



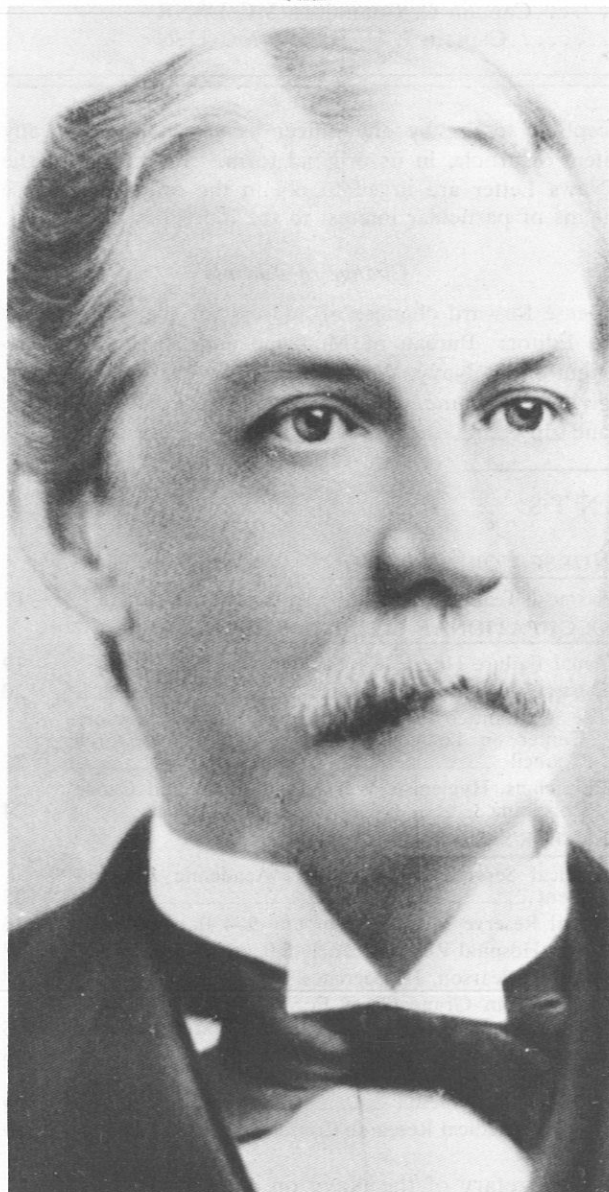
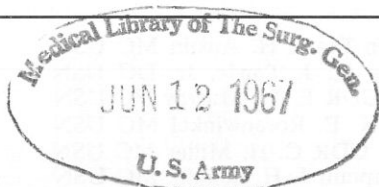
# UNITED STATES NAVY

## Medical News Letter

Vol. 49

Friday, 26 May 1967

No. 10



### Surgeons General of the Past

(The twelfth in a series of brief biographies)

Francis M. Gunnell, twelfth Chief of Bureau and eighth Surgeon General of the Navy, was born in Washington, D.C. on 27 November 1827. He received his M.D. from Columbian College (now George Washington University) in 1846, and was appointed Assistant Surgeon in the Navy by President Zachary Taylor 29 March 1849. Doctor Gunnell served in the Pacific Squadron and then was on the storeship Supply when CDR David Farragut was establishing the Navy Yard at Mare Island. During the Civil War he was attached to the North and South Atlantic Blockading Squadrons and to the naval hospital in Washington, being promoted to Surgeon in 1861. He next joined the European Squadron and had another tour in Washington, becoming Medical Inspector in 1871 and Medical Director in 1875. Later duty included Fleet Surgeon of the Atlantic Fleet and of the Asiatic Squadron. He was appointed Chief of the Bureau of Medicine and Surgery on 1 April 1884 by President Chester A. Arthur and served 4 years. During his term of office a naval hospital at Widows Island, Maine was commissioned in 1887 which accommodated yellow fever patients until 1903. Surgeon General Gunnell retired from active duty on 27 November 1889, but performed special duty in the Bureau of Medicine and Surgery from 6 December 1902 to 31 March 1903. He was also President of the Medical Examining Board on 2 September 1903 and also from 25 September 1903 to 10 September 1907, being then almost 80 years old. Doctor Gunnell thereafter resided in Washington until he died on 10 June 1922 at the age of 94½ years, a record for longevity among the Navy's leading physicians. Contemporaries described him as above middle height, rather slender, pleasant and affable in manner, and very erect in carriage even in his nineties.

*United States Navy*  
**MEDICAL NEWS LETTER**

Vol. 49

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No. 10

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

# ENIGMATIC FEVER AND PELVIC THROMBOPHLEBITIS\*

## RESPONSE TO ANTICOAGULANTS

*Leo J. Dunn MD† and Lee W. Van Voorhis MD‡ Iowa City, Iowa.  
New Eng J Med 276(5):265-268, February 2, 1967.*

Since the early descriptions and considerations of Virchow, Hunter and Welch an extensive literature has been accumulated regarding thrombophlebitis and its related disorders. De Bakey, in 1954, listed more than 400 references in his review of thrombophlebitis. The diagnosis of the disease, the risks from embolism and the varieties of therapeutic regimens are well known. Less well known is the entity of septic pelvic thrombophlebitis. The disorder is relatively uncommon, and in our experience the diagnosis has been overlooked in many patients for inordinate periods.

The purpose of this report is to review a particular form of septic pelvic thrombophlebitis that frequently eludes diagnosis because of the absence of positive findings. Our recent experience with this entity has been of interest because of the striking effect of anticoagulation.

Involvement of the major pelvic veins by an extensive pelvic infection such as puerperal sepsis or septic abortion is the commonly reported description of septic pelvic thrombophlebitis. In such cases the examination of the pelvis gives many positive findings such as tenderness, induration, purulent discharge and perhaps abscess formation. Death by embolism from pelvic thrombophlebitis or metastatic abscess formation bears testimony to the seriousness of this complication. Prevention and therapy of these sequelae of pelvic thrombophlebitis have been the subjects of considerable debate.

Septic thrombophlebitis can follow childbirth or pelvic surgery, with few or no positive physical findings on pelvic examination. Under these circum-

stances, the course may be regarded as a "fever of unknown origin," and the patient may be treated by aggressive antibiotic therapy without response. Cognizance of this diagnosis in the absence of conclusive physical findings can be found in the reports of Collins and Nelson, Wolf, Burns and Schulman and Zajtchuk. The typical history is one of a post-partum obstetric patient or postoperative gynecologic patient who has a low-grade fever attributed to such conditions as endometritis, operative-site infection and hematoma. Soon thereafter, high, spiking temperatures, usually in the range of 103 to 104°F., develop. In contrast with the dramatic temperature excursions noted in the chart the patient gives no evidence of distress but is quite comfortable except during the febrile peaks. At these times the symptoms consist of chills, headache and malaise. Physical examination often reveals nothing at all, or perhaps some localized tenderness in the pelvis. Occasionally a cordlike induration suggestive of a thrombosed vein is found. Edema or any other findings in the legs are absent in these cases. Use of the term septic seems justified in view of the nature of the fever and the high incidence of positive blood cultures.

In most cases therapy with high doses of multiple antibiotics is instituted in spite of a negative physical examination. The presence of septic pelvic thrombophlebitis is first suspected after many days of unsuccessful antibiotic therapy. It has been our experience, and that of others, that the symptom complex has not suggested the proper diagnosis to generalists, internists and obstetrician gynecologists alike. This sequence is well illustrated by a case referred to our hospital in 1964 after unsuccessful antibiotic management at another hospital (Case 4). As described below, the patient was admitted to the hospital with amnionitis. Labor was induced, and premature twins were delivered. After many days of high, spiking

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temperatures with no response to large doses of antibiotics, an internist was called in consultation. In his opinion the patient, when first seen, was not toxic and was not nearly as acutely ill as the temperature pattern suggested. Furthermore, culture studies

were more or less unrevealing, and blood cultures were all negative. The generous doses of various antibiotics had had no effect whatever on the febrile course of the illness, and there were no localized complaints or even very dramatic physical findings.

TABLE 1. Summary of the Pertinent Data.

CASE No.	AGE yr.	PROCEDURE	ANTE-PARTUM COMPLICATIONS	ABNORMAL PHYSICAL FINDINGS DURING FEBRILE ILLNESS	BLOOD CULTURES	MAXIMUM WHITE-CELL COUNT	EMBOLISM
1	31	Vaginal delivery	Premature rupture of membranes; amnionitis.	Small vaginal laceration, with good healing; 2 episodes of hypotension, with fever spikes.	Bacteroides; alpha-hemolytic streptococcus on 18th day.	35,350	None
2	22	Premature vaginal delivery	Diabetes mellitus; Premature rupture of membranes; 2d-trimester bleeding.	None	<i>Esch. coli</i> on 10th day	20,150	None
3	23	Vaginal delivery of twins	Mild toxemia; anemia; rapid labor.	None	Negative (2 specimens)	12,600	None
4*	27	Cesarean section; hysterectomy.	None (para VIII)	Cellulitis & abscess of vaginal cuff	None recorded	55,000	None

\* See text.

### Case Reports

Four of the 5 cases seen and treated between 1962 and 1965 are recorded briefly in Table 1. The remaining case is described below in detail for illustration.

D.B. (U.H. 64-8730), a 20-year-old gravida III, para II, was admitted to another hospital in the 7th month of pregnancy with a temperature of 101.6°F. and a foul vaginal discharge. On examination the fetal heart tones were not audible, a foul vaginal discharge was present, and amnionitis was diagnosed. An intravenous drip containing chloramphenicol was started. On the following day the temperature was normal, and induction of labor was begun. Within 30 minutes the temperature rose to 105°F., and she had chills. Antibiotic therapy was continued, and the temperature gradually returned to normal. The labor was normally progressive, and twins were delivered 6 hours later. Both infants were living at birth and had intact amniotic sacs but died soon after delivery.

Immediately after delivery the patient became hypotensive, and therapy at that time consisted of

chloramphenicol, penicillin, streptomycin, sodium hydrocortisone succinate (Solu-Cortef) and whole-blood transfusions. On the 5th post-partum day antibiotic therapy was changed. During this time the physical examination remained entirely negative, and blood cultures were also reported as negative. Febrile agglutinins, malaria smears, salmonella cultures and so forth were taken and were negative. The white-cell counts never rose above 13,000, and on the 8th post-partum day, a dilatation and curettage was performed, apparently to rule out infected retained products of conception. The curettage was negative, and the febrile course continued without any demonstrable change. The patient was seen in consultation by an internist, whose comments are referred to above. All antibiotic therapy was discontinued from the 10th to the 17th post-partum day to rule out drug fever. There was no change in the course. The patient was transferred to this hospital on the 17th post-partum day.

Physical examination was entirely negative, and blood cultures drawn at this time were later reported as showing nonhemolytic streptococci, beta-hemolytic streptococci and *Escherichia coli*, with sensitivity



to penicillin, chloramphenicol and tetracycline. The diagnosis on admission to the obstetric service was septic pelvic thrombophlebitis. A transfusion was given because of a hemoglobin of 10 gm. per 100 ml., and an intravenous infusion containing aqueous penicillin was begun.

