down's Syndrome.

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# ADRENALECTOMY FOR DISSEMINATED BREAST CANCER

Sir Stanford Cade\* KBE, CB, FRCS, FRCP, FRCOG, Brit Med J 2(5514): 613-615, September 1966.

The incidence of breast cancer in women in England and Wales has risen progressively for the past 40 years, and during 1964, 9,860 women died of it. The cause of death in these cases is metastatic spread of the disease.

Huggins and Bergenstal (1952) showed that control of metastases from breast cancer can be achieved in a proportion of patients by adrenalectomy. This report is based on a personal series of 348 patients (including three males) with a disseminated breast cancer, submitted to bilateral adrenalectomy and gonadectomy during the past 14 years.

The operation is effective in about half of those submitted to it, and the results in hormone-dependent tumours are unsurpassed by any other form of treatment as regards degree of response and length of period of remission, and only equalled by the results of hypophysectomy.

### Clinical Material

The ages of the patients varied from 24 to 76 years, but the majority were in the fourth and fifth decades. The series included 24 patients with bilateral mammary cancer and nine with pregnancy or

lactational cancer. There is no evidence that the younger age group responded differently from the older; neither was success or failure in any way related to the pre- or post-menopausal state of the patient.

The operative mortality, defined as death within one month of the operation, was 4.3% in the overall series and 1% in the last 100 patients. The technique of the operation in all cases was by the posterior route through the bed of the 11th and 12th ribs. In almost all patients the operation was done in two stages: left adrenalectomy and bilateral oophorectomy followed one week later by right adrenalectomy. No correlation was observed between the histological variety of breast cancer and the response to adrenalectomy.

Site of Metastases.—The commonest site of metastases was the skeleton; in many patients both skeletal and visceral metastases were present, in others lymph nodes were involved, and in some there were cutaneous recurrences. The distribution of metastases is shown in Table I. The histological examination of the ovaries and adrenals showed that 40% of the adrenal glands and nearly 30% of the ovaries were found to be involved by metastases (Lumb and Mackenzie, 1959).

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### Choice of Patients for Adrenalectomy

Only half of those submitted to adrenalectomy are likely to benefit from it. The choice of patients for bilateral adrenalectomy therefore presents some difficulty, as there is today no simple, reliable, and generally applicable test to predetermine "hormone-dependence." The response to adrenalectomy is not solely determined by the biological factor of hormone-dependence, and other factors should be taken into consideration.

### Extent, Type, and Site of Metastases

The extent of metastatic involvement and the interference with vital functions increase the operative hazard and influence the response to treatment.

The size of the metastases and the type of invasion and spread are more important than the site. Thus hepatic metastases have been reported as less likely to respond than skeletal metastases, but a study of patients with hepatic metastases indicates that a large number of small metastatic nodules may regress completely, whereas one or two large massive deposits will not be affected.

Similarly, pulmonary metastases revealed radiologically as multiple, discrete, spherical shadows may regress completely after adrenalectomy, whereas infiltration of the pulmonary lymphatics (lymphangitis carcinomatosa) invariably fails to respond. Similarly, intracranial metastases at the base of the skull or cerebral or cerebellar metastases may respond if small although multiple, whereas large tumours may kill the patient from a sudden haemorrhage and raised intracranial pressure. These observations indicate that adrenalectomy should be undertaken as soon as metastases are diagnosed and not as a last resort.

Confusion of thought between failure to respond, owing to hormone-independence of the cancer and functional failure of the organ the seat of metastases, led to the belief that visceral metastases are less hormone-dependent than skeletal metastases.

#### "Free Period"

The best-known factor in the assessment of the likely response or lack of response to adrenalectomy is the length of the so-called "free period"—the interval between the first treatment (mastectomy) and the occurrence of metastases.

If this free period is short, 12 to 18 months or less, adrenalectomy is not likely to benefit the patient. After a free period of four years or more a favourable response to adrenalectomy occurs in almost 50% of patients.

TABLE I.—METASTASES IN 348 PATIENTS

Bone	212 (61%)
Bone and viscera	172 (50%)
Lung and pleura	
Liver	
Eye	
Brain	
Heart	4 (1%)
Local recurrences of primary tumour	90 (26%)

Personal experience over 14 years indicates that if adrenalectomy proves to be effective it is so irrespective of the site of metastases. In this series several patients with involvement of the liver have shown regression of the hepatic metastases with remission for periods up to three years.

#### Previous Hormone Treatment

A review of 165 patients in this series previously treated by oestrogens, androgens, or cortisone and subsequently submitted to adrenalectomy shows that (1) lack of response to androgens, oestrogens, or oophorectomy does not mean that adrenalectomy will not control the metastasis; (2) aggravation of symptoms by oestrogens indicates hormone-dependence and so does improvement after oophorectomy; (3) the periods of remission after the administration of androgens or oestrogens, with or without cortisone, are shorter than periods of remission following adrenalectomy; (4) the incidence or frequency of regression is higher after adrenalectomy than after androgens, oestrogens, and steroids; (5) adrenalectomy following prolonged hormone treatment is less frequently effective than adrenalectomy performed as the initial treatment. This is especially the case in pulmonary metastases, as the response to androgens and steroids in these patients is of short duration and is often followed by widespread recrudescence and rapid deterioration of the patient's state, which precludes adrenalectomy.

Many patients submitted to this "medical" trial with a favourable initial response survive a few months only. Dao and Nemoto (1965), in a critical evaluation of adrenalectomy and androgen therapy in disseminated breast cancer, conclude that adrenalectomy should be "performed at the onset, when metastases first become demonstrable, as a primary therapy." The present series confirms their experience, especially as regards pulmonary metastases. They conclude that "the data from this study provide evidence that patients with pulmonary metas-

tases, unless they receive immediate effective treatment, die within a few months. Treatment of such patients with hormonal therapy is equivalent to procrastination."

Critical observation of this series of patients adrenalectomized for disseminated breast cancer indicates that not infrequently the preliminary trial of "simpler" hormonal treatment by androgens, oestrogens, or steroids has proved detrimental to the patient and has rendered "inoperable" a previously "operable" patient. If the chances of a favourable response to adrenalectomy in the previously untreated patient are 50%, this chance is reduced in those previously submitted to medicinal hormone therapy who prove resistant to it and in whom the metastases continue to grow in number and size. Study of these patients makes clear the fallacy of the argument: "there is no harm in trying hormone therapy, and if or when it fails there is still adrenalectomy to turn to."

Many metastases remain for a time clinically silent and undetectable, as shown by the considerable number of ovaries and adrenals found to be involved on histological examination and the discovery at laparotomy of hepatic metastases previously unsuspected. Bilateral adrenalectomy has proved of greater value when undertaken early, both by the number of remissions and by prolonged periods of control.

### Remission and Regression

Objective evidence of a favourable response to adrenalectomy is the regression or disappearance of visible and palpable lesions, healing of ulceration and radiological evidence of regression of pulmonary metastases, healing of pathological fractures, recalcification of osteolytic metastases, and restoration of function—for instance, vision after regression of intraocular metastases.

Regression of lesions can be complete or partial, lasting or temporary. The length of remission varies from a few months to several years. Reactivation of the disease is shown by the appearance of fresh lesions, although no recurrences may develop at the actual site of previous lesions which have regressed following adrenalectomy. The periods of remission achieved in this series are shown in Table II.

Prolonged survival—for periods of 5 to 12½ years—in patients submitted to adrenalectomy between 1952 and 1959 is shown in Table III.

This series of 348 patients with disseminated breast cancer includes three with involvement of the heart and pericardium, necessitating aspiration of

TABLE II.—DURATION OF REMISSION FOLLOWING
ADRENALECTOMY

Duration of	Pati	Patients		
Remission	No.	%	Assessed	
Nil (failures)	109	32)	227	
Up to 6 months	45	13	337	
1 year	61	19	320	
2 years	35	11	313	
3 years	20	6.5	309	
4 years	10	3.4	297	
5 to 12½ years	19	7	272	

blood-stained pericardial effusion prior to adrenalectomy; one patient who submitted to oesophagectomy for an oesophageal metastasis from breast cancer, before cortisone became available and adrenalectomy could be undertaken, subsequently developed skeletal metastases, for which adrenalectomy was done. Two patients required post-adrenalectomy gastric resection, and one patient vagotomy and gastro-enterostomy for haematemesis; all three gave a history of previous peptic ulceration, and this was aggravated when cortisone had to be given. Hypercalcaemia in the presence of extensive osteolytic skeletal metastases required pre-adrenalectomy treatment by steroids to render the patient fit for surgery. Primary carcinoma of the breast of en cuirasse type proved hormone-independent.

### Illustrative Cases of Prolonged Remission and Regression

The clinical histories of eight patients with prolonged survival following bilateral adrenalectomy and oophorectomy are summarized.

Case 1.—Married woman aged 43. Nullipara, pre-menopausal. This case has been described and illustrated (Cade, 1955). The patient developed a local recurrence two years after radical mastectomy for carcinoma of the left breast. The lesion was not controlled by radiotherapy. Bilateral adrenalectomy and oophorectomy in 1953, with rapid and total regression of the lesion. Well and free from recurrence to date, 12½ years later.

Table III.—Prolonged Survival Among 272
Patients Submitted to Adrenalectomy
(1952-9)

Years	5	6	7	8	9	10	12	121/2	Total	
No. of										
patients	8	4	1	3	1	1	1	2	19 (7%)	

Case 2.—Married woman aged 47. Multipara, pre-menopausal. Radical mastectomy in August 1950 for stage I carcinoma of the right breast. Two years and two months later pain developed in right buttock and leg, which continued for 18 months. Bilateral adrenal ectomy and oophorectomy in November 1953 for osteolytic metastases in the left humerus, right ischium, and ninth rib. All the lesions recalcified. Well and free from disease to date, 12½ years later.

Case 3.—Married woman aged 56. Multipara, six years post-menopausal. Radical mastectomy in May 1948 for stage II carcinoma of right breast. Postoperative radiotherapy given. In January 1952 paralysis of left vocal cord developed. In July 1952 x-ray examination showed bilateral pulmonary metastases and paralysis of right diaphragm. Treated by radiotherapy and androgens. Four months later the supraclavicular nodes were enlarged. In February 1954 there were bilateral pulmonary metastases and a mediastinal mass, with paralysis of left vocal cord and of right leaf of diaphragm. Metastases in right supraclavicular lymph nodes and choroidal metastasis in left eye. Bilateral adrenalectomy and oophorectomy in February 1954. Choroidal metastasis regressed completely, with recovery of vision; supraclavicular lymph nodes could no longer be felt. X-ray examination of chest showed complete regression of pulmonary metastases, but paralysis of vocal cord and diaphragm persisted. Well and free from active disease, with complete regression of all metastases to date, 12 years after adrenalectomy.

Case 4.—Spinster aged 48. In July 1950 radical mastectomy for a stage III carcinoma of right breast, previously treated by radiotherapy. In October 1953 a right pleural effusion and paralysis of the right vocal cord developed. Bilateral adrenalectomy and oophorectomy in October 1954. At laparotomy liver contained metastases. Histological examination showed metastases in left adrenal and left ovary. Following adrenalectomy complete remission of all lesions till June 1961—that is six years and eight months-when skeletal metastases appeared in the left pubic ramus and left femur. These were treated by radiotherapy and androgens. Death occurred on 10 June 1963. Following adrenalectomy the patient survived nine years, with complete remission for six vears and eight months, although at the time of adrenalectomy there were metastases in the mediastinum, pleura, liver, ovary, and adrenal.

Case 5.—Married woman aged 35. Multipara, pre-menopausal. Radical mastectomy in June 1946 for a stage II carcinoma of left breast. Post-operative radiotherapy given. In December 1957, 10 years

after mastectomy, the patient then aged 45 became pregnant but aborted spontaneously in 10th week. During pregnancy local recurrences developed in scar and metastases were found in the supraclavicular lymph nodes on biopsy. Bilateral adrenalectomy and oophorectomy in December 1957 resulted in complete regression of enlarged lymph nodes and of local recurrence. In January 1964, 17 years after the mastectomy and seven years after adrenalectomy, patient developed carcinoma of the opposite (right) breast and underwent a radical mastectomy. Well to date, nine years after adrenalectomy. No other case where mammary cancer developed several years after adrenalectomy and oophorectomy has been recorded.

Case 6.—Married woman aged 49. Nullipara, pre-menopausal. Radical mastectomy for stage II carcinoma of right breast in December 1954. In March 1957 laparotomy revealed extensive carcinomatous involvement of parietal and visceral peritoneum, omentum, mesentery, and liver. Bilateral adrenalectomy and oophorectomy was done; both ovaries and adrenals contained metastases. All the lesions regressed and patient is alive and clinically free from disease to date, nine years after adrenalectomy.

Case 7.—Married woman aged 56. Nullipara, post-menopausal. Radical mastectomy for carcinoma of right breast in 1947 and post-operative radiotherapy. In August 1954, seven years after mastectomy, metastases developed in both humeri with pathological fractures. Within four months there was widespread blood-borne dissemination; the skeleton was extensively involved by metastases in skull, both humeri, both femora, left scapula, left clavicle, and several ribs. Liver grossly enlarged to level of umbilicus by multiple metastases proved by biopsy at laparotomy for oophorectomy. Bilateral adrenalectomy and oophorectomy on 4 January 1955. Ovaries and adrenals free from metastases. The response to adrenalectomy was rapid, with healing of pathological fracture, recalcification of all skeletal metastases, and regression of hepatic metastases. Patient returned to full work as schoolteacher and led a normal life. Remission lasted for over seven years, when skeletal metastases became active. Post-adrenalectomy survival: seven years eight months.

Case 8.—Married woman aged 43. Hysterectomy for fibroids in 1954. Radical mastectomy for carcinoma of right breast in 1956. In 1959 metastases in right lung and skeletal metastases in skull, ribs, pelvic bones, and both femora. At that time a large

duodenal ulcer was shown on barium-meal examination. Bilateral adrenalectomy and oophorectomy in March 1960. Metastases found in one right adrenal and in one of two accessory adrenal glands. Two years later, in 1962, vagotomy and gastrojejunostomy for activation of duodenal ulcer. At that time there was no longer any radiological evidence of pulmonary metastases, and all skeletal metastases had recalcified. Remains well and free from recurrence to date, six years after adrenalectomy.

### Summary and Conclusions

The paramount indication for adrenalectomy is disseminated breast cancer, and the natural history of the disease shows clearly that a "solitary" metastasis is evidence of dissemination and that a metastasis remains "solitary" for a short time only.

Pre- and post-adrenalectomy management by cortisone is now fully understood and easily achieved. The operation presents no special difficulty in the hands of a surgeon of average skill; the operation

mortality is now 1%. Life on cortisone is almost normal. The earlier adrenalectomy is undertaken the greater the chances of prolonged remission. The response to previous hormonal treatment is not a reliable indication of hormone-dependence, and preliminary hormone therapy often precludes a favourable response from adrenalectomy.

Restoration of function, such as recovery of vision following regression of intraocular metastasis and recovery from various cranial-nerve paralyses from metastatic involvement of the base of the skull, has been achieved following adrenalectomy.

In hormone-dependent tumours, relief of pain is achieved almost immediately after adrenalectomy.

Survival for periods of up to twelve and a half years has been achieved with complete regression of skeletal and visceral metastases.

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### MEDICAL ABSTRACTS

### RENAL HYPERTENSION—DIAGNOSIS AND SURGICAL TREATMENT

W. M. Kirkendall MD, Annette E. Fitz MD, and M. S. Lawrence MD, (From the Cardiovascular Research Laboratories, Department of Internal Medicine and Surgery, University of Iowa, and the Medical Service, Veterans Administration Hospital, Iowa City, Iowa.) New Eng J Med 276: 479-485, March 2, 1967.

One purpose of the authors of this article is to present information concerning the value of some widely used tests, as well as examinations of peripheral and renal-vein blood for renin, as tools for predicting operative success. Also, they report the results of operative treatment for renal hypertension in patients followed until death or for one to four years.

Fifty patients with hypertension who had operations between 1 January 1962, and 1 February 1965 are the basis for this report. Twenty-four of these (48 percent) were classified as cured or improved at the end of the follow-up period.

According to the authors, brief duration of hypertension is the most helpful historical factor in predicting the patients most likely to benefit from

operation. In the young, nonatherosclerotic patient a low-pitched abdominal bruit, particularly if coupled with unexplained hypokalemic alkalosis, was a good indication of correctable renovascular hypertension. Differential determinations of renal vein renin were helpful in predicting surgical success in eight patients. Intravenous pyelography and radioactive renography were good screening techniques. Aortography and renal arteriography were useful in demonstrating both parenchymal and vascular disease; many patients who had abnormalities on pyelography, radioactive renography, and aortography were unimproved by operation. For the best prediction of surgical success, the significance of these tests must be confirmed before operation by differential determinations of renal-vein renin or split renal-function studies or both.

### ACUTE MYOCARDIAL INFARCTION IN PATIENTS THIRTY-FIVE YEARS OF AGE AND UNDER

A. S. Kaplan MD, Dis Chest 51: 137-147, February 1967.

Dr. Kaplan, in this article, reviews the medical literature on the subject of myocardial infarction

in patients below 40 years of age and presents a series of 59 cases of clinically proved myocardial infarction in patients 35 years old or younger taken from an unrelated urban population in a community of approximately 50,000 people during the period 1951-1963. Twenty-six percent of these were negroes; all cases were selected from the records of the Norfolk General, De Paul, Leigh Memorial, and Community Hospitals, and the office of the State Medical Examiner, Norfolk, Virginia. In his discussion of problems and relationships which predispose to coronary artery disease in the young group, he takes these up under the headings of Family History, Obesity, Hypertension, Diabetes Mellitus, Cholesterol, Smoking, and Physical Activity and Occupation, and in addition he discusses the problem of the young woman with coronary disease and the problem in Negro women.

The group from Norfolk was comprised of 46 white men, 12 (26 percent) of whom died; four white women, of whom two died; five Negro men, of whom four died; and four Negro women, of whom four died. Hypertension occurred in 34 percent of the cases, diabetes mellitus in 18 percent, obesity was a factor in 27 percent, and elevated serum cholesterol (over 250 mg/100 ml) in 84 percent. Predominant involvement of the left anterior descending coronary artery was found in the 17 who were autopsied. Clinically, the electrocardiographic infarction pattern was found to be as frequently anterior as posterior in distribution with lateral extension about one-half as frequent.