Anticoagulation therapy was started immediately after admission with heparin, and 6 hours later, the temperature dropped suddenly to 98°F. The temperature remained at that level except for a slight rise on the 25th post-partum day. All therapy was discontinued on the 25th post-partum day, and the patient remained well thereafter.

### Discussion

These cases illustrate the most important aspect of this entity of enigmatic septic pelvic thrombophlebitis—mainly, the absence of indicative physical findings. It is interesting that these cases and those reported by Collins and others were largely obstetric, and perhaps some specific vascular change related to pregnancy predisposes to this complication. Therefore, this diagnosis should be strongly considered in a post-partum patient or any patient after pelvic surgery who has continued spiking temperatures in the absence of physical findings and who does not respond to antibiotic therapy. The use of anticoagulation appears to be very important in the therapy of this disorder. Although in each case the question of spontaneous resolution or change in antibiotics could be raised to explain the patient's

course, the dramatic response to anticoagulation in repeated cases strongly suggests a cause-and-effect relation. This supports the similar observations by Wolf, Burns and Schulman and Zatuchni. When we applied the same anticoagulant regimen to febrile patients with recognized wound infections or pelvic cellulitis, no similar "antipyretic effect" as suggested by Wolf was noted. This apparent specificity of effect has caused Schulman and Zatuchni to suggest the use of anticoagulation as a diagnostic test for pelvic thrombophlebitis.

In the reports mentioned, little or no information was offered regarding bacteriologic studies. Blood cultures obtained in 4 of our cases were positive in 3. This similar finding led Collins and Nelson to the conclusion that "Blood cultures are of value if the result is positive . . . if negative, it in no way rules out the presence of suppurative pelvic thrombophlebitis."

### Summary

Five recent cases of septic pelvic thrombophlebitis in obstetric patients are reported. The diagnosis was delayed in each because of the lack of suggestive physical findings. Consideration of this diagnosis was evoked when an enigmatic fever did not respond to antibiotic therapy. A prompt response to anticoagulation was a striking finding in these cases.

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

## THE STRAIGHT-BACK SYNDROME: RADIOGRAPHIC MANIFESTATIONS<sup>1</sup>

Homer L. Twigg MD, Antonio C. de Leon MD, Joseph K. Perloff MD, and Massoud Majd MD. *Radiology* 88(2):274-277, February 1967.

Absence of the normal thoracic kyphosis is a relatively recently accepted cause of "pseudoheart disease." The clinicoradiographic condition has come to be known as the "straight-back syndrome." The diagnosis can readily be suspected on viewing routine postero-anterior and lateral roentgenograms of the chest. The thoracic malformation was first re-

ported by Rawlings in 1960, and subsequent reports have appeared in the literature.

### Material

During the past two years, we have studied 24 patients—12 men and 12 women—in whom loss of thoracic kyphosis was the only somatic fault. A constant clinical feature of all 24 was a heart murmur for which they were referred to the cardiology service of our hospital. The age range was twelve to thirty-six years. Each patient had at least one stand-

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ard 12-lead electrocardiogram, and thoracic wall phonocardiograms were obtained in all subjects. Seven underwent right heart catheterization during which appropriate hemodynamic tests were performed. The other patients were not catheterized because information derived from the first 7 cases enabled us to recognize the entity with assurance at the clinical level.

Radiographically, each patient had one or more sets of postero-anterior and lateral chest films. Radiologic assessment included the cardiothoracic ratio, the cardiac configuration, the degree of shift of the cardiac silhouette, and the prominence of the main pulmonary artery.

To gain further information concerning deviations from normal thoracic dimensions, the following measurements were made in the 24 patients and in a normal group of 50 men and 50 women of comparable age: (a) anteroposterior diameters along a perpendicular line from the posterior border of the sternum to the anterior border of the eighth thoracic vertebra and (b) transthoracic diameters at the level of the diaphragm. The ratio of the anteroposterior to the transthoracic diameter was then determined. In the control group the arithmetic means and the standard deviations were obtained separately for men and women.

### Results

Most patients were asymptomatic, and the loss of the normal thoracic kyphosis was apparent on physical examination. The appearance of the thorax was often typical, with the decrease in the anteroposterior diameters of the chest obvious.

In each of the 24 patients, there were superficial ejection systolic murmurs that varied in intensity from grade 1 to 3 (out of a possible 6). The murmurs were best heard in the second left interspace. They tended to become amplified during full expiration. Since this study, two of the authors (A.C. de L.

and J.K.P.) have observed in some cases amplification of the murmur by chest wall compression. Diastolic murmurs were uniformly absent in our series, although they have been reported. Twelve electrocardiograms had vertical axes and rsr patterns in leads V<sub>1</sub> or AVR. The hemodynamic data were normal except for elevated right ventricular and end-diastolic pressures in one patient. Pulmonary function studies defined mild restrictive defects in 3 of 8 subjects so studied. These clinical and laboratory data appeared in detail in a previous report.

It is important to note that in many patients organic heart disease could not be excluded on clinical grounds. The abnormalities prominently considered were atrial septal defect, mild pulmonic stenosis, or idiopathic pulmonary artery dilatation, but cardiac catheterization substantiated their absence.

The most striking and consistent radiographic finding is the loss of the normal kyphotic curvature of the thoracic vertebrae seen on the lateral chest radiograph. This alteration in thoracic configuration is readily apparent when compared to a normal chest and is the cause of the narrow distance between the vertebral column and sternum. Data derived from measurements of anteroposterior and transthoracic dimensions were compared with similar measurements in 100 normal controls (Table 1). For the 100 normals the mean anteroposterior diameter for males was 14.2 cm, and for females 11.96 cm; and the mean anteroposterior transthoracic ratio was 47 for males and 45.7 for females. In the patients with straight-back syndrome, however, the mean anteroposterior diameter for males was only 10.65 cm, and 9.81 cm for females; and the mean ratios were 35.83 for males and 37.29 for females. It is noted that not only were these mean figures lower than in the normals, but the highest figure in each range was also below the normal mean. Nine of each measurement were also outside two standard deviations from the mean.

TABLE I

	No.	Age (yr.)		A-P Diameter (cm)		A-P/Transthoracic Ratio (%)	
		Ave.	Range	Mean	Range	Mean	Range
<i>24 Patients with Straight-Back Syndrome</i>							
Males	12	20.50	14-29	10.65	8.5-13.0	35.83	29.8-41.6
Females	12	21.33	12-36	9.81	8.2-10.6	37.29	31.8-43.2
<i>100 Normals</i>							
Males	50	32.74	12 to 49	14.20	10.82 to 17.58	47.0	36.7 to 57.3
Females	50	32.28	12 to 50	11.96	8.72 to 15.20	45.7	32.3 to 59.0

In 11 patients, the radiographic appearances of the heart were normal. A "pancake" aspect in the postero-anterior projection simulated cardiomegaly in 4 patients. This was caused by its compression between the sternum and the inwardly displaced thoracic spine. A leftward shift of the heart was noted in 9 patients, and this displacement and rotation produced prominence of the main pulmonary artery in 5. Two of these cases were studied by angiocardiology, and the prominence on the postero-anterior chest film was found to be the result of a leftward shift in position of the heart together with superimposition of the left pulmonary artery, and not to dilatation of the main pulmonary artery.

The right ventricular angiocardiograms demonstrated the proximity of the right ventricle and pulmonary artery to the posterior border of the sternum. This displacement may produce an exaggeration of the normal ejection vibrations and may explain the common occurrence of systolic murmurs in the second left interspace. In some cases, an obliteration of the retrosternal space and a decrease in the retrocardiac space were quite apparent.

#### Discussion

Absence of the normal thoracic kyphosis is thought to be developmental in origin and may begin as early as the eighth week of fetal life before ossification occurs in the vertebral bodies. Most children have "straight" thoracic spines before they begin to stand. There is no radiographic evidence of intrinsic bone disease, and the vertebrae are normally mobile. The straightback is an asymptomatic skeletal defect. As the spine straightens and the anteroposterior dimension of the chest decreases, a forward and leftward displacement of the heart and

great vessels may result in clinical signs which simulate organic heart disease. Right ventricular enlargement or pulmonary artery dilatation is frequently mistakenly inferred.

It is important for the radiologist to recognize this entity in any patient referred to him for cardiac evaluation. Suggesting this diagnosis to the clinician may prevent an expensive and unnecessary cardiac diagnostic investigation, and the patient can generally be assured that he does not have an organic heart lesion.

#### Summary

Loss of the normal kyphotic curvature of the thoracic spine can produce clinical signs which mimic organic heart disease. Twenty-four patients with straight thoracic spines were studied clinically and radiographically. The auscultatory and electrocardiographic findings suggested a number of congenital cardiac abnormalities. Roentgenographically, the heart was usually normal in size and configuration, but in some cases it had a "pancake" appearance simulating cardiomegaly and in other patients it was displaced to the left with prominence of the pulmonary arteries. The ratios of the anteroposterior to transthoracic diameters of these patients were found to be uniformly below the mean normal of those derived from 100 normal subjects. Recognition of this syndrome is important to the radiologist who may prevent unnecessary cardiac investigations by suggesting the correct clinical diagnosis.

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

## MANAGEMENT OF TRAUMATIC HYPHEMA A REVIEW OF 109 CASES

*Joseph L. Darr (MD), Major (MC), and Jack W. Passmore (MD), Colonel (MC)*  
*Washington, D.C. Amer J Ophthal 63(1):134-136, January 1967.*

In recent years, a great deal of attention has been focused on traumatic hypHEMA. Its frequency and

the serious nature of its complications have been emphasized by several authors. A variety of therapeutic measures and precautions have been attempted in efforts to arrest bleeding, promote more rapid absorption of blood from the anterior chamber and prevent the occurrence of secondary hemorrhage

From the Ophthalmology Service, Walter Reed General Hospital, WRAMC. This material has been reviewed by the Office of The Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any endorsement of the opinions advanced or any recommendation of such products as may be named.



with its attendant high incidence of secondary glaucoma which can be so devastating. Several reports in the recent literature describe aggressive therapy for those patients in whom secondary glaucoma has already occurred, including irrigation of the anterior chamber with fibrinolysin. Obviously, associated damage to the uveal tract, including iridodialysis, ciliary body and choroidal ruptures, retinal damage and intravitreal hemorrhages, with their individual contributions to poor prognosis, are not necessarily reversed by management. It is disconcerting, however, to see the eye or useful vision lost by reason of secondary hemorrhage, when the initial injury and the hyphema so induced were of small enough extent to expect full or considerable return of function. The purpose of this report is to present a method of management of traumatic hyphema by which secondary hemorrhage with its inherent complications can be minimized.