## INITIAL TREATMENT OF CARCINOMA OF THE BREAST, STAGES I AND II

CDR L. C. Getzen MC USN, (From the Surgical Research Unit, Naval Hospital, San Diego, California). Amer J Surg 113: 358-362, March 1967.

This study, for purposes of uniformity in comparison, was limited to Caucasian women who had unilateral radical mastectomies for stages I and II carcinoma at the Naval Hospital, San Diego, California during the period 1948-1962 and is based on a total of 217 patients.

Twenty-five percent had surgical treatment only. In addition to surgery, 21 percent had oophorectomy and cobalt 60; 19 percent radiation; 18 percent cobalt 60; 11 percent oophorectomy, thio-TEPA, and cobalt 60, and six percent thio-TEPA and

cobalt 60. In his summary, the author states that postoperative radiation therapy produced a lower five year survival rate in patients with carcinoma of the breast, stages I and II after radical mastectomy than in patients who did not receive radiation therapy; the decreased survival rate was especially significant in patients with stage I disease; the highest survival rates were achieved in patients who had oophorectomy, thio-TEPA, or both, together with radical mastectomy, with or without postoperative radiation therapy. He feels that the host resistancetumor virulence balance probably exerts the greatest influence on survival of patients with cancer of the breast and that the balance may be unfavorably altered by postoperative radiation or may be enhanced by oophorectomy, thio-TEPA, or both.

# CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS

M. H. Grieco MD, New York, (From the Allergy Laboratory, Department of Medicine, St. Luke's Hospital Center, New York). Arch Intern Med 119: 141-145, February 1967.

Skin sensitizing antibody has been demonstrated to sodium cephalothin, cephaloridine, and 7-aminocephalosporinic acid in a patient studied five months after anaphylactic reaction to oral penicillin G. It is suggested that all cephalosporin C derivatives be used with the same caution as are penicillin derivatives in patients with a past history of penicillin allergy.—Authors' Summary.

### "ANAPLASIA CLINIC" AID IN THE DIAGNOSIS AND TREATMENT OF PRE-INVASIVE CERVICAL LESIONS

W. M. Kramer MD and Saul Kay MD, (From the Department of Surgical Pathology, Medical College of Virginia, Richmond, Va.). Cancer 20: 202-209, February 1967.

A specialized "Anaplasia Clinic" has been of value in evaluating women with abnormal vaginal cytology and no obvious invasive cervical lesion. Using cytology, colpomicroscopy and biopsy as preliminary diagnostic tools, 163 cases of anaplasia, 75 of carcinoma in situ and 8 of invasive cancer have been detected from 339 referrals. Of the patients with biopsy-provided lesions 89 percent were in the

childbearing age group. Three instances of progression from anaplasia to carcinoma in situ have occurred in untreated patients. Biopsy alone produced cytologic regression in 50 of 80 anaplasia cases. Biopsy strongly influences the natural history of anaplasia. Cauterization was effective in causing regression in 17 of 28 cases with persistent abnormalities on smear following biopsy and would appear to be an effective form of therapy for anaplasia.—Authors' Summary.

### CARCINOMA OF THE UTERINE CERVIX— A STUDY OF 864 PATIENTS

I. C. Nielson MD, R. R. Smith MD, J. R. McLaren MD, and J. E. Scarborough MD, (From Emory University School of Medicine, Department of Surgery, Robert Winship Memorial Clinic, Atlanta, Ga.).

Cancer 20: 86-92, January 1967.

This is a report of 864 patients who had primary treatment for cervical cancer at the Emory University Hospital from 1937 through 1964. Fifty-three had adenocarcinoma, 118 carcinoma in situ, and 693 invasive squamous carcinoma. All were studied with respect to age, stage of disease, and mode of therapy.

The annual incidence of invasive carcinoma declined progressively while that of carcinoma in situ increased, not only when compared to all new tumors added to the registry but also when carcinoma of cervix alone was considered. The annual incidence of stages I and II disease increased while that of the later stages of III and IV decreased progressively during the period of study. Among the small groups of patients with adenocarcinoma. the 5-year survival was slightly lower than that for invasive squamous cancer. No patient with in situ cancer has experienced recurrence or has died as a result of the disease; of this group, 80 were treated by hysterectomy, 9 were managed with conization alone, and the rest, 29, received radiation therapy alone or in combination with surgery. Among those with invasive squamous carcinoma, the over-all 5-year survival was 68 percent; the more significant survival as determined by stage was 87 percent, 60 percent, 17 percent and 4 percent for stages I through IV respectively. The incidence of major complications of treatment was approximately 1 percent; treatment failures as evidenced by local recurrence occurred in 16.8 percent of the total number of patients treated.

### DENTAL SECTION

### DENTISTS AND THE MEDICO-DENTAL TEAM

H. Lamont Pugh MD,\* Reprinted with permission from Virginia Med Monthly 94: 64-66, January 1967.

"But he who dares refuse
All aid of men, must be a god or fool."
W. W. Story ("A Contemporary Criticism")

Active duty in the Armed Services provides members of the medical profession with a particularly favorable opportunity to become acquainted with members of the dental profession, and to acquire an awareness of the role they play and the manner and measure in which the two professions can mutually augment the mission of each other.

There are no more elite units in any of the branches of our National Defense establishment than

the Dental Corps of the Army, Navy and Air Force.

Scholastically, from the standpoint of academic requirements for admission to a dental school in the United States, and the mastery of a curriculum requisite to graduation, as well as in a postgraduate sense, the profession of dentistry has kept abreast of the profession of medicine in a remarkable measure.

In general, devotees to the profession of dentistry are imbued with certain qualities commonly associated with artists. The dentist is quite significantly endowed with pride of workmanship and pride of accomplishment similarly as is an artist who paints a picture. Many physicians are likewise so endowed,

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of course. Dentists are as unequivocally dedicated to their calling as are physicians to theirs. A high level of ethical consciousness and practice is equally applicable to both professions.

Physicians and dentists who recognize that they have valuable allies in each other will profit immeasurably from such a realization, and so will their patients. And may it be observed in passing that while the patient clientele of either profession includes many members of the other profession, many more physicians are the beneficiaries of dental treatment than vice versa. Let us ever be grateful to and for our dental colleagues.

That infection in the body is detrimental to the health of individuals, regardless of where the infection may be, is a commonly accepted fact. It is when the infection involves the teeth that the situation assumes a dental bearing. Cases of acute nephritis, arthritis or iritis in which the mischiefmaker may be traced to infected tonsils, infected paranasal sinuses and infected teeth are too common and well known to warrant more than casual mention. In such conditions as diabetes and hyperthyroidism the alert physician will take particular cognizance of infections of any sort, including infection of the teeth and gums. A statistically significant percentage of cases of bacterial endocarditis has been attributed to dental infection. A flare-up in an old endocarditis is sometimes precipitated by the transient bacteriemia that follows extraction of infected teeth. In rheumatic heart disease the physician's responsibility does not end with the treatment of the heart condition but must take into account oral infection. Glomerular nephritis, pyelitis, or pyelonephritis are often secondary to and always aggravated by extraneous sources of infection, the teeth rating high on the list of possible offending foci.

Not only are the services of our dental confreres highly important in the management of a wide list of systematic maladies that may stem from oral infection as a contributing—if not a solely causative—factor, but frequently the dentist, because he is accustomed to viewing the oral tissues, may assist greatly in the arrival at an early diagnosis of diseases which have oral manifestations. Diabetes, leukemia, pellagra, scurvy, Hodgkin's disease, hyperthyroidism, pernicious anemia, Addison's disease, syphilis (primary, secondary or congenital), lichen planus, purpura hemorrhagica, erythema multiforme, poisoning by heavy metals (notably lead), and finally—and few will gainsay the most important of all—oral cancer fall into this category of diseases.

To consider now another facet of this matter, the dentist in the pursuit of his profession will not infrequently need to turn to the physician or to the appurtenances generally regarded as those belonging more strictly in the province of the physician. In addition to the dependence by a fair number of dentists upon an M.D. or a nurse anesthetist when a general anaesthetic is desired, dentists must recognize the need for laboratory assistance, such as blood and urine examinations, basal metabolism or protein bound iodine tests and biopsy as aids in diagnosis. Laboratory examinations of this nature, prompted by an oral clinical picture, may quite likely reveal the existence of systemic diseases or deficiencies that possibly had not been suspected. As examples of conditions in which the dentist would consider clinical laboratory findings and collaboration with a physician to be in order the following are cited: A predisposition to hemorrhage from the gums or oral mucosa in the absence of trauma or when routine procedures do not control postoperative hemorrhage; when there is marked pallor of the oral mucous membrane; when there is definite evidence of atrophy of the papillae of the tongue; the presence of sore spots on the tongue or buccal mucosa which persist in the absence of local irritation; when there is excessive thirst or dryness of the tongue or oral mucosa; (Sjögrens syndrome) when there is an extraordinary odor to the breath—especially a fruity or ammoniacal odor or when a remarkable discoloration of the tongue, lips or face is evident. The existence of a ranula is sometimes first noted by a dentist.

Because of the complex embryology of the head and neck, developmental anomalies of a nonconsequential character are not uncommon around the head, neck and mouth and may, by those not altogether familiar with this field, be mistaken for neoplasms. Median rhomboid glossitis, Fordyce's disease and various exostoses such as torus palatinus, or torus mandibularis are conditions in point. The dentist who is accustomed to seeing these conditions can frequently prevent or dissipate a cancerophobia in an apprehensive or frightened patient.

In pregnancy, collaboration with dentists is nowadays more or less routine, although the old theory which would have it that for every child a tooth has been exploded under the focus of brighter light brought to bear by either physicians or dentists or both. There remains, however, one interesting indication for a pregnant woman's seeking dental care and guidance. Reference is made to pregnancy gingivitis and "pregnancy tumors"—a soft tissue

gingival nodule—varying in size from that of a grape seed to that of a green pea.

Before the advent of the antibiotics, it was not uncommon for a relatively simple dental infection to progress with such rapidity as quickly to constitute a major medical or surgical problem calling for prompt and vigorous—even, sometimes heroic treatment. Problems of this character and magnitude used to be encountered in fulminating facial and cervical cellulitis originating from infected teeth. This process occasionally would extend to and invade the fascial planes and spaces of the neck. The pharyngeal and submandibular spaces could become so involved as to interfere with a patent airway, and to provide for relief, indeed probably to avert imminent death, a tracheotomy was sometimes expeditiously done. If these infections eroded into the pretrachea and prevertebral fascial tracts their spread into the mediastinum was not an unlikely possibility. Physicians and sugeons used occasionally to see a cavernous sinus thrombosis originating from an area drained by the angular vein. An infection from an upper anterior tooth can be conveyed to and by this vein. The venous return from the teeth also enters the pterygoid plexus of veins. The pterygoid plexus communicates with the ophthalmic veins which empty into the cavernous sinus. During recent years, incident to the use of antibiotics and of anticoagulants, these complications stemming from dental infections have become far less common in the United States, and while they are cited more for academic than actual reasons, their potentiality does still exist and in some foreign countries whose health, medical and dental standards are inferior to ours, medico-dental problems of this character are not unlikely to be encountered.

Nowhere are the benefits of physician-dentist cooperation better seen than in the management of traumatic fractures of the jaw bones, whether they are or are not (and they frequently are) complicated by other injuries. The ultimately complete restoration of the patient's chewing ability in these cases depends upon expert management. Therefore, it is essential not only that the fractures be initially reduced and that the bone fragments be properly immobilized, but that the dental arches be so restored as to provide normal occlusion for the patient and that the position of the condyles in the temporomandibular joints be taken into account. The same may be said with respect to numerous more basically plastic procedures involving the face. The

assistance of a dentist in repair of cleft palates will certainly be found advantageous; particularly if the surgeon is only an occasional operator in this field. After having witnessed the management, by dentists, of a few jaw fractures, it will be a rare orthopedic or plastic surgeon indeed who will gainsay that the treatment of injuries of this nature belongs in the realm of dentistry.

### OSSEOUS HEALING AFTER OBLIQUE OSTEOTOMY OF THE MANDIBULAR RAMUS

P. J. Boyne, J Oral Surg 24(2): 125-133, March 1966.

In six adult Macaca rhesus monkeys, an oblique osteotomy of the ramus was performed bilaterally, and the osseous repair studied, using tetracycline labeling of bone. Only minimal decortication was performed. The monkeys were killed at intervals, having received doses of 10 mg/kg body wt tetracycline intramuscularly before sacrifice. Ground undecalcified sections were made from that portion of the specimen sectioned parasagittally through the osteotomy site. The sections were examined under an ultraviolet microscope and the findings correlated with decalcified, hematoxylin-eosin (I) stained sections from the same specimens. Monkeys tagged at 9-10 days and killed after 20 days showed no fluorescence at the osteotomy site itself, although some new bone was visible in the I sections. Monkeys tagged at 14-15 days and killed at 25 days had fluorescent new bone in the marrow vascular spaces adjacent to the osteotomy line, and the I section showed primary bony callus at the 25-day-old surgical site. Monkeys tagged at 14-15 and 19-20 days and killed at 30 days exhibited a fluorescent pattern, indicative of 14-15 days labeling, and another, representative of latter primary bony callus formation extending into the space between the fragments. In the same sections, new bone formation at the attachment of the external pterygoid muscle as well as remodeling of the bone of the condyle was seen. Cortex-to-cortex contact offers ample opportunity for osseous healing, surgical procedure produces changes in condylar relationship, and immobilization should be maintained for four weeks in these instances.

(Abstracted by: Dan J. Kaznelson, From: Oral Res Abs 1(7): 650.)

### PERSONNEL AND PROFESSIONAL NOTES

### NEWLY STANDARDIZED ITEM OF INTEREST TO DENTAL OFFICERS

Attention is invited to a recently standardized item which is now available and may be of value in various training and teaching programs of dental activities. The item description is:

FSN 6910-926-1367 Model, Anatomical,

Human Skull-\$103.00

This item provides a life-size model of the adult human skull with two interchangeable mandible and maxilla sets, one with normal complement of teeth, and the other demonstrating common dental pathologies.

#### DENTAL FACILITY ATLAS

The Dental Division maintains an atlas for each dental facility both afloat and ashore. This atlas

contains photographs of representative spaces, schematic scale drawing or blueprint, and the current DD Form 477-1 of each dental facility. In order for each atlas to be kept in a current status, cognizant dental officers are reminded to comply with the provisions of article 6-151 of the Manual of the Medical Department whenever alterations or major changes have been accomplished.

Furthermore, it is requested that dental facilities provide the Dental Division, on a continuing basis, with photographs of operatories and other spaces as the dental equipment modernization program progresses. Such information as the name of the facility, the space photographed, the date of the photograph and any other amplifying data should be included on the back of each photograph.

### NURSE CORPS SECTION

# NURSING CARE OF THE PATIENT RECEIVING EXTERNAL RADIATION THERAPY

By LCDR Martha V. Pearce NC USN, Instructor, Nuclear Medicine Department, National Naval Medical Center, Bethesda, Maryland.

Increasing technology in nursing practice provides numerous learning opportunities for the professional nurse of the twentieth century. Rapid developments in the field of nuclear medicine have necessitated considerable changes in the practice of nursing. One aspect of nuclear medicine is the use of Cobalt-60 and supervoltage X-ray units as sources of external radiation for teletherapy. In the care and treatment of these patients, it is essential that the ward nurse instruct her personnel in the signs and symptoms to expect from radiotherapy. There are many misconceptions about radiation which may cause patients and staff to attribute unrelated complaints to this type of therapy. Teletherapy is felt to directly affect only the area being treated. A frank, honest explanation of the effects of radiation on specific areas of treatment will often allay symptoms caused by fear.

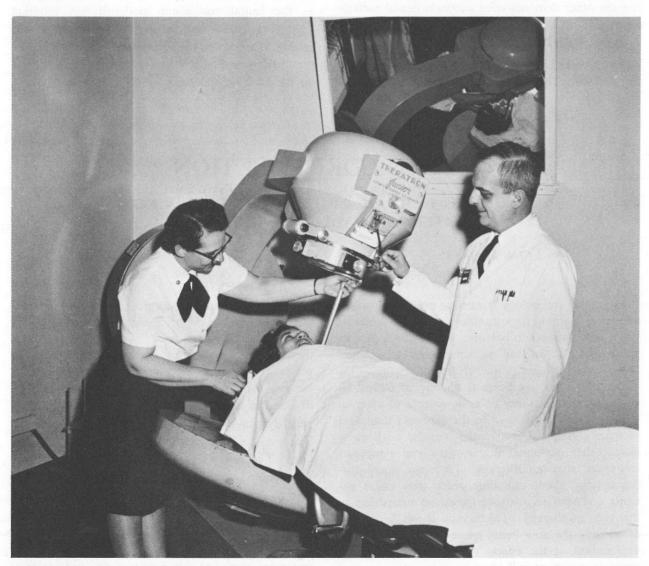
There is a certain degree of tissue destruction in the treatment area which frequently causes symptoms. Measures must be taken to recognize these symptoms and to control them before the patient's discomfort becomes severe. Therapy involving mucous membrane causes mucositis, then dryness; laryngeal therapy produces transient hoarseness, dysphagia and possible respiratory impairment. The use of a humidifier usually relieves mucosal dryness. Therapy which includes the eye may cause photophobia, corneal damage, or some pain; radiation to the gastrointestinal tract causes irritation of the area treated with possible nausea, vomiting or diarrhea as a complicating factor; hair follicles are depressed by radiation causing loss of hair in the treatment area; the skin becomes dry and reacts as if to sun exposure. Clean dry skin tolerates therapy best; therefore topical applications must not be used on the treatment area until therapy is completed.

Since radiation is known to destroy tissue, it is important that the patient maintain a high protein diet. If the patient develops dysphagia or nausea, steps must be taken to provide antiemetics and high protein liquids to meet his nutritional requirements. A change from a full to a soft diet with frequent between meal feedings is often all that is necessary when the mouth, throat or esophageal areas are being irradiated. Prompt recognition and recording of symptoms related to therapy will allow the radiologist to institute measures to keep them to a minimum. Comprehensive nurses' notes which contain physical as well as psychological signs and symptoms are of prime importance to the radio-

therapist since he sees the patient for only a few minutes each day.