#### Previously Reported Series

In previously reported series, secondary hemorrhage rates vary but the average has been about 30 percent. Greater than 50 percent of these cases of rebleeding develop secondary glaucoma with results ranging from severe impairment of visual acuity to loss of the eye by enucleation. Shea, in 1951, reported a secondary hemorrhage rate of 13 percent in a series of 113 cases. Thygeson, in 1952, reported a series of 34 cases with a rate of 38 percent rebleeds. Loring, in 1958, reported 56 cases with a rebleed rate of 30 percent. Gregerson, in 1962, reported a series of 200 cases with a rebleed rate of 6 percent. Cole, in 1964 reported 100 cases with a rebleed rate of 30 percent. In both Shea's and Gregerson's series, the rate of secondary hemorrhage was significantly below the previous average, 13 percent and 6 percent, respectively (Table 1). There was one common denominator in both these series: all cases were managed in an extremely con-

TABLE 1

SECONDARY HEMORRHAGE IN PREVIOUSLY REPORTED SERIES

	No. Cases in Series	Rebled Rate
Thygeson	34	38%
Loring	56	30%
Cole	100	30%
Shea	113	13%
Gregerson	200	6%

servative manner, consisting of strict bedrest, with binocular patching for approximately one week, and the avoidance of any type of miotic or mydriatic.

#### Observations in a Series of 109 Cases

In the past 10 years, we have compiled a series of 109 cases, 75 of which were treated according to a strictly enforced plan of conservative management (Group I), and 34 in which the conservative regimen was not applied (Group II). In Group I, all patients were examined and admitted within 12 hours after injury. In Group II, 29 were admitted within 12 hours after injury, while five were admitted at intervals varying from three to 14 days post-trauma. No penetrating injuries of the globe are included in either group, and no selection is allowed according to the severity of associated uveal tract injuries, or according to the size of the initial hyphema.

Group I was managed according to the following plan: (1) strict bedrest for five to seven days; (2) complete binocular occlusion; (3) strict avoidance of either miotics or mydriatics; (4) sedation of all children and apprehensive adults; and (5) elevation of the head in patients with macroscopic hyphema. We believe that the latter step probably lessens the risk of secondary glaucoma, if the blood is allowed to clot inferiorly, leaving the superior angle clear of macroscopic blood.

In Group II, treatment deviated from this plan as follows: six were not kept at strict bedrest, four were not bilaterally patched, 17 received mydriatics, three received miotics, one received both miotics and mydriatics, two were neither patched bilaterally nor kept at bedrest, and one received conservative management for two days only (Table 2).

In Group I, managed strictly according to our

TABLE 2

DEVIATIONS FROM CONSERVATIVE MANAGEMENT IN GROUP II

Management	Patients	Rebled
1. Not kept at bedrest	6	2
2. Not binocularly patched	4	1
3. Neither patched nor kept at bedrest	2	2
4. Received mydriatics	17	4
5. Received miotics	3	1
6. Received both miotics and mydriatics	1	1
7. Treated for two days only	1	

regimen, there were four instances of secondary hemorrhage, providing a rebleed rate of 5.3 percent. Three cases of secondary glaucoma developed, all

TABLE 3

RESULTS IN 75 CASES CONSERVATIVELY  
MANAGED (GROUP I)

4 secondary hemorrhages	Rebleed rate 5.3%
3 cases of secondary glaucoma	
3 cases required surgery	

occurring in patients who rebled (Table 3). These cases required evacuation of the anterior chamber blood either by paracentesis with irrigation, or by removal of the clot after corneal-scleral section.

In Group II, there were 11 instances of secondary hemorrhage, constituting a rebleed rate of 32 percent. There were seven cases of secondary glaucoma, all occurring in patients who had experienced secondary hemorrhage. Five of these required surgical intervention. Three of these went on to absolute glaucoma and two eventually required enucleation for a blind painful eye. The other two were controlled medically with oral Diamox (Table 4).

TABLE 4

RESULTS IN 34 CASES MORE LIBERALLY MANAGED  
(GROUP II)

11 secondary hemorrhages	Rebleed rate 32%
7 cases of secondary glaucoma	
5 cases required surgery	
2 eyes eventually enucleated	

In the cases that require surgical measures to relieve secondary glaucoma, it is our experience that the clot can be removed from the anterior chamber with greater ease and with more predictable success in reducing intraocular pressure by performing a 120-degree corneal-scleral section or a linear corneal section, as advocated by Callahan. It is his contention that it is often impossible to remove all of a

clot through a small opening even with excessive irrigation, and that the postoperative course is frequently complicated by further bleeding and return of elevated intraocular pressure. In most eyes in which a corneal section with evacuation of clot was performed, further complications did not develop. Neither course of action was taken except in those cases in which intraocular pressure was elevated and corneal blood staining was imminent or beginning.

#### Summary and Conclusions

1. It is recognized that the disastrous complications of traumatic hyphema occur chiefly following secondary hemorrhage.

2. A study has been made of 109 cases of traumatic hyphema, 75 of which were managed according to a strictly enforced conservative plan, and 34 cases in which deviation from this plan occurred in one or more of the following ways: failure to keep the patient at strict bedrest, failure to patch binocularly, or the use of mydriatics or miotics in the first week post-trauma. In the conservatively managed group, there was a secondary hemorrhage rate of 5.3 percent. In the more liberally managed group, the secondary hemorrhage rate was 32 percent, which agrees with the average rebleed rate of other series reported in the last 15 years.

3. Our method of conservative management is described. We believe that the low rate of secondary hemorrhage experienced in the group so managed is significant and warrants continued practice.

4. Some ophthalmologists advocate the routine use of atropine in the management of traumatic hyphema and there appears to be more disagreement on this single point than with any other item in our protocol. Consequently, we have begun a second study wherein all hyphema patients are treated conservatively as described, with one exception—alternate patients receive atropine once daily. The results of this study will be the subject of a future report.

*Walter Reed General Hospital (20012).*

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

## DIAGNOSIS AND TREATMENT OF ABNORMAL BREAST SECRETIONS

*Ann B. Barnes MD, Boston, New Eng J Med 275(21):1184-1187, Nov. 24, 1966.*

The etiology and treatment of abnormal breast secretions are perplexing to those in practice and research alike. Abnormal function of the female breast may appear at any time of life from infancy to old age as indicated by the "witch's milk" of the newborn and postmenopausal discharges. Breast secretions are also observed in men, young and old. In diagnosis both intramammary and neurohumoral mechanisms must be considered. The investigation needed may range from a simple review of the history and physical examination to costly radiologic and laboratory tests and possibly extensive surgical procedures.

The incidence of unilateral in contrast to bilateral secretions in association with various diseases is not generally known. In theory, discharges arising from neurohumoral mechanisms should tend to be bilateral, and local processes should cause an ipsilateral discharge. However, a "local" process such as cystic disease may involve both breasts, and one breast may initially be more responsive to hormonal stimulation. Further complexities exist as shown by Russfield's description of 2 cases of chromophobe adenoma of the pituitary gland in which bilateral breast discharges were associated with unilateral mammary carcinoma. The practitioner must be alert to a wide range of possible underlying conditions in patients with breast secretions.

### Intramammary Conditions

#### Malignant Lesions

Discharges in the presence of an associated mass must usually be diagnosed by excisional biopsy. More abstruse are discharges without associated masses, and an immediate concern is the possibility of occult carcinoma. The character of the discharge, whether serous, bloody or opalescent, is of little assistance in identifying a malignant growth. In all patients presenting nipple discharges the reported incidence of cancer ranges from 4 to 52 percent, the variation doubtless reflecting the prior selection in the several series, depending on the methods of referral and on the accuracy of recording discharges.

Only 1 to 5 percent of all patients with carcinoma of the breast have a discharge. In cases of discharge without a palpable tumor adenofibrosarcoma, fibrosarcoma, liposarcoma, malignant melanoma as well as the more common adenocarcinoma have been reported. In males with breast discharges carcinomas are more frequent than benign tumors. Neurogenic sarcoma in the breast has been reported in 1 unusual case. The malignant nature of Paget's disease and its common moist lesion of the nipple is well recognized.

#### Benign Lesions

In 3 series, representing over 5,400 cases of benign breast disease, 10 percent of the patients had a nipple discharge. About 30 percent of those with discharges had fibrocystic disease, 10 percent intraductal papilloma, and 7 percent papillary cystadenoma. In half the cases of intraductal papilloma there was a discharge, but papillomas were less common than fibrocystic disease. With papillomas a discharge recurred after operation in 10 percent of cases; this was explained by the presence of additional papillomas overlooked at the initial operation. Other conditions found with a discharge and no palpable mass include sclerosing adenosis, chronic cystic disease, duct ectasia, galactoceles, abscess, keratosis of the nipple, variocoeles, fat necrosis and acute mastitis. Tuberculosis of the breast is occasionally seen with a bloody discharge, but only once has a milklike secretion been reported. Tuberculosis more usually presents as an enlargement of the breast with a *peau d'orange* sign and a palpable ipsilateral axillary lymph node. Toxoplasmosis involving the breast and causing a discharge has been reported. Eczema of the nipple may cause a discharge, and the cause is generally apparent on inspection.

Chemical analysis of mammary secretions is rarely accomplished because of difficulty in collecting a sufficient volume. Cytologic examination, when satisfactory, approaches 80 percent accuracy. Kjellgren obtained unsatisfactory smears in 16 percent of 235 patients with nipple discharge. In the remainder



there were 16 percent false-negative and 4 percent false-positive smears. Jackson and Severance noted a higher false-positive rate: 26 percent. They estimated that 76 percent of secretions with anaplastic cells represent intraductal papillomas and 24 percent carcinomas. Kline and Lash warned that in postpartum patients with bloody discharge, cytologic studies are particularly difficult to interpret and commonly provide false-positive smears. Transillumination of the breast, as suggested by Cutler can help locate small intraductal tumors in the periphery of the breast tissue. Sandbloom and Lofgren popularized mammography in 1952. However, Kjellgren pointed out that about a third of these are technical failures; he mentioned aspiration biopsies as an additional diagnostic measure.

#### Unidentified Local Causes

The treatment of nipple discharges arising from unidentified local causes has run the gamut from radical mastectomy for suspected carcinoma to temporizing observation. Babcock, in 1938, advocated dilating a diseased duct from the nipple, followed by a wedge resection of the area drained by the duct. Haagensen and his associates considered manipulation of ducts dangerous and preferred an anatomic dissection and excision of the discharging duct with its area of drainage. They did not recommend simple mastectomy or radical mastectomy in the absence of a specific diagnosis but emphasized careful follow-up study.

#### Neurohumoral Causes

The effect of the pituitary gland in the initiation of lactation was first recognized in 1928. Recently, a mediating hormone of the anterior pituitary gland, prolactin, has been isolated from sheep pituitary glands. This hormone is a polymer with a molecular weight of 24,200. At present, prolactin activity is measured by a pigeon-crop assay. In man pure prolactin has not been identified since all substances from the human pituitary gland with lactogenic effects have some growth-promoting activity as well. It is currently thought that the tuber cinereum of the hypothalamus reacts directly to the circulating target-organ hormones such as estrogens and progesterone. The reaction of the hypothalamic centers produces "releasing" factors, which are carried via the hypothalamic-pituitary portal system to the anterior pituitary gland and induce lactogenic-hormone secretion. Whether the hypothalamic factors are excitatory or inhibitory to anterior pituitary function is not yet

clear. Prolactin may have a permissive rather than an obligatory effect since it produces mammary growth in rats only in the presence of progesterone, estrogen and growth hormone. As a possible pathologic variant, Russfield et al. suggested that reproductive organ failure may lead to pituitary hyperplasia or neoplasia, which in turn alters prolactin secretion.