Signs and symptoms unrelated to radiation must not be neglected. The presence of fever in a patient who is receiving teletherapy may be due to infection or dehydration. The patient's lowered resistance may make him more susceptible to infection, but fever must be controlled by treating its specific cause; it is seldom directly due to radiation. Any complaints not directly associated with therapy should be evaluated immediately before complications arise.

Above all else, a confident sympathetic attitude is most valuable in assisting apprehensive patients. Nursing personnel should exhibit an attitude of confidence which can only be acquired through their own knowledge of radiation therapy.



CAPT John H. Ebersole MC USN, Chief of Nuclear Medicine, NNMC, Bethesda, Md. and LCDR Martha V. Pearce NC USN.

### AEROSPACE MEDICINE SECTION

### CAPT M. H. GOODWIN MC USN RETIRES

CAPT Merrill H. Goodwin, whose most recent duty was as Commanding Officer of the Naval Hospital, Pensacola, Florida, since 1963, retired on 31 January 1967 after 29 years of continuous active naval service. He was relieved as Commanding Officer, Naval Hospital by CAPT L. R. Riddle MC USN.

CAPT Goodwin graduated with a B.S. degree from Ball State College in Muncie, Indiana and received the degree of Doctor of Medicine from Indiana University School of Medicine in 1936. He interned at the U.S. Marine Hospital, Baltimore, Maryland, entering the U.S. Navy in August 1937. He was designated an Army Air Corps Flight Surgeon in 1938, a Naval Flight Surgeon in May 1939 and a Naval Aviator in 1944.

Doctor Goodwin has been appointed to be the Executive Vice President and Managing Editor of the Journal of the Aerospace Medical Association. He arrived on 1 February 1967 at the Headquarters, National Airport, Washington, D. C. and is residing in McLean, Virginia.—AEROMED, BUMED.

### POST HOSPITALIZATION FLIGHT PHYSICAL EXAMINATIONS

Delay in receipt of a post hospitalization flight physical examination on aviation personnel after a Medical Board.

#### Discussion

Aviation personnel undergoing hospitalization leading to a Medical Board are considered to be in a grounded status from the time of admission to the hospital until such time as a favorable flight physical examination has been performed by a Flight Surgeon and approved by the Chief, Bureau of Medicine and Surgery and the Chief of Naval Personnel (or the Commandant of the Marine Corps). The Aviation Physical Qualifications Branch, BUMED, is unable to determine the flight status of these individuals without a current (post hospitalization) flight physical examination. Since these individuals are often unaware of this requirement, excessive time is required to contact them through their commanding

officer. The resulting delay not only deprives the individual of this flight pay, but also the Navy of the efficient utilization of his services as an aviator or naval flight officer.

#### Action

Naval hospital commanders are requested to please comply with MANMED, art. 18-11(4) which requires that the official orders on aviation personnel, returning them to a duty station to await the Navy Department action on the Medical Board, will direct them to obtain a complete flight physical examination, with submission of the reports (SF 88 and other reports deemed necessary) to BUMED (Code 511) prior to resumption of any duties involving flying. Medical officers at Naval Air Stations and other Flight Surgeons should screen all aviators returning to duty from hospitalization to assure that this requirement is met.—AEROMED, BUMED.

### ROYAL NAVY EXCHANGE OFFICER BILLET

The Chief of Naval Operations informed BUMED that the Commander, British Navy Staff, Washington, D. C. had advised that the Royal Navy Exchange Officer assigned to the Naval Aerospace Medical Institute will not be relieved, since they are unable to provide another medical officer qualified in aerospace medicine at this time. The Ministry of Defense has proposed that an exchange in the field of underwater medicine be arranged. The Chief of Naval Operations has been advised that an exchange of medical officers in the field of underwater medicine is considered to be of mutual benefit to both nations. The requested exchange program will be initiated in May 1967. The current U.S. Navy exchange billet at the Royal Naval Air Medical School, Seafield, England, will be transferred to the particular facility chosen by the Royal Navy. The first assignment will be of LCDR R. L. Sphar MC USN to Staff, Flag Officer Submarines, HMS DOLPHIN, Gosport, England. The Royal Navy exchange billet will be established at the Naval Submarine Medical Center in New London, Connecticut. The minimum period of assignment of medical officers to these billets should be 24 months.

—AEROMED, BUMED.

#### DISORIENTATION SYMPOSIA

In late January 1967 scientists from the Army, Navy. Air Force, universities, industry and several foreign countries visited the Naval Aerospace Medical Center at Pensacola, Florida for a symposium on the role of inner ear organs in space exploration. The symposium was sponsored by the National Academy of Sciences and the National Research Council with assistance from the Office of Biotechnology and Human Research, National Aeronautics and Space Administration. The meeting was held at Pensacola where military and civilian investigators have been performing extensive research in vestibular physiology, and the Institute has special research equipment, such as the slow rotation room. This third symposium of its kind heard, and discussed, 30 scientific papers, including five by scientists from Canada, England, Italy, Scotland and Sweden.

Under the combined auspices of the Naval Aerospace Medical Institute, Pensacola, Florida, and the Aerospace Medical Research Department, the Naval Air Development Center Johnsville, Pa., was host for a 3-day symposium on Vertigo as a problem in Aerospace Medicine beginning February 7. Approximately 40 national and international military and civilian authorities on vertigo attended and participated in the symposium, which was held at the Warrington Motel. Each of the three day sessions was introduced by a formal presentation concerning one particular phase of vertigo in aerospace medicine. This was followed by a round table discussion led by a five-member panel. Among the problems examined during the meeting were:

The significance of vertigo as a cause of accidents; facts and theories about causes of vertigo; psychophysiology factors contributing to vertigo in aerospace crews; the possibilities and limitations in the use of operational vertigo trainers; experimental devices for physiological testing in equilibration measurements of vertigo, and the relationship of the degree of realism achieved in simulation to the value of the simulator.

CAPT Frank B. Voris MC USN, Assistant to the Director of the Research Division, Navy, Bureau of Medicine and Surgery, delivered the symposium opening remarks. CAPT Edward M. Wurzel MC USN, Director of the Center's Aerospace Medical Research Department, and Dr. Ashton Graybiel,

Director of Research, Naval Aerospace Medical Institute, Naval Aerospace Medical Center, Pensacola, Florida, served as general symposium moderators. Guest lecturers included: CAPT Frank H. Austin MC USN, Office of the Deputy Chief of Naval Operations (AIR); CAPT Richard Luehrs MC USN, Naval Aviation Safety Center, Norfolk, Virginia; Dr. A. J. Benson, Institute of Aviation Medicine, Farnsboro, Hants, England; Dr. Brant Clark, Ames Research Center, Moffett Field, California; and Dr. F. E. Guedry, Aerospace Medical Center, Pensacola, Florida.—AEROMED, BUMED.

### **EMERGENCY EJECTIONS**

Because of the number of vertebral fractures of varying degrees of severity occasioned by emergency ejections from Navy and Marine Corps aircraft, a program of radiographic study of the vertebral column of flight applicants is being initiated at the Naval Aerospace Medical Institute.

It is anticipated that by screening individuals for spinal column abnormalities, the incidence of back injury can be reduced to a minimum.

A primary impetus for this program came from the Aeromedical Department of the Naval Aviation Safety Center after a continuous study and review of ejection injuries over the past several years. The program has been strongly supported by the Bureau of Medicine and Surgery, and implementation became possible through continued efforts of the Institute and the Naval Aerospace Medical Center.

—AEROMED, BUMED.

### PHYSICAL EXAMINATION AND PSYCHO-LOGICAL TESTING FACILITY

The Naval Aerospace Medical Institute at the Aerospace Medical Center, Pensacola, Florida, has been designated as the physical examination and psychological testing facility for prospective Naval Test Pilot School students. The first group of T.P.S. students included two Marine and eight Navy officers. Examinations will be more comprehensive than test pilots have had before and will require an entire week for completion. This will be an interesting group on which to do follow-up studies as part of the Institute's continuing study on the effects of aviation duty, the aging processes, etc. This very select group will be given special attention like the "Thousand Aviator" group which has been under study for many years. Included will be comprehensive vestibular psychomotor, and disorientation tests. Examination of the test pilots is being conducted at the request of the Commander, Naval Air Test Center at Patuxent River, Maryland.—AEROMED, BUMED.

# HISTORY OF EFFORTS TO DEVELOP A COMMON MEDICAL OFFICER'S REPORT OF AIRCRAFT ACCIDENTS

In 1964 an attempt was made to standardize definitions concerning aircraft seat ejection phases and components for the U.S. Air Force and U.S. Navy by CAPT R. E. Luehrs MC USN, Head, Aeromedical Department, Naval Aviation Safety Center, and COL E. C. Lentz MC USAF, Director, Life Sciences Division, Office of the Inspector General, Headquarters, U.S. Air Force. This was accomplished, and later a proposal was made by Dr. Luehrs to develop a Tri-Service Medical Officer's Report of Aircraft Accident for approval by higher authority in each service, for use in conjunction with accident reporting. Dr. Lentz concurred and the first of three formal meetings was held 2-4 June 1964 in Norfolk. Representatives of the three services attended and outlines of work were tentatively agreed upon. The Air Force began work on the Biomedical part of the form while the Army took the Sociopsychological section and the Navy the Biophysical (Safety and Survival) part. Two subsequent meetings were held in Norfolk and innumerable exchanges of proposed sections, liaison visits and telephonic messages and letter traffic ensued. The Coast Guard sent representatives to Norfolk for liaison on this project. Commonality was sought in four essential areas:

- 1. Definition of medical factors (Dorland 23rd Edition).
  - 2. Coding (DDDIC).
  - 3. Terminology of items other than medical.
  - 4. Similarity of items coded.