Milk ejection is mediated through oxytocin, a peptide containing 8 amino acids. Oxytocin is found at nerve endings arising from the supraoptic and paraventricular hypothalamic nuclei. It is liberated from these endings into the portal system and thence to the posterior pituitary gland where it is stored. Suckling triggers the release of oxytocin, and this reflex is mediated in part by nerve fibers that traverse the paraventricular area of oxytocin production. Yet to be explained in this scheme is the role of placental lactogenic hormone. This was discovered by means of certain immunologic properties common to growth hormone and a lactogenic substance in the placenta and term serum.

Mechanical stimulation of the breast has long been recognized as a way of inducing lactation. Mead described nulliparous and menopausal women in primitive tribes putting adopted infants to their breasts. In Western society women who have long since weaned their infants may continue to secrete milk as a result of their own manipulation or of illfitting garments. Eliciting a history of manipulation, besides requiring awareness of the possibility, demands tact on the physician's part and perhaps several visits before the patient's confidence allows her to speak freely.

Milk secretion may follow trauma to the chest wall. Lactation has been observed repeatedly in patients recovering from thoracoplasty. Breast secretions also occur subsequent to pneumonectomy, mammoplasty and herpes zoster. No relation between the day of the menstrual cycle on which the trauma occurred and subsequent secretion has been recognized. The mechanism is probably similar to that in suckling and is associated with stimulation of the second to sixth thoracic nerves, leading to hypothalamic-pituitary activity.

In normal pregnancy hypothalamic-pituitary lactation results from hormonal stimulation rather than through peripheral nerve pathways. Pregnancy, whether of recent termination or several months past, is the most usual cause of lactation and must always be considered. After pregnancy rare conditions such as pituitary necrosis (Sheehan's syndrome) may be manifested by persistent or late on-

set of lactation before other symptoms of pituitary insufficiency are apparent. The Chiari-Frommel syndrome might be considered a *forme fruste* of Sheehan's syndrome, and is characterized by persistent post-partum lactation, amenorrhea, uterine atrophy and a low urinary excretion of follicle-stimulating hormone (FSH).

A similar syndrome unassociated with pregnancy has been described by Forbes and her associates and also by Argonez and Del Castillo. The patients are usually obese, complain of headaches and amenorrhea and have uterine atrophy, lactation and a low urinary level of FSH. Forbes and her co-workers speculated that this complex arises from dysfunction of pituitary eosinophilic cells that attenuates the normal hypothalamic-pituitary suppression of prolactin production. The eosinophilic cells are implicated because these are seen in pituitary tumors associated with lactation. However, Russfield et al. gave a reminder that although with usual trichrome stains, cells appear either acidophilic or basophilic, these probably are 1 cell type, the amophil. They described such cells in patients with acromegaly and chromophobe adenomas who had breast secretion. In 7 of their 8 patients with chromophobe adenoma the following abnormalities were present: 1 male and 3 females had breast secretions; 2 females had breast carcinoma and secretions; and 1 female had cystic disease. However, a specific cell type associated with endocrine function need not be present since a patient with pituitary angiosarcoma may also have abnormal lactation, and this implies that a space-occupying mass distinct from a functioning tumor may alter the hypothalamic-pituitary balance controlling lactation.

Milk secretion has been described in both hypothyroid adolescent girls and hyperthyroid women. Some authors speculate that there is a single hypothalamic defect inducing both lactation and the abnormal thyroid state. Analysis of the mammary secretion from the hypothyroid girls reveals less lactalbumin than is ordinarily found in human milk. Treatment of the thyroid condition usually results in cessation of mammary secretion. Levin suggested that the adrenal glands as well as the pituitary gland have a key role in lactation. Breast secretions were seen in 2 male patients with metastatic adrenal carcinoma to the ribs, but it is not clear whether this resulted from local irritation due to the metastasis or from abnormal pituitary function. Postencephalitic lactation has been reported. Ehni and Echles described lactation without ejection after pituitary-

stalk section for metastatic mammary carcinoma. These reports confirm the preponderant influence of the central nervous system rather than peripheral causes such as the adrenal glands.

At the Massachusetts General Hospital, of 32 women in a series of 80 patients who had had pituitary-stalk section for advancing diabetic retinopathy, frank lactation developed in 1, and 3 had moderate breast engorgement after the surgical operation. In addition to those treated by pituitary-stalk section, 67 diabetic patients with advancing retinopathy and with significantly more advanced renal and peripheral vascular disease received Bragg-peak-proton-beam irradiation of the pituitary gland. Of these, 26 were women of whom 1 complained of progressive breast enlargement, and another of breast fullness several months after treatment. This experience is too limited to establish whether the more localized irradiation is associated with fewer breast symptoms than surgical operation of the pituitary stalk. The menstrual histories of the patients with breast symptoms were no different from those of other women with diabetes of similar severity. In the patients with stalk section diabetes insipidus developed within a day after operation, and no predilection was recognized for the breast symptoms to appear on the same side as the frontal craniotomy.

Factors acting on the hypothalamus alone are also implicated in nonpuerperal lactation. After the wide use of tranquilizers reports of lactation appeared in the psychiatric literature. In succeeding years nearly all phenothiazines, as well as reserpine and methyl-dopa, were noted to induce lactation. Males and females may have unilateral or bilateral secretions. This side effect has not been noted with barbiturate sedatives. The appearance of lactation appears to be related to higher doses of the phenothiazines, and when they are discontinued, lactation ceases. Therapy may be resumed at lower doses without recurrence.

More difficult to comprehend within the framework of present understanding is posthysterectomy lactation. Equally intriguing is Cooke's report (1915) of chorioepithelioma of the testis, without metastases, associated with mammary hypertrophy and colostrum-like secretions. Three previous examples of this syndrome had been reported.

The treatment of abnormal lactation of neurohumoral origin is not entirely satisfactory. The necessity of treating antecedent tumors may cure the lactation. Occasionally, warnings to patients about

breast manipulation or cessation of drug therapy may be sufficient. In the Chiari-Frommel, Forbes-Albright and Argonez-Del Castillo syndromes, as well as cases that follow pituitary-stalk section and hysterectomy, treatment may not be necessary because of spontaneous cures. Nonspecific measures to relieve breast engorgement, including binding of the breasts, fluid limitation and cold packs, may be of value.

Estrogen therapy has not been successful in the suppression of lactation, but Cohan reports success with progesterone. Christiansen was the first to achieve the reinstatement of menses with pregnant mare's serum and human gonadotropin in a case of the Chiari-Frommel syndrome, but he failed to comment on the course of lactation. Kaiser reported ovulation in lactating patients with the Chiari-Frommel syndrome after administration of clomiphene citrate.\* Jones and DeMores-Ruehsen described encouraging results in lactating patients with the Argonez-Del Castillo syndrome with sequential human menopausal urinary gonadotropin † and human chorionic gonadotropin. ‡ In these cases the hormones were more effective than clomiphene. These authors inferred control of lactation as well.

\* In the form of Clomid, W.S. Merrell Company, Cincinnati, Ohio.  
† In the form of Pergonal-25, human menopausal gonadotropin, Istituo, Farmacologis, Serono, Rome, Italy.  
‡ In the form of Follutein, human chorionic gonadotropin, E.R. Squibb and Sons, New York City.

## GANGRENE OF THE HAND FOLLOWING INTRA-ARTERIAL INJECTION

*Donald L. Hager MD and James N. Wilson MD, Los Angeles.  
Reprinted from the Arch Surg 94:86-89, January 1967, Copyright 1967,  
by American Medical Association.*

The intra-arterial injection of medications in the upper limb may result in serious impairment or loss of part of the extremity. When one reflects on the frequency and casualness with which medications are injected intravascularly into various parts of the upper limb, it is remarkable that there should be so few untoward incidents reported.

The textbooks of pharmacology and anesthesiology comment to a varying degree on the complications associated with the intra-arterial injection of drugs. With the exception of thiopental sodium and

From the Orthopaedic Hospital, Los Angeles.

## Conclusions

A woman with a breast secretion unrelated to pregnancy and without mass may present a difficult problem in differential diagnosis. The history, in addition to excluding pregnancy and related conditions, may provide data on abnormal suckling, irritation, drug therapy, local surgery or trauma. A physical examination with special attention to neurologic and endocrine findings may give evidence for pituitary tumor or dysfunction. Cytologic studies, cultures, chemical analysis of the discharge, mammography, transillumination, hormone assays for follicle stimulating hormone, 17-ketosteroids and 17-hydroxysteroids in the urine can be helpful although seldom is any one test conclusive. Biopsy of discharging ducts may be helpful when local processes are at fault.

Once therapy, medical or surgical, is instituted, vigilance for signs of an occult cancer of the breast or pituitary gland or another etiologic factor must be maintained. Follow-up observation of patients not only will lead to early recognition of associated problems but also will add to the currently imperfect understanding of the mechanisms underlying secretions of the breast.

I am indebted to Dr. Richard A. Field for making available the records of patients with diabetes at the Massachusetts General Hospital.

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

contrast media, there is little in the medical journals concerning these complications. A number of other compounds have been incriminated; for example, promazine HC1, chlorpromazine HC1, ether, and mephenesin (Myanesin). A number of reports attribute arterial thrombosis and gangrene to idiosyncrasy or local irritation. It is more likely that these cases reflect the intra-arterial injection of the drug.

Reported here are three cases involving: (1) amobarbital sodium, (2) meperidine HC1 and promethazine mixture, and (3) promazine HC1.

In all of our cases, medical-legal implications prevented procurement of some of the clinical data.



## Report of Cases

Case 1.—A middle-aged woman received an unknown quantity of amobarbital sodium in a left dorsal wrist vessel. Within several minutes, the hand and distal forearm became cold and cyanotic. Therapy with anticoagulants was instituted. Three weeks after the injection, the fingers and tip of the thumb were amputated because of gangrene.

Case 2.—A middle-aged woman received a mixture of merperidine HCl, 50 mg, and promethazine HCl, 25 mg, in a left antecubital vessel. She experienced immediate pain in the distal forearm and hand. Within one hour there was a blotchy discoloration of the forearm and by two hours, the hand and distal forearm were cold and anesthetic. The patient was treated with stellate ganglion block, anticoagulants, and papaverine. Progressive gangrene of the fingers and thumb ensued. Seven weeks later amputation was performed through the distal forearm.

Case 3.—A middle-aged woman received an unknown quantity of promazine HCl in a right antecubital vessel. She experienced immediate pain in the hand. A bluish discoloration and coldness rapidly followed. Treatment with stellate ganglion blocks, anticoagulants, and totazoline HCl was instituted. Gangrene of the distal segment of the thumb developed, necessitating amputation three weeks later.

## Pathogenesis

The pathogenesis of the ischemia and gangrene following intra-arterial injection of medications is not well understood. The usual necropsy findings are grossly described and little is said about the condition of the small vessels. If surgical exploration of the antecubital space is done, it is usually performed many hours after the injection in this area. At this time, intravascular damage or thrombosis of the brachial artery and its branches is apparent. What is not apparent are the changes which have occurred during the initial critical stages.

Cohen, in 1948, reviewed 12 cases of intra-arterial injection of thiopental sodium of which six required forearm amputation. He concluded that spasm of the distal arterioles and late thrombosis of the arteries were the significant lesions. In three of the patients reported on by Cohen, the radial pulse disappeared after a period of 8, 10, and 16 days postinjection to be followed by gangrene.

Attempts have been made, experimentally, to clarify the pathogenesis of the ischemia. Burn and Hobbs perfused rabbit ears with thiopental sodium

and concluded that vascular constriction was due to local liberation of norepinephrine. Kinmonth and Shepherd injected thiopental sodium into the femoral artery of the rabbit. They observed only a transient contraction of the artery. However, when this drug was injected into the central artery of a rabbit's ear, edema and inflammation, followed by gangrene after three to four days, developed. Engler and his co-workers describe an experimental technique with dogs. The femoral artery was occluded for one minute prior to injection of one of the following test substances: promazine HCl, ether, dextroamphetamine, or sulfobromophthalein. Gangrene of the leg consistently developed. These authors described the gross and microscopic findings and concluded that early intimal damage was rapidly followed by necrosis and thrombosis of artery walls. These changes appeared earliest in the arterioles and small arteries. They suggest that the effect of occlusion of the femoral artery was to allow the drug to be transported undiluted with the arterial system.

## Clinical Picture

The clinical picture has been well described by a number of writers. Immediate, severe, burning pain in the hand and forearm is most characteristic. If the patient is being anesthetized, he may respond to pain by flexing the forearm, groaning, and writhing on the table. The induction may be prolonged due to pain. Also, if the drug being injected is the inducing agent, it will be carried distally within the artery. There may be an initial flushing of the extremity, to be followed rapidly by blanching and a variable amount of cyanosis. The distal pulses may disappear at this time or may persist, only to disappear hours or even days later. Occasionally, the pulses may vanish, return, and then become absent again. The skin may become a mottled blue or blue-green in patches distal to the injection. Rarely, a prominent feature is tremendous edema of the forearm and hand. Subsequently, ischemia changes and a variable amount of gangrene of the hand and forearm follow.

## Treatment

The management of these patients is controversial. Ideally, the goals are to eliminate arterial spasm, prevent thrombosis, and to restore blood flow to the limb. Pharmacology and anesthesiology texts recommend a variety of measures: surgical intervention, intra-arterial procaine, sympathetic block, anticoagulation, vasodilators, and local infiltration of substances to counteract irritation and reduce spasm.

Surgical intervention is one of the more controversial measures. Cohen concluded that early exploration with arteriotomy and extraction of the clot may be worthwhile, but that late exploration or arteriectomy are worthless and may even be detrimental. It would not appear that adventitial stripping at a localized area has much merit when one considers that the entire arterial tree is involved. It is almost universally agreed that immediate intra-arterial injection of several milliliters of 1% to 2% procaine through the same needle that introduced the offending drug, is of value. However, Kinmonth and Shepherd could not demonstrate any salutary effect of 4% procaine following the injection of 10% thiopental sodium in the rabbit ear. They did find that sympathetic denervation and anticoagulation resulted in a reduced amount of necrosis and gangrene. There is general agreement that repeated brachial plexus or stellate ganglion blocks are indicated. Immediate heparinization is advocated by many writers. Vasodilators are of dubious value.

If the incident occurs at the onset of a surgical procedure, it is desirable to terminate the operation unless it is one of great urgency. The suggestion has been made that the vasodilatation of the general anesthesia is beneficial. However, it would seem more logical that all of one's efforts should be directed toward securing adequate blood flow to the limb. This is no time for procrastination, ice packs, and complacency. If the operation has begun or must be done, subsequent heparinization will add the complication of bleeding from the operative site. Bleeding may also occur at the site of sympathetic block. These hazards must be accepted.

How long should one continue treatment? The duration of the therapy must be individualized.

#### Prevention

How does one avoid this catastrophe? Anesthesiologists have long been alerted to the noxious effect of thiopental sodium in the higher concentrations. It is suggested that the concentration of this drug not exceed 2½%. Even so, Dundee describes a patient who apparently had pain in the forearm while receiving a 2½% thiopental sodium injection while under general anesthesia. And Fell reports on a patient who complained of pain in the hand and forearm after receiving the 2½% preparation in a distal forearm artery. The use of a test dose followed by a pause is often advocated as a routine precaution. Stuart reports a case in which a test dose of 1 ml of a 5% solution of thiopental sodium did not elicit

any symptoms; however, further injection of 5 ml produced the typical pain and ischemic changes. The injection in this patient was in an aberrant ulnar artery at the elbow.

Many writers have commented on the presence of aberrant or superficial arteries at the antecubital, forearm, wrist, and hand level. Gagnon's analysis of the reported cases of gangrene following intra-arterial injections includes a discussion of the anatomy of aberrant vessels.

Swerdlow's report contains a photograph of an angiogram demonstrating an aberrant ulnar artery in the forearm. In Baillie's article, there is a photograph which illustrates an artery on the dorsum of the hand. A dissection of 188 cadaver limbs by Hazlett revealed a superficial ulnar artery in 6 (3.1 percent). The artery is superficial to the muscles of the forearm, but it may be either deep or superficial to the deep fascia. In 542 medical and dental students, a superficial ulnar artery was found in 15 (2.7 percent). It was noted that a tourniquet obliterated the pulsation in the superficial artery. This superficial ulnar artery may be an extremely close companion of a vein in the medial antecubital space. McCormack and co-workers report an incidence of 14.27 percent high origin of the radial artery in their cadaver limb dissections. The radial artery, unlike the ulnar artery, will usually assume its normal position along the brachioradialis muscle at the elbow level, and thus is rarely superficial here.

The risk of placing a needle in an artery of a struggling or obese patient should be well appreciated. Obviously, a too-tight tourniquet will prevent arterial pulsation, but how many of us check for a distal pulse prior to a venipuncture? Hyperextension of the elbow may cause the arteries to become relatively superficial and is to be avoided. Particular awareness should be used on the medial side of the elbow where a superficial ulnar artery may be confused with a median cubital vein. And finally, adequate lighting is a prerequisite of safe venipuncture.

#### Conclusion

Three cases of intra-arterial injection of medications with resultant ischemia and gangrene have been described. The pathogenesis, treatment, and prevention of this complication have been discussed. It is hoped that physicians will report their experiences so that the nature and scope of the problem will be better clarified. There would appear to be a need to demonstrate experimentally the rationale and value of certain forms of treatment.

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

#### Generic and Trade Names of Drugs

Amobarbital sodium—*Amytal Sodium*.

Merperidine HCl—*Demerol HCl, Pro-Meperdan*.

Mephenesin—*Myanesin, Tolosate*.

Promethazine HCl—*Phenergan*.

Promazine HCl—*Sparine HCl*.

Chlorpromazine HCl—*Thorazine HCl*.

Thiopental sodium—*Pentothal Sodium*.

Tolazoline HCl—*Priscoline HCl, Arterodyl TT*.

Dextroamphetamine—*Dexedrine*.

## MEDICAL ABSTRACTS

### THE HAND AS AN INDICATOR OF GENERALIZED DISEASE

G. B. Greenfield MD, C. H. Escamilla MD, and Hildegard A. Schorsch MD, (*Cook County Hospital, Chicago, Illinois*), *Amer J Roentgen* 99: 736-745, March 1967.

At the outset, the article states that roentgenograms of the hands often reflect the picture of generalized disease; that in evaluating roentgenograms of the hands, the careful analysis of features applicable to bone disease in general should be used; and that the latter comprises independent observation of periosteum, cortex, medulla, location of lesion, bone production or destruction, erosion, resorption, and soft tissue changes. The following categories are listed as those into which the predominating pathological changes fall: (A) Periosteal Changes; (B) Soft Tissue Changes; (C) Changes in the Tufts; (D) Changes in the Wrists; (E) Destructive & Lytic Changes; and (F) Diffuse Changes.

Following this introduction there are descriptions of diseases by groups with representative photographs of roentgenograms. Under periosteal changes, pulmonary osteoarthropathy, thyroid acropachy, and hyperparathyroidism are described. Hemangiomas and lymphedema are described under soft tissue changes; scleroderma, leprosy and acromegaly under changes in the tufts; lead intoxication, rickets, and brown cysts of hyperparathyroidism under changes in the wrists; metastasis, gout, enchondromatosis, and sarcoidosis under destructive and lytic changes; and thalassemia, pituitary dwarfism, rheumatoid arthritis, and nerve injury under diffuse changes.

### LOCAL ANESTHETICS SYNERGISTIC TOXICITY

The practice of combining a local anesthetic possessing rapid onset of action with one having pro-

longed action is not uncommon. It is also potentially hazardous. The authors determined the LD<sub>20</sub> dose of individual anesthetics, then noted the toxicity of various combinations of the LD<sub>20</sub> doses. Tetracaine was tested with lidocaine, mepivacaine, chlorprocaine, and propitocaine. Each combination was employed in 100 mice. Only 10 animals survived the lidocaine-tetracaine combination, 20 survived the chlorprocaine-tetracaine combination, and 12 each survived the mepivacaine-tetracaine and propitocaine-tetracaine combinations.—Akamatsu & Siebold (Seattle, Wash.), *Anesthesiol.* 28:238 (Jan-Feb), 1967.

[Tetracaine-‘Pontocaine’, Winthrop; lidocaine-‘Xylocaine’, Astra; mepivacaine-‘Carbocaine’, Winthrop; chlorprocaine-‘Nesacaine’, Maltbie.]—Republished from CLIN-ALERT No. 45, March 9, 1967, by permission of Science Editors, Inc.

### KRIESELMAN RESUSCITATOR HOSPITAL ALERT

The Krieselman resuscitator Model 24-TPM has a bare stainless-steel tube coming from the filter. The tube is so placed that it is readily seen when the unit is approached to connect the suction tubing. The outlet to which rubber tubing is supposed to be attached comes from a bottle attached to a front leg of the unit. This bottle is hidden by the sterile drape usually placed over the unit. It is easy for an inexperienced person, especially one in a hurry, to connect the suction catheter to the outlet pipe. Such an accident recently occurred at the U.S.N.H., St. Albans, N.Y. The incorrectly attached suction catheter was passed into the stomach of an infant, with resulting near-fatal abdominal distention. All 24-TPM Krieselman resuscitators should be modified by making a 45° flare in the end of the outlet tubing, making it impossible to slide a rubber tube onto it.—Wander (St. Albans, N.Y.), *New England J. M.*



276: 349 (Feb. 9), 1967—Republished from CLIN-ALERT No. 51, March 9, 1967, by permission of Science Editors, Inc.

#### ANGIOKERATOMA—A CLINICO-PATHOLOGICAL STUDY

*Roland Imperial MD and E. B. Helwig MD, (From the Dermal Pathology Branch, Armed Forces Institute of Pathology and the Registry of Dermal Pathology, Washington, D.C.) Arch Derm 95: 166-175, February 1967.*

The authors describe an angiokeratoma which they consider to be different from those classified as angiokeratoma, Mibelli type; angiokeratoma, Fordyce type; angiokeratoma, Fabry type; and angiokeratoma circumscriptum. They examined angiokeratomas from 116 patients. Eighty-three percent of these were solitary lesions. They occurred on all parts of the body but the incidence was greater on the lower extremities than elsewhere and they are described as bluish to black, rough, warty growths. A most important consideration which they point out is that they must be considered in the differential diagnosis of malignant melanoma. In 15 percent of their series, the clinical diagnosis had been melanoma and a wide surgical excision had been carried out. They propose the designation angiokeratoma, solitary or multiple for the lesion which they describe.