Two and one half years of work by over forty medical, paramedical and digital computer personnel have gone into the present proposed form. The final version which has been directed to be submitted by the Surgeons General of the Military Services will be compiled during the April Aerospace Medical Association Meeting. Adoption by the various services is expected following a brief field evaluation period.

The Common (MOR) Medical Officer's Report may be utilized by Great Britain and Canada through arrangements of the Joint Committee on Aviation Pathology which is providing the strength for the adoption of this MOR by the various United States services.

In addition, the proposed MOR is the subject for a STANAG for ratification by the member nations of NATO. A central data repository is being sought which will contain the output of all users of the MOR and this storage will constitute a far greater sample than the data banks of the individual services.—Naval Aviation Safety Center.

### HUMAN ERROR RESEARCH AND ANALYSIS PROGRAM—HERAP

Because of the fact that over one-ha'f of all Navy/Marine aircraft accidents are human caused (total or partial causation factor present), the Navy/Marine Air Board, in June 1964, following a presentation on the subject by the Aeromedical Department of the Naval Aviation Safety Center, directed the Center to "provide a program . . . which will alleviate the problem." A program proposal was submitted and was favorably endorsed by the Chief of Naval Operations on 7 August 1964, stating in part, "It is imperative that immediate positive action be initiated to reduce the human error caused accidents in order to further reduce the loss of lives and aircraft."

Implementation of a longitudinal man-machine-environment-management systems analysis began. Initially, the program called for four to five years' contractual program development and operation with Safety Center "in-house" capability phasing in until ultimately HERAP would be conducted in all aspects by the Center.

Phase One, or Program Definition Phase (Definition and Feasibility), was completed early in 1966 by the Human Factors group of Douglas Aircraft Company. Phase Two, which calls for commencement of the work, has been in progress for four months and the formation of a data bank on a Douglas IBM 7090 for ultimate transfer to the Safety Center's Honeywell 1200 ensues.

HERAP is a far reaching program which systematically delineates many areas not presently known or sufficiently appreciated. Studies embracing parameters of man's capabilities with respect to his management of an Airborne Weapons System in variable environments are being undertaken. Measurement of the interfaces and description of the degradation of "best" performance of the man module in the loop is being attempted using old and new tools. Methodologies have been described.

Bench mark problems have been completed. Rigorous research designs are being constructed and applied to the myriad problems. The Aeromedical Department of Naval Aviation Safety Center has been designated as "action agency" and to that end has conducted HERAP from the beginning.

In addition, highly qualified officers and enlisted and civilian personnel contribute significantly. Administrative and support people are inadequate in supply but the number is growing.

Funded by the Naval Air Systems Command and supported by the Chief of Naval Operations, HERAP has begun.—Naval Aviation Safety Center.

#### HYPERBARIC CHAMBERS

Hyperbaric chambers have recently been installed at Physiological Training Units located at Castle AFB, Calif.; Edwards AFB, Calif.; Ellsworth AFB, S. D.; Brooks AFB, Texas; and Wright Patterson AFB, Ohio. Additional chambers are programed for units at Otis AFB, Mass.; Weisbaden AB, Germany, and Howard AFB, Canal Zone. These chambers are installed primarily for treatment of decompression sickness in accordance with the provisions of AFR 161-19, Use of Compression Chambers for Treatment of Dysbarism.—From USAF Medical Service Digest XVIII(1), AFRP 160-1, January 1967.

# HYPOXIA EPISODE OF TWO NAVAL AVIATORS IN THE TF-9J AIRCRAFT AND IMPROPER UTILIZATION OF THE H-2 EMERGENCY OXYGEN SYSTEM

CDR Leroy B. Cochran MSC USN, Aviation Physiology Training Unit, Marine Corps Air Station, Cherry Point, N. C.

Narrative: Two pilots briefed for an early take off in a TF-9J aircraft. Pre-flight was normal and both noted that the bailout bottles, attached to their MB-A5/A5A seats, registered full.

Their take-off and climb-out was normal and the flight proceeded at a flight level of 35,000 feet as cleared and cabin pressure was maintained at 23,000 feet. The early part of the flight was uneventful. After approximately 1.0 hour of flight the pilots noted a feeling of tiredness and heaviness of limbs which did not particularly alarm them at this time. After approximately 1.5 hours of flight both pilots became mildly nauseated and faint. The control of the aircraft was exchanged allowing the other pilot a chance to check all oxygen equipment, including tightening their masks. All equipment checked out normally with oxygen regulators on 100% and safety pressure on. During this time, control of the aircraft was erratic. The pilots held their breath and/or slowed respiratory rate.

When none of these maneuvers improved their symptoms, the pilots suspected hypoxia or oxygen contamination. During this time they reported slowed responses, mild faintness, instrument fascination, etc.

At this point the command pilot realized that they were in trouble and were being affected by some fault of the oxygen system. Both oxygen regulators

were then secured and the H-2 bailout emergency oxygen supply activated. For a period of 60-90 seconds the oxygen flow was excessive, blowing out about the oxygen mask seals. After this period, the flow was not sufficient to support respiration. (It may be noted here that the MC-3A quick disconnect was not separated from the aircraft oxygen hose.) Their symptoms did improve, however, during this time. After apparent exhaustion of emergency oxygen, the pilots removed their oxygen masks, breathing cabin air while making an emergency descent to 7,000 feet. Upon leveling off, the canopy was opened and the pilots felt symptomatically improved immediately. The "IFR" flight plan was cancelled and landing was made at destination approximately ten minutes after the emergency descent.

#### Findings:

- 1. An investigation of all components of the oxygen source and system, from converter to mask hose, was negative for evidence of contamination.
- 2. One oxygen mask was improperly fitted and a defective laminar seal was found in the other.
- 3. The Flight Surgeon concluded that the pilots were most probably hypoxic due to the use of defective oxygen masks.

Discussion: Needless to say, in this mishap the two pilots involved were very fortunate that more serious results did not occur. Using the emergency H-2 bailout bottle in this situation was warranted but proper procedures were not followed. When used as emergency oxygen equipment in the event of failure of the regular aircraft oxygen system, the proper procedures are:

- 1. Pull the ball handle immediately after malfunctioning of the regular oxygen system is noted.
- 2. Disconnect the mask tube connector from the aircraft breathing tube.
- 3. Descend to an altitude at which the use of oxygen is not required, within an interval of 10 minutes or less.

It should be emphasized again that the H-2 emergency bailout oxygen cylinder is designed to supply sufficient oxygen for bailouts and other emergencies up to an altitude of 50,000 feet. The flow time of this equipment is approximately 10 minutes.

The oxygen flow controller metering element is calibrated so that oxygen flow upon activation will be 10-12 liters per minute and about 1 liter per minute during the tenth minute of flow. Therefore, if utilized properly the H-2 emergency oxygen system provides pressure breathing for protection above 35,000 feet and oxygen diluted with air for continued protection at lower altitudes. The mask hose should be open to allow air to enter to supplement the diminishing oxygen flow from the cylinder. Design features of the MC-3A connector are such that resistance to inhalation may be felt approximately 2 minutes after activation.

Two Low Pressure Chamber runs were made, simulating the cabin altitude of 23,000 feet and the H-2 emergency oxygen bottles were activated with oxygen regulator secured and MC-3A oxygen hose connected. The findings approximated those reported by the pilots. These tests were performed to ascertain if the H-2 bottles were properly charged.

The NATOPS Manual is not specific and clear on use of the H-2 Emergency Oxygen System. The two pilots involved were under the impression that the H-2 emergency oxygen bottle would support required respiratory volume for a duration of 8 to 10 minutes without breaking the MC-3A disconnect.

After talking with several other members of the squadron involved, it was found that a great majority of the pilots were of the opinion that in case of an emergency, the H-2 oxygen supply would provide adequate respiratory volume for some 8 to 10 minutes duration while remaining at altitude. When flight personnel are continually being transferred from one squadron to another, where aircraft have different emergency oxygen systems, proper checkout and retraining is mandatory. The Aviation Physiology Training Units have a specific responsibility in this area. There are perhaps many other flight personnel who have been instructed in the functions of "minireg" emergency oxygen equipment and who assume that the H-2 system works the same way.

Recommendations: That all Aviation Physiology Training Units and Flight Surgeons review this aspect of their training program and emphasize the following:

- 1. Purpose, function and correct procedures for utilization of the H-2 Emergency Oxygen System.
- 2. The importance of pre-flight and in-flight checks on the oxygen mask.

#### **ANNOUNCEMENT**

The Sixth Scientific Session of the Joint Committee on Aviation Pathology will be held at Ottawa, Canada 12-14 September 1967.