#### RENAL ARTERY ANOMALIES AND HYPERTENSION—A STUDY OF 340 PATIENTS

*P. W. Robertson MD FRCP, D. H. Hull MA MB MRCP, A. Klidjian MB FRCS, M. L. Dyson DMRD, Wolverhampton, England. Amer Heart J 73: 296-307, March 1967.*

This is the second study by the authors of patients with hypertension. Renal arteriograms were obtained in each instance. Two hundred twenty-five patients were assessed as having idiopathic or essential hypertension and of these, 152 (67 percent) had renal artery anomalies. In the earlier, smaller series, the incidence was 70 percent. In the two series taken together, a total of 461 hypertensive patients, about 68 percent of those with essential hypertension had renal artery anomalies. The findings support the view of the authors that the association

between renal artery anomaly and idiopathic hypertension may be significant, and confirm observations made by others in this field.

#### EFFECTS OF HEAT ON BLOOD PIGMENT ABSORPTION RATE IN TRAUMATIZED MUSCLE

*LCDR Jean L. Heath MSC USN, Phys Ther 47: 9-21, January 1967.*

The purpose of this investigation was to conduct a pilot study (1) to determine the effects of ultrasound, microwave diathermy, massage, and combined microwave diathermy and massage on the rate of absorption of blood pigments from traumatized rabbit skeletal muscle; (2) to make a relative comparison of the apparent rates of absorption obtained by these treatment methods; and, (3) to seek some physiological evidence as the basis for the clinical use of these forms of treatment in hastening reabsorption of extravasated blood after severe muscle contusion.

The thighs of experimental animals were traumatized by two methods, bruising and injection of autogenous blood. Treatments, to one traumatized thigh of each animal, were administered twice daily for two days beginning twenty-four hours after trauma. Animals were sacrificed at intervals of four, six and twelve days post trauma. After sacrifice, certain of the heme pigments were extracted from the traumatized muscle homogenates. The concentration of extracted heme pigment in each muscle was determined spectrophotometrically and a comparison was made of rates of absorption of heme pigments from treated and untreated traumatized muscle. Additional information was obtained from some of the animals by radioisotope (Fe 59) studies, gross and microscopic observations, and determination of bilirubin concentration.

This study demonstrated no significant difference in the rate of absorption of blood pigments from traumatized rabbit skeletal muscle after treatment when compared with untreated muscle. It was felt, however, that a larger sample size at the four and six-day sacrifice intervals would afford a more representative picture upon which valid conclusions might be drawn.

Collagen fibers were grossly visible in the area of trauma three days after injury. Adhesions extending across fascial planes were evident by eight days.

Further studies would be desirable to (1) elucidate further the differences in rates of absorption of blood pigments, and (2) to demonstrate possible differences in collagen formation of treated and untreated sides.—Author's summary.

Adapted from a thesis submitted to the faculty of the Graduate School of the University of Minnesota, Minneapolis, in partial fulfillment of the requirements for the Master of Science in Physical Therapy degree, June 1965.

## DENTAL SECTION

### DIARRHEA FROM DIETETIC CANDIES

*J. D. Gryboski, New Eng J Med 275: 718, September 1966.*

In recent years "sugarless" candies and soft drinks containing sorbitol, mannitol or both as replacement for sucrose and starches have been consumed in increasing quantities by children. The hexitols, recommended for the prevention of dental caries, present the advantage of being acted upon slowly by bacteria of the oral cavity and of being slowly absorbed through the gastrointestinal tract. Because of these very properties diarrhea may follow the ingestion of sufficient quantities of the sugar alcohols.

Therefore, it should be incumbent upon the dentist to advise the parent of this possible sequela when prescribing these substitute foods in a preventive dentistry program.

(Abstracted by: LCDR William K. Bottomley DC USN.)

### EFFECTS OF PLASTER-OF-PARIS IMPLANTS IN SURGICAL DEFECTS OF MANDIBULAR ALVEOLAR PROCESSES OF DOGS

*Colhoun, Neiders and Greene, J Oral Sug 25: 122, March 1967.*

Plaster-of-paris was studied as a possible material for rebuilding of alveolar ridges by implanting the material in defects created surgically in the mandibles of dogs. In the pilot study, three dogs showed a great increase in the height of the alveolar bone in the surgical defect. In a later study, however, in which the plaster was implanted in the surgical defects in the alveolar processes of twenty-four dogs, no difference in healing or height of bone formation was detected. Plaster-of-paris did not slow healing and was resorbed within thirty days.

(Abstracted by: CAPT Howard S. Kramer DC USN.)

## PERSONNEL AND PROFESSIONAL NOTES

### WORKSHOP IN PERIODONTOLOGY

A Periodontics Workshop was held from 3-6 April 1967 at the Naval Dental School, Bethesda, Maryland, to obtain solutions to many problems that exist in the present Navy periodontal practice and to accomplish, more effectively, the periodontal mission within the Navy and Marine Corps.

Prior to the convening of the workshop, a comprehensive questionnaire was sent to all instructor officers assigned to training billets in periodontics. The answers were submitted to Dental Division, Bureau of Medicine and Surgery, where they were compiled, edited, prepared and distributed to the participants ordered to the workshop. Eighteen officers attended. The participants divided into Sub-

groups and each was assigned a problem area for development. The Subgroups, upon completion of their assignments, reconvened in General Assembly and each problem area was discussed and solutions agreed upon.

The Professional Branch, Planning and Logistics Branch, and the Preventive Dentistry Section of the Professional Branch of the Dental Division, participated in the General Assembly discussion periods. The agenda included problems from twelve broad areas: Training, Preventive Periodontics, Periodontal Research, Operating Room, Instruments and Supplies, Record Keeping and Reporting, Periodontics Syllabus, Treatment Planning, Personnel, Bulletins, Billeting and the American Academy of Periodontology meetings.

The Chairman of the four-day workshop was RADM Francis J. Fabrizio DC USNR-R. CAPT Peter F. Fedi, Jr. DC USN and CDR Gerald M. Bowers DC USN served as coordinators.

#### DENTAL TREATMENT OF VIETNAMESE CIVILIANS

During calendar year 1966, a total of 35,821 Vietnamese civilians received 69,747 dental treat-

ments. These treatments were rendered by the dental personnel of III MAF, 1st MARDIV, 3rd MARDIV, and 1st MAW as a humanitarian service in addition to their duties of rendering routine dental treatment and preventive dentistry to U.S. Navy and Marine Corps personnel. The impact on the Vietnamese people of the dramatic relief from pain, arising from dental care, was of great importance in our pacification efforts.

## NURSE CORPS SECTION

### SURGICAL TEAM (MILPHAP) IN VIETNAM

Two Navy Nurse Corps officers are assigned to the Surgical Team called MILPHAP in Vietnam. This is the Military Provincial Health Assistance Program which assists the Vietnamese civilians in improving medical and nursing practices in their hospitals. Nurse Corps officers selected for this assignment are highly qualified in surgical nursing, operating room methods, and teaching practices. They are to serve as consultants and advisors. However, in order to bring about much needed improvement, they must teach by doing. They work directly with the medical and nursing Vietnamese practitioners in an attempt to promote higher standards of patient care by introducing more up to date nursing practices.

At present the Nurse Corps officers assigned to MILPHAP are: LCDR Elizabeth A. Wilson NC USNR, LCDR Winifred L. Copeland NC USNR and LTJG Gerald G. Hasaka NC USNR (anesthetist). A letter received by CAPT Veronica M. Bulsheski NC USN from LCDR Winifred L. Copeland is printed in this edition for our readers interest.

"I received your letter pertaining to gathering historical information and pictures of this area and assignment. Both Miss Wilson and I are working toward compiling such information and pictures and plan to send them to you in the next few months. We hope that it will be useful.

"Our team arrived in Saigon on the 9th of February after some 26 hours enroute via Northwest Orient Airlines. We were taken to Koepler Army Compound in Saigon for the in-processing and the beginning of many briefings. Since there are no facil-

ities at Koepler for women, Miss Wilson and I stayed at the USAID\* guest house and commuted by taxi. The army briefings, though interesting, and well organized were more geared to the jungle fighting soldier.

"Saigon was interesting but hectic. We arrived at the beginning of TET or Vietnamese New Year, which resembles a combination of Christmas, New Years, Thanksgiving and Fourth of July. One notes the elements of the Fourth of July very readily with the firecrackers going off day and night. Apparently the Vietnamese sleep very little during this holiday. The crowds, heat and dirt of the city made the delta sound appealing. We were not too sorry to leave Saigon after a week.

"From Saigon to Rach Gia was an hour and a half by Beechcraft. The pilot pointed out the interesting landmarks enroute including the mountains along the Cambodian border. The rivers cross the delta in a very picturesque fashion and the whole area is deceptively peaceful from the air. Travel here is primarily done by air because the VC have mined many of the roads, and blown up the bridges. The pilots maintain as high an altitude consistent with safety for as long as possible because of the instances of rifle fire from the ground. Also the pilots won't land here at Rach Gia until they can recognize "friendly" transportation on the ground. Since communications of all kinds are difficult here, the pilot signals his wish to land by buzzing the town—notably the doctors' house and the hospital. Such buzzing will bring 2 or more men to the air strip, in a Jeep and with weapons.

\* United States Agency for International Development.



"Our hospital is considered to be one of the best in Vietnam. It is very old and unscreened so that the insect and rodent population on every ward is unbelievable. The wards are crowded with patient and family who set up camp during the illness. The patient furnishings on the wards consist of an iron bed with wooden slats, covered with a straw mat. The only mattresses that I have seen are in the recovery room and the postoperative ward. As soon as a patient feels well enough he "escapes"—or leaves unannounced. This is often done just before scheduled surgery, but may occur at any time. It is most disconcerting to our medical officer to find that his patient in traction has "escaped" traction and all. Apparently we have rather stiff competition from the local practitioner of "Chinese Medicine". This is the local witch doctor who gives us many "headaches" by attempting to treat diphtheria, for example, by kneading the skin on the neck of an infant. We get the child just in time for a tracheostomy but too late for much in the way of therapy.

"We have not had an American hospital administrator here since last October. I have been attending to the administrative matters with the very capable assistance of Miss Wilson. I have always felt that hospital administration would be a challenge but what a place to begin! We are currently preparing all reports, answering communications from Public Health on the number of cases of cholera, diphtheria, etc, and reporting on immunization programs in our province. Our hospital administrator is due to arrive on April 15 and we shall welcome him.

"Our nursing time is divided among the operating room, emergency room and recovery room. The number of surgical cases is going up because of war casualties and we have asked for more surgical beds and an additional operating room. The VC continue their harrassment by mining roads and blowing up local buses enroute to neighboring towns. The role

of nurse advisor is challenging, though not without its problems. The cultural setting is so different and nursing standards as we know them do not exist. Last Monday, I was privileged to attend the opening of a workshop for Vietnamese chief nurses. The workshop lasts two weeks and is an attempt to teach the chief nurse what his job is. Almost all chief nurses here are men. I hope to work closely with Mr. Cao when he returns from the workshop in the organization and administration of the nursing service here. We will have to begin from the very beginning! Mr. Hasaka is giving anesthesia and instructing two Vietnamese in anesthesia. He is also helping with administrative duties.

"Our house is located 5 blocks from the hospital and we have a car (International Scout) to drive to work. Miss Wilson and I are sharing the house with 2 USAID nurses. There is plenty of room and by VN standards the house is a good one. We are having problems with the electricity and water—in that they are both off sometimes for 12 or 24 hours at a time. The local "power and light company" turn the generators down too low and blow the fuses. We have obtained a good supply of candles, flashlights and one battle lantern. Now if we could just find a way to keep the food from spoiling. We have two very willing maids who speak only Vietnamese. Most of our food is obtained from the local economy since the nearest commissary is in Saigon. We can get some canned goods through supply channels but it is difficult.

"We have made several interesting rural health visits. One was down river to a navy junk base. The medical officer, Miss Wilson and I held sick call and were almost overrun by the villagers. We saw 200 patients and it was a very long hot day. The afternoon temperature has been between 115 and 120. We are told that this is a prelude to the monsoons."

# OCCUPATIONAL MEDICINE SECTION

## RENAL FAILURE DUE TO CARBON TETRACHLORIDE

*Thomas N. Markham MD, Ann Harbor, Michigan. JOM 9(1):16-17, January 1967.*

A man was referred to the Occupational Medicine Service by the Internal Medicine Service for evaluation of liver and renal failure following exposure to carbon tetrachloride.

### Case Report

#### Personal Medical History

This 29-year-old college instructor had been entirely well until 8 days prior to admission, when he noted mild malaise which he attributed to a viral infection. The following day he became anorexic and nauseated, and began to vomit. He continued to vomit 10-12 times in the next 2 days. By the third day he was able to drink 1-2 glasses of water over a 24-hr. period. Coincident with the vomiting, his urinary output fell to about 180 cc. during the third day. He was seen by a local physician, who felt he was dehydrated and hospitalized him on the fifth day at another hospital for hydration. Over the next 4 days he received 4 L. of fluid per day, gaining 5 lb. in weight, but he remained oliguric.

#### Environmental History

Upon admission to this hospital, history revealed that this patient had had an alcoholic intake of 1/2 to 1 pint of whiskey per day for 6 years. Eighteen hours later it was discovered that on the day of his initial symptoms, he had spent approximately 30 min. cleaning his bathroom tiles with carbon tetrachloride and consumed 1 or 2 cocktails during the cleaning process. He also reported that the bathroom was inadequately ventilated and he had noted a strong odor of carbon tetrachloride while he worked. There was no other history of exposure to toxic agents.

#### Physical Examination and Subsequent Course

Examination revealed a well-developed, dyspneic male in moderate distress. The temperature was 99.6° F., the pulse was regular at 130, and the respirations were 28. The blood pressure was 196/70.

There were scleral and subconjunctival hemor-

rhages. There was no evidence of venous distention. The breath sounds were diminished in the lung bases, and scattered coarse, moist rales were present over the anterior lower lung fields. The cardiac border extended to 13 cm. left of the midsternal line and there was a diffuse point of maximal impulse. A Grade I-VI systolic precordial murmur was heard best at the base, and a protodiastolic extra sound was present at the apex. The abdomen was distended, and shifting dullness was present. The liver was palpable 7 cm. below the right costal margin. The spleen and kidneys were not palpable, but there was bilateral costovertebral angle tenderness posteriorly. The lower extremities showed a trace of pedal edema.

The urine gave a 4 plus reaction for protein, a 1 plus reaction for glucose, and revealed 10-12 white cells and 1-2 fine granular casts in the urinary sediment. The hematocrit was 48% and the white-cell count 11,400/cc., with a normal differential. Serum electrolytes were: sodium, 125 mEq./L.; potassium, 5mEq.; chloride, 78 mEq.; and carbon dioxide, 19 mEq. The blood urea nitrogen was 140 mg./100 ml. and serum creatinine 22 mg./100 ml. An x-ray film of the chest revealed marked hilar congestion.

In view of the azotemia, the patient was placed on fluid restriction as well as a low-salt, low-protein diet and was started on peritoneal dialysis. The pulmonary congestion increased, and the following day he required phlebotomies to control pulmonary edema. During the first 14 hr. of treatment, he lost 11 lb. in weight. In the next 13 days, he continued to have severe electrolyte disturbances consisting of hypo- to hypernatremia and persistent hyperkalemia. His liver-function findings gradually improved, with the bilirubin dropping from a total of 3.8 mg. with direct fraction of 2.9 mg./100 ml. to 0.6 mg. and 0.3 mg./100 ml., respectively, during the first 3 days of hospitalization. During a similar period, his glutamic oxaloacetic transaminase fell from 204 to 36 units and his glutamic pyruvic transaminase dropped from 1,260 to 395 units. However, he remained oli-

guria, and on the tenth hospital day he developed a persistent fever ranging between 100° and 104° F. Cultures of the peritoneal dialysate grew *Proteus morganii*. He was started on large doses of antibiotics and hydrocortisone. Two days later, he went into peripheral vascular collapse and, despite all efforts, he died on the fourteenth hospital day.

One breath analysis was obtained on his tenth post-exposure day and revealed a peak in the carbon tetrachloride region of 4 ug./L. Subsequent breath samples were unsatisfactory because of the patient's condition.

A postmortem examination revealed pulmonary congestion of the left lung and marked fibrinopurulent exudate on all peritoneal surfaces. The microscopic examination of the liver indicated centrilobular necrosis, with collapse of the reticulum and slight fatty infiltrates. The kidney demonstrated a flattening of the tubular epithelium, some hyalinized glomeruli and acute passive congestion of the medulla.

#### Comment

The potentiation of carbon tetrachloride toxicity by ethanol has been recognized for many years, and numerous clinical and experimental observations have supported this action. However, the mechanism of action has not been identified. Several theories have been postulated to explain this potentiation. Guild et al. postulated the formation of an ethylchloroformate which is toxic to both the liver and kidneys. The toxicity of this compound is unknown, as yet. New et al. suggested that an alcohol-induced choline deficiency for prolonged periods may point to the source of this potentiation, but damage has been noted when alcohol and carbon tetrachloride were ingested simultaneously. Attempts have been made to relate the liver injury to the

greater concentration of lipid-soluble carbon tetrachloride within ethanol-induced fatty accumulations in the liver. However, Bahor has shown that the potentiation of toxicity is independent of liver lipids.

More recent experimental evidence suggests that carbon tetrachloride may act through stimulation of lipid peroxidation and the formation of free radicals, but this remains unproved.

Guild et al. and New et al., in presenting 39 cases of renal failure following carbon tetrachloride poisoning, observed that renal damage is most frequently associated with inhalation, while severe liver damage more frequently follows ingestion. They observed that following inhalation, although their were initial findings of liver damage in several of the cases. These findings rapidly cleared by the third day, while the anuria or oliguria frequently was not evident until the third day, with a range of 1-8 days for its appearance. All their cases deal with renal failure and, therefore, prevent determining the proportion of cases of severe renal injury to those of severe liver injury.

The case presented here appears to follow the general pattern usually seen in carbon tetrachloride poisoning involving renal failure. The exposure is frequently minimal and the patient frequently has been in good general health. He usually has a history of significant ethanol intake, generally over a prolonged period. The overall prognosis in these cases appears to be 80-90% recovery when artificial dialysis is used. Death in nearly all cases is a result of the renal failure and not liver injury.

Diagnosis—Carbon tetrachloride intoxication; acute renal failure; and acute generalized peritonitis.

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

## DUSTS, FUMES AND GASES

*W. L. Ball PhD, Accident Prevention News-Record 1st half FY 67, pages 21-24.  
Prepared by Dept of Army, Office Chief of Engineers Safety Office.*

### *Dusts and Fumes*

The detection, measurement and control of dusts and fumes, both being airborne particulates, may be considered together. All dusts and fumes are potentially harmful although some appear to cause only nuisance and discomfort. Others initiate allergies that may produce symptoms such as hay fever and

skin or digestive disorders. Minerals such as silica and asbestos may cause incurable lung damage. Chemical dusts and fumes may be irritating, corrosive or poisonous.

Dusts may be of animal, vegetable, or mineral origin. Their physiological action is influenced by their state of division. There is a particle of critical size which is retained in the lungs. Smaller particles



are exhaled, and larger ones are trapped in the nose and throat.

Technical advances in drilling, excavating, and grinding have increased dust control problems because the machinery used produces more and finer dust than did hand methods and, even with modern ventilation systems, the dusts in the air may not be entirely removed.

Metal fumes present somewhat similar problems to those of dust even though their origin is different. At high temperatures metals volatilize and form finely divided particles called fumes. Except for the very toxic metals such as chromium, arsenic, lead and beryllium, metal fumes are not a serious toxicity hazard. Although metal fume fever may result from welding and torch cutting it is of short duration.

The action of toxic metals on the body depends on the form in which they occur. Metallic chromium, for example, is harmless but when it is in solution as chromate it can cause painful ulcers where it contacts the skin. Its solution as a mist may perforate the nasal septum (the dividing wall inside the nose), if breathed. Some chromium compounds are toxic; others are not. When combined with organic compounds metals tend to be more toxic. Striking examples of this phenomenon are the organo-phosphorous insecticides, lead tetraethyl and the organo-mercuric fungicides.

#### Assessing Exposure

In assessing the exposure to dusts and fumes the investigator will require such information as:

1. Chemical composition of the dust or fume
2. Size of dust and fume particles
3. Concentration of respirable dust or fume in the worker's breathing zone
4. Number of exposures and their total length
5. Severity of the effort (heavy work increases the depth of breathing)
6. Efficiency of protective devices and measures.

#### Control Measure

The ideal first line of defense against dust and fumes is efficient ventilation with local exhausting that removes it at source. Water supplied at the point of cutting or impact of a tool is a valuable supplement to ventilation. Provision of dust masks does not answer the personal protection problem because workers often find them unbearable to wear. All methods of dust control should be supplemented by dust assessment and medical examination of the workers.

#### Gases

Every year hundreds of gassing accidents occur. Carbon monoxide from internal combustion engines and heating devices is the most frequent cause but death may follow gas leaks in mining, chemical and other operations.

The poisonous gases are the most dangerous of the chemical toxicants not only because they are inherently toxic but also because their gaseous form allows them to escape from any vessel that is not completely tight and to diffuse into all corners of their containing space.

Medically, gases can be considered in three groups: simple asphyxiants, biological poisons and irritants.

##### 1. *Simple Asphyxiants*

The simple asphyxiants dilute the atmospheric oxygen to the point where it will no longer support respiration. Nitrogen, methane and carbon dioxide are in this group. Death occurs fairly rapidly when the oxygen content of the air is depleted below half the normal level of 20.5 percent by volume.

Nitrogen is not a serious hazard in chemical or manufacturing industries. In mining and the sinking of wells and shafts it is, however, a potential danger.

Methane not only displaces atmospheric oxygen but, with air, may form an explosive mixture. It is found in coal mines where it was formerly known as "fire damp".