Individuals desiring to present papers or attend this Session should communicate with:

> Surgeon Commander Henry D. Oliver, RCN Canadian Defense Building 2450 Massachusetts Avenue, N. W. Washington, D. C. 20008

### EDITOR'S SECTION

The first of a series of articles on Molecular Biology, 1967 appeared in The New England Journal of Medicine 276: 502-511, 2 March 1967 and the others in succeeding numbers under the heading Medical Progress. An Editorial in the 2 March issue states "Enough principles of nature have been revealed in detail by the methods of molecular biology that they can now be explained coherently, sometimes even simply." Unfortunately the articles are too long to be reproduced in the U.S. Navy Medical News Letter and too packed with information to be abstracted satisfactorily. The use of the word "simply" by the editor is high praise indeed for now some understanding of this complex discipline will be possible by many, perhaps most of us.

A letter to the Surgeon General of the Navy from John H. Walters MD, Chairman, Committee on Nursing and Paramedical Personnel requests assistance in the Program of the Missouri State Medical Association to alleviate the presently serious and increasingly severe shortage of Nurses in Missouri. The Committee is anxious to have names of enlisted men trained in Nursing or Medical services during their military service prior to discharge from Military Service for referral to schools in Missouri seeking faculty as well as students in the Nursing profession.

The American Journal of Cardiology for January 1967 (19: 1-116) includes a symposium on Echocardiography (Diagnostic Ultrasound). After an introduction by the Guest Editor, Bernard L. Segal MD, FACC, there are twelve articles by investigators in the United States and from abroad with the following titles:

Ultrasonic Engineering in Heart Diagnosis Ultrasoundcardiography in Mitral Valve Stenosis Correlation Between Ultrasoundcardiography, Hemodynamics and Surgical Findings in Mitral Stenosis

Echocardiography. Clinical Application in Combined Mitral Stenosis and Mitral Regurgitation Echocardiography. Clinical Application in Mitral Regurgitation

Pre- and Postoperative Evaluation of Mitral Stenosis by Ultrasound

Reflected Ultrasound in the Diagnosis of Tricuspid Stenosis

Echocardiography in Congenital Heart Disease. Preliminary Observations

Use of Reflected Ultrasound in Detecting Pericardial Effusion

Echoaortography

Clinical Application of Ultrasound in the Analysis of Prosthetic Ball Valve Function

Another Look at Echocardiography. Concepts in Biomedical Engineering

### REGIONAL MEETING OF AMERICAN COLLEGE OF PHYSICIANS—1967

A memorandum has been received from The American College of Physicians announcing a 1967 regional meeting of the A.C.P. members in the District of Columbia and Maryland to be held Saturday, December 2, 1967, at the University of Maryland Hospital, Baltimore, Maryland.

Dr. Richard B. Hornick is the chairman in charge of arrangements and the University of Maryland Medical School will be host for the morning program from 9 am to 11 am. A Program Committee will select papers for the remainder of the morning and afternoon program. There will be a noon luncheon with Edward C. Rosenow, Jr. MD FACP, Executive Director of the College, and another College officer as guest speaker.

Abstracts of papers for consideration by the Program Committee should be sent to either of the Program Co-Chairmen as soon as possible, but not later than August 15, 1967.

Papers from the District of Columbia should be sent to:

John F. Maher, M.D. Georgetown University Hospital Washington, D. C. 20007

Papers from Maryland should be sent to: Alan Bernstein, M.D. 819 Park Avenue Baltimore, Maryland 21201

### NSA X-RAY DEPARTMENT

The U.S. Naval Support Activity, DaNang Station Hospital staff, acknowledged to be operating the finest field hospital in the history of warfare, is composed of many highly skilled units; among them is the "crack" X-ray Department.

A helicopter swings in, a casualty is lifted off, and the wheels of medical technology are in motion. The patient is rushed to the emergency ward where the immediate concerns are to eliminate any danger of death, and to alleviate pain and discomfort. A preliminary diagnosis of wounds is made; then internal diagnosis, and the X-ray team goes into action.

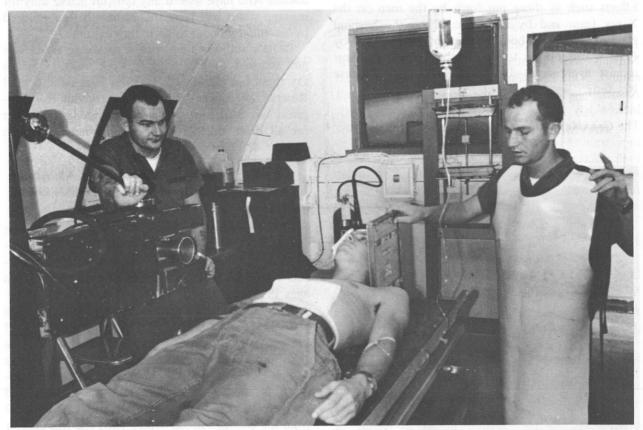
A number of vital questions must be answered for the hospital surgeons—How deep are the wounds? Are they endangering vital organs? Are there any broken bones? How much shrapnel is inside the victim, and where is it located?

The head of the X-ray Department, LCDR James R. Moyers of San Diego, California, and his staff of eight technicians provide these answers in a surprisingly short period of time. A multiple

wound victim (one who has been hit in the head, chest area, and all four extremities) can be completely X-rayed and on his way to surgery with developed pictures for use by the surgeon in less than 15 minutes. A routine X-ray can be shot, developed and delivered in approximately seven minutes.

Dr. Moyers commented, "The devotion to duty of my men is marvelous. They understand the extreme importance of their task and react with a sense of urgency that is so important in treating combat injuries."

One particularly harrowing night saw 20 casualties arrive at the same time. The call came up from the emergency room to X-ray. "Get ready!" Ready they were. In less than two hours, all 20 men were through the Department, and on their way to surgery. Two hundred and twenty X-rays had been taken and developed. "Performances like this help make the Support Activity hospital the finest medical complex in Vietnam," said Dr. Moyers.



ROAD TO RECOVERY. . . . Combat Casualty is X-rayed by Hospitalmen Second Class W. C. Griggs (left) and W. C. Ellis. Patient will be on way to surgery with developed pictures for use by the surgeon in about 7 minutes.—Photo by PH1 Joe Dyer.

Hospitalman Second Class William Ellis of Jacksonville, Florida, was on duty last October 1st. The word came, "Bring a portable X-ray machine to the emergency ward immediately. We have a Vietnamese soldier here with a live mortar round in his side. We need pictures."

"I was stunned," Ellis said. "I thought, some-body has to be kidding. I hurried down to the ward, and saw it was not a joke. The round was laying just under his skin. It was evident what it was. I just did my job. He was moving around somewhat, which added to the difficulties. I was sure glad when it was over." His pictures aided CAPT Harry Dinsmore, chief of surgery at the hospital, to successfully remove the mortar round and save the patient.

The X-ray unit also handles a variety of routine jobs. Over 12,700 patients have been through their clinic since the hospital opened in Jan., 1966. An average of 90 per day are now serviced.

The X-ray Department provides invaluable "eyes" for the Support Activity's doctors and surgeons. Efforts such as those put forth by the men on the X-ray team and by all personnel on the hospital staff represent another key element in the drive by Free World Forces to rid South Vietnam of communist aggression.—By Vern Krol YN3, Release No. 6-67.

# NAVMEDSCOL GLOBAL MEDICINE SERIES LAUNCHED



CAPT John H. Stover, Jr., MC USN, Commanding Officer, Naval Medical School, National Naval

Medical Center, Bethesda, Maryland, presents one of the first units of NAVMEDSCOL's Global Medicine Synopsis Series to RADM Harry S. Etter MC USN, Commanding Officer, U.S. Naval Hospital, Bethesda. Looking on is CAPT George H. Tarr, Jr., MC USN, Chief of Medicine, U.S. Naval Hospital, Bethesda. Approximately 40 units of the Global Medicine Synopsis Series will be mailed to some 30 Naval Hospitals and other selected medical activities.—NNMC, Bethesda, Md.

### RESERVE STATUS PHYSICIANS FACE POSSIBLE ACTIVE DUTY

Defense Department has authorized the services to order active duty tours up to 24 months for about 100 draft age physicians holding Reserve commissions.

This authorization was given by Congress in 1957. The law specifies that those under 35 years of age may be ordered to active duty for as many as two years.

The Army, Navy and Air Force plan to call up those without any prior active duty service. Those doctors who have served any time on active duty for training status will have the 24-month tour reduced by an amount equal to their training time.

DOD's authorization applies to young physicians not assigned to organized Reserve units. Officials say these individual calls will not lessen the overall Reserve effectiveness, and will carry out the Congressional intent of providing equitable treatment for all draft age physicians.—Commanders Digest 3(16): 4, February 25, 1967.

### NAVAL OFFICER SELECTED AS AN "OUTSTANDING YOUNG WOMAN OF AMERICA"

ENS Patricia Rae Evans MSC USNR has been selected to appear in the 1966 edition of Outstanding Young Women of America, an annual biographical compilation of outstanding women between the ages of 21 and 35.

ENS Evans graduated from the Hobart High School, Hobart, Indiana in 1958 in the top 5% of her class and attended Indiana University on a scholarship from the Gary, Indiana chapter of Sigma Kappa Pi. During her sophomore year she was governor of the Tower Quadrangle, on campus, and received the outstanding leadership award of 1959 from the college. In her senior year, she was charter president of the Phi Theta Professional Fraternity for physical therapy students at the Indiana University Medical School. She graduated from that

school in 1962 with a degree in physical therapy and was employed as Chief Physical Therapist at Porter Memorial Hospital, Valparaiso, Indiana for the next four years.



ENS Evans was appointed in the Navy Medical Service Corps on 19 April 1966. She graduated with distinction from the Naval Women's Officer School, Newport, Rhode Island in May 1966. At that time she was presented with the Leadership Award by the Aquidneck Business and Professional Women of Newport. She is currently a member of the professional staff of the Naval Hospital, Great Lakes, Illinois.—Public Affairs Office, BuMed.

In the Sunday Post Tribune (Gary, Indiana) of 5 March 1967, ENS Evans is listed as one of the ten best dressed women (in her uniform) of Lake County, Indiana.—Editor.

### ADMIRAL McDONALD RE-ELECTED PRESIDENT NAVY MUTUAL AID ASSOCIATION

The Board of Directors of the Navy Mutual Aid Association at their Annual Meeting on 14 March 1967 announced the re-election of Admiral David L. McDonald, USN, as President. Other officers elected by the membership were Admiral George W. Anderson, USN, Ret., First Vice President; Vice Admiral V. R. Murphy, USN, Ret., Second Vice President; Lieutenant General R. C. Mangrum, USMC, Third Vice President; Vice Admiral K. K. Cowart, USCG, Ret., Fourth Vice President; and, Commander S. J. Barcay, Jr., MC, USN, Vice President-Medical Director.

Elected to the Board of Directors were:

Rear Admiral L. A. Bachman, USN, Ret.
Admiral Arleigh Burke, USN, Ret.
Major General P. J. Fontana, USMC
Rear Admiral R. B. Fulton, II, USN
Rear Admiral H. J. Goldberg, SC, USN
Rear Admiral J. B. Heffernan, USN, Ret.
Rear Admiral A. C. Husband, CEC, USN
Captain S. H. Kinney, USN
Rear Admiral W. I. Martin, USN
Rear Admiral W. H. Schleef, SC, USN, Ret.
Vice Admiral B. J. Semmes, Jr., USN
Rear Admiral R. L. Townsend, USN
Vice Admiral P. E. Trimble, USCG
Major General R. G. Weede, USMC
Lieutenant General F. L. Wieseman, USMC, Ret.

A highlight of the year's operations was the further increase in 1966 in the additional death benefit from \$3,500 to \$4,000, making the total death benefit \$11,500. This increase in death benefit was at no increase in cost to the members.—Navy Mutual Aid Association, Washington, D.C.

### ACUTE CHLOROQUINE-PRIMAQUINE AND DAPSONE TOXICITY

Personnel returning from Southeast Asia are routinely issued antimalarial tablets containing 300 mg. of chloroquine base and 45 mg. of primaquine base. These drugs are a potential source of accidental poisoning, and several such cases involving children have recently been reported. In addition, U.S. Army personnel leaving Viet Nam receive a 30-day supply of 25 mg. Dapsone tablets and the same possibility of poisoning exists for this drug.

The toxic dose of chloroquine base for children is approximately 20 mg/Kg and the lethal dose is approximately 100 mg/Kg. Although the toxic and lethal doses are not known for adults, it is felt that children are more sensitive. The manifestations of acute chloroquine poisoning include myocardial depression, disturbances of cardiac conduction, arrhythmias, hypotension, central nervous system stimulation with convulsions, and eventual paralysis of the vital brain centers. The impressive feature is the rapid appearance and often fatal outcome of chloroquine toxicity, frequently occurring within 2 hours of ingestion. Because of the early and severe consequences of chloroquine toxicity, it is imperative that therapy be initiated rapidly. Since gastrointestinal absorption of chloroquine is rapid, vomiting should be induced as early as possible if the affected

individual is conscious and danger of aspiration minimal. Gastric lavage should be performed as soon as possible in the comatose patient; prior intubation with a cuffed endotracheal tube is recommended to prevent aspiration. Equipment should be available for support of respiration. Convulsions, if they occur, will have to be controlled. Vasopressors, such as norepinephrine, are indicated for hypotension. The use of intravenous sodium bicarbonate, or molar sodium lactate, has been recommended because of its synergistic effect with sympathomimetic agents in treating hypotension and because of its beneficial effect in treating the cardiac manifestations of quinidine toxicity. Renal excretion of chloroquine is increased with acidification of the urine (a minor objection to the use of alkali, as mentioned above). Because of the slow elimination of chloroquine from the body, prolonged observation of the patient is indicated.

Primaquine reaches its maximum plasma concentration in about 6 hours and is rapidly metabolized. Methemoglobinemia is a manifestation of toxicity of quinoline compounds and can be treated with intravenous administration of aqueous methylene blue. In individuals with glucose-y-phosphate dehydrogenase deficiency, an acute hemolytic anemia may develop.

Dapsone may also produce methemoglobinemia. In addition, since sulfones act as electron donors, some increased erythrocyte hemolysis may occur in individuals with normal levels of glucose-6-phosphate dehydrogenase. Central nervous system stimulation has also been observed following acute intoxication with Dapsone.—PrevMed Div, BuMed.

### CAPT HARRY H. DINSMORE MC USN RECEIVES THE NAVY CROSS

Citation:

For extraordinary heroism on 1 October 1966 while serving as Chief of Surgery at U.S. Naval Support Activity, Danang, Republic of Vietnam. With full knowledge of the serious hazards involved and with complete disregard for his own personal safety, CAPT Dinsmore volunteered to perform a surgical operation to remove a live 60 mm mortar shell from the chest wall of Private First Class Nguyen Luong, Army of the Republic of Vietnam. The impact fuse of the mortar shell was partially activated and could easily have detonated at any time during the operation, resulting in certain death to CAPT Dinsmore and his patient. Exhibiting outstanding professional skill and calmness, CAPT Dinsmore took command of the situation and successfully removed the shell. By his heroic conduct and fearless devotion to duty, CAPT Dinsmore saved the life of the patient and upheld the highest traditions of the United States Naval Service.

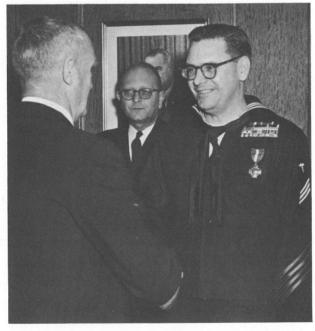


CAPT Harry H. Dinsmore MC USN

## RAYMOND D. CLAY HM USN RECEIVES THE NAVY CROSS

Citation:

For extraordinary heroism as a Platoon Corpsman, 1st Platoon, Company "G", 2d Battalion, 7th Marines in the Quang Tri Province, Republic of Vietnam on 24 September 1966. When a Marine from his platoon suffered a severe head wound shortly after the company encountered a North Vietnamese force estimated at regimental strength and employing intense mortar and small-arms fire, Hospitalman Clay, without hesitation, crawled approximately twenty meters through intense fire to aid the wounded Marine. As he began to treat the wounded man, an enemy grenade exploded about ten meters away. Although bleeding profusely from wounds caused by flying shrapnel, Hospitalman Clay continued treating the Marine until two more grenades landed near him, one falling so close to his legs that he immediately kicked it into the bushes, while the second grenade fell next to him and the



In a ceremony in the Navy Hospital, Bethesda, on 16 March 1967, VADM Robert B. Brown MC USN, Chief, Bureau of Medicine and Surgery, congratulates Hospitalman Raymond D. Clay USN, after presenting the Navy Cross to Clay for heroic actions in Vietnam, as RADM H. S. Etter MC USN, Commanding Officer, Naval Hospital, Bethesda, looks on.

wounded Marine. Hospitalman Clay quickly threw himself between the grenade and his patient and, in so doing, absorbed the shrapnel and shock with his own body, saving the wounded Marine from further injury and possible death. The force of this explosion hurled Hospitalman Clay into the bushes, where yet another grenade exploded, increasing the number of his wounds. He then laboriously and with great pain crawled to the rear. Hospitalman Clay's exceptional spirit and fortitude greatly increased the morale of the wounded Marines around him. His inspiring and courageous actions in jeopardizing his own life in order that his patient might live were in keeping with the highest traditions of the United States Naval Service.

### LCDR R. L. SMITH RECEIVES LETTER OF COMMENDATION

The following is a letter of Commendation to LCDR Robert L. Smith MSC USN from VADM R. B. Brown MC USN, Surgeon General.

"The Bureau has received and reviewed your revision to the Pharmacology and Toxicology Sections, Chapter 7, Handbook of the Hospital Corps, U.S. Navy.

This revision represents about eight months of arduous effort, above and beyond your regular duties. You are not assigned this task, but assumed it on your own initiative, having realized the need. As a self-imposed assignment, you did not allow it to interfere with your daily routine, but did most of the work on your own time.

The Pharmacology and Toxicology Sections of the Handbook of the Hospital Corps, have not been revised since 1961. Portions of the text had become obsolete and a need for additions has been generated by technological advances. Your revision more than satisfies all the requirements imposed by the dynamic nature of the subject matter. Your extreme attention to detail has allowed complete coverage of the material, while your presentation has been tailored to the level of the user of the Handbook. Your excellent cross-indexing of trade, patent, and generic names is an example of the care annd precision with which you approached these labors.

Your conduct has been in the highest tradition of the naval service, and you are commended for your most significant accomplishment."

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