Carbon dioxide asphyxiation is a danger after fires, particularly in mines, and from the slow biological combustion that occurs in stored grain. It gives more warning than nitrogen because headache starts when the dangerous level is reached.

##### 2. *Biological Poisons*

Carbon monoxide is the chief killer of the biological poisons because it occurs so widely. Among its common sources are: electric furnaces, blast furnaces, gas manufacturing plants, oil refineries, charcoal ovens, refuse plants, silver and coal mines. Anyone who works where power or heat is being generated by a combustion process may be exposed to carbon monoxide. Motors running in unventilated spaces or with faulty exhaust systems are a frequent source of carbon monoxide poisoning. Persons making long automobile trips may receive significant exposure to this gas.

Carbon monoxide is taken up about 200 times faster by the blood stream than is oxygen. This means it will steal more and more of the blood's oxygen capacity. Also the haemoglobin gives up the carbon monoxide with difficulty.

Surveys have shown that carbon monoxide lowers the visual threshold, especially if associated with an oxygen deficiency. Even the small amount of carbon monoxide inhaled by a smoker may cause slight impairment of visual acuity.

Hydrogen sulphide is a biological poison that paralyzes the respiratory system. Unfortunately the olfactory nerves become insensitive to its strong odour of rotten eggs and toxic levels may not be noticed. Permanent injury is infrequent in non-fatal cases. The gas is found in the sulphur dye industry, tanneries, the production of carbon disulphide and in oil refining. It occurs in natural gas and petroleum products and in some mining and ore refining operations. At 50–100 ppm it irritates the eyes and throat. A half hour exposure to 500 ppm causes dizziness and headache followed by unconsciousness. At around 1,000 ppm death is instantaneous. If exposure to hydrogen sulphide cannot be avoided, a mask that protects the eyes while preventing inhalation of the gas is necessary. In severe poisoning artificial respiration supplemented with carbon dioxide and oxygen may be necessary.

Hydrogen cyanide, with its odour of bitter almonds, is one of the most deadly poisons known. It may be used completely sealed only, in industry. It is released from its salts by acids. Fortunately it is liquid below 26° C. It has caused comparatively few injuries in industry because its poisonous nature is well known and precautions are taken.

The asphyxiant action of hydrogen cyanide differs from that of carbon monoxide in that it decreases the supply of oxygen to the tissues. Poisoning may

follow absorption through the skin or cuts and abrasions or inhalation and ingestion.

First symptoms are headache, nausea and dizziness. Odour is not a quick enough warning of a dangerous concentration.

Cyanides are used in silver and gold extraction, case hardening, pickling, electroplating and photography. The gas is also used as an insecticide or fumigant.

### 3. Irritant Gases

Exposure to irritant gases causes edema, necrosis and inflammation rather than the burns that result from contact with acids. Because high concentrations of irritant gases can produce damage quickly, duration of exposure is not as significant as it is with the asphyxiant gases. Very soluble irritants, such as ammonia, attack the mucosa of the mouth and nose. Moderately soluble ones, in low concentration, may affect only the eyes. Chlorine is an example of this type. Gases of low solubility (phosgene and nitrogen oxides) cause little irritation of the upper respiratory tract but can damage the lungs. The more soluble irritants are less dangerous because the victim will not long tolerate them if escape is possible. The less-soluble ones penetrate deeply because the individual is unaware of their presence.

Among their irritants may be included ammonia, acrolein, formaldehyde, chlorine, hydrogen fluoride, ozone, nitrogen dioxide, sulphur dioxide and phosgene. Recently the exhaust products from motor vehicles have been receiving attention. Under the action of sunlight, the hydrocarbons and oxides of nitrogen react to produce ozone, ozonides, peroxides and other oxidants that cause eye irritation, reduce visibility and vegetation damage.

## THE COMMITTEE ON TOXICOLOGY AND THE ADVISORY CENTER ON TOXICOLOGY OF THE NATIONAL RESEARCH COUNCIL

*Ralph C. Wands, Director, Advisory Center on Toxicology,  
Ltr of 21 March 1967 to Dr. Rosenwinkel.*

### Historical

The Committee on Toxicology was organized in 1947 by Dr. W. Albert Noyes, Jr. as Chairman of the Division of Chemistry and Chemical Technology. It was intended to be a domestic counterpart to the *Commission de Toxicologie* of the International Union of Pure and Applied Chemistry. The first

members were Dr. H. H. Schrenk (chairman), Dr. L. T. Fairhall, Dr. D. O. Hamblin, Dr. D. D. Irish, Dr. J. H. Sterner, Major General Alden H. Waitt, and Dr. W. P. Yant. Dr. H. C. Hodge, Dr. A. J. Lehman and Colonel John Wood were also appointed in 1949.

The Committee promptly recognized that in addition to its duties as a spokesman in international affairs for the U.S. professions of toxicology and industrial hygiene, there were many important domestic needs for its services. Foremost among these, and in keeping with the fundamental purpose of the National Academy of Sciences-National Research Council, was the need of the Armed Forces for advice and assistance on problems of toxicology. Over the years this aspect of the Committee's activities has grown to include the needs of other Federal Agencies. These domestic services now occupy a considerable portion of the Committee's attention with very little being devoted at present to international affairs.

It was suggested in 1950 by one of the Committee members that a "unified industrial hygiene and toxicology center" be established. In June 1953 Admiral C. J. Brown, Acting Surgeon General, U.S. Navy, formally proposed that the Committee establish a center to inform and advise the Armed Forces on matters pertaining to toxicology. A memorandum of agreement between the Army, Navy, Air Force, and Atomic Energy Commission was executed on 26 June 1956. The National Aeronautics and Space Administration, the Coast Guard, and the Division of Air Pollution, U.S. Public Health Service, have subsequently joined the roster of fiscal sponsors of the Center.

The Center began operating in January of 1957 when Dr. Harry W. Hays took office as its first Director, a position which he filled until July 1966.

#### Committee on Toxicology

The Committee on Toxicology serves the National Research Council and serves as a spokesman representing a consensus of U.S. toxicology experts. In addition it has the following specific responsibilities to the fiscal sponsoring agencies and the Center:

- a. Respond to questions of broad policy brought to it through the Center by the sponsors.
- b. Recommend interim operating allowable concentrations of air contaminants, especially in cases where data are insufficient to enable official agencies to act.
- c. Recommend initiation of specific toxicological testing or research.
- d. Recommend elimination of duplication of toxicological research when unnecessary duplication is discerned.

- e. Provide advice on, and if necessary, participate in field studies presented by a sponsor through the Center.

- f. Advise the Division of Chemistry and Chemical Technology with regard to scientific policies and direction for the Center.

In carrying out these responsibilities the Committee on Toxicology meets at least once a year with all the liaison representatives of the sponsors for formal and informal discussion. It meets at other times as often as required by the problems presented, usually three to four times a year. Members are appointed for a definite term of office by the Chairman of the Division of Chemistry and Chemical Technology. They are chosen for their recognized professional ability, judgement and integrity. They bring to the Committee's deliberations a technical competence and objectivity permitting a dignified and unbiased perusal of the problems presented. They serve without compensation in response to a personal sense of patriotic and professional duty. They are only reimbursed for expenses incurred in conjunction with Committee activities.

#### Sponsoring Agencies

The responsibilities of each sponsoring agency include the following:

- a. Annual review of the budgetary requirements of the Committee and the Center and provision of fiscal support. This is accomplished through designated representatives to the fiscal sponsors committee. Funds are administered through the Office of Naval Research.

- b. Annual designation of a liaison representative serving as a formal channel for the communication of official inquiries between the various operating units of the sponsor and the Center.

- c. Contributions to the Center of toxicological information available within the sponsoring agency providing the Center conforms to the applicable security regulations.

The liaison representatives present to the Center requests for assistance from their agency. They also distribute within their agency the replies from the Committee and the Center. They arrange, wherever feasible, for automatic distribution to the center of toxicological information developed within the agency and assist the Center when necessary in obtaining other pertinent data.

The Fiscal Sponsors Committee usually meets an-



nually prior to expiration of the current contract in order to provide for uninterrupted service by the Center.

#### Advisory Center on Toxicology

The scientific policies and direction of the Center are the responsibility of the Division of Chemistry and Chemical Technology with the advice of the Committee on Toxicology and in consultation with the Division of Biology and Agriculture and the Division of Medical Sciences.

The responsibilities of the Advisory Center on Toxicology are basically those of providing a central source of information and technical staff to enable the Committee on Toxicology to advise the sponsors on scientific and technical questions relating to the health hazards to military and civilian personnel from the toxic properties of sponsors' materials. Specifically the Center is:

- a. A source of information and advice to supplement the toxicological activities of the sponsors.
- b. A clearinghouse for storage and exchange among the sponsors of unclassified and classified toxicological information and evaluations of such data from governmental, industrial, academic and other sources.
- c. A source of suggestions for declassification and publication of toxicological information.
- d. A medium of communication between the sponsors and the Committee on Toxicology.
- e. An aid to the Committee by providing appropriate toxicological data from its collection and by providing administrative support.
- f. A recipient and custodian of proprietary toxicological information from commercial sources as a basis for recommendations.
- g. An agency to perform such other functions related to toxicology as it may appropriately be called upon to do and which do not interfere with the foregoing primary responsibilities.

In performing its share of these responsibilities the Advisory Center on Toxicology maintains a small, efficient staff of professional, technical, and clerical personnel assisted by the staff of the Academy-Research Council. The Center maintains thorough coverage of the toxicological literature for input to its files by subscriptions and interlibrary loans. Similar study of toxicological information developed in governmental laboratories is accomplished by acquisition of the reports when issued. Information in private laboratories is solicited when

needed. These sources are supplemented by personal contact through visits and participation in meetings whenever feasible. Close contacts are also maintained with the liaison representatives so that communication regarding their problems may be prompt and mutually understood.

The Center does, on occasion, accept requests for assistance from other governmental agencies and private enterprises with the proviso that such services are complementary to the interests of the sponsors and do not interfere by an undue requirement of time with the Center's responsibilities as outlined above. The Center frequently finds that other federal agencies and private corporations are excellent sources of needed information and thus such cooperation is mutually beneficial to all concerned.

#### PHYSICIANS, HYGIENISTS WARNED ON ACCIDENTAL OZONE POISONING

*Environ Health Ltr 6(2): 3, January 15, 1967.*

The Public Health Service has warned that there is no exposure to ozone in industry without some risk to health and the danger of undesirable health effects "far outweighs any benefits presumed to be derived from the industrial or institutional use of ozone for control of odors or bacteria in air."

Even in low concentrations, PHS notes, inhaled ozone may cause dryness of the mouth, throat irritation, coughing, headaches, and pressure or pain in the chest, followed by difficulty in breathing. Varying in individuals, ozone may impair the sense of smell, disguise other odors with a continuous odor of ozone, alter taste sensation and produce neurological impairments.

The greatest use of ozone is in the suppression of mold and bacterial growth, such as in the treatment of drinking water supplies and industrial wastes, and the sterilizing of food products. Other uses of ozone include the rapid aging of wood, the aging of liquor, rapid drying of varnish and printing ink, production of peroxides, bleaching of oils, waxes, textiles and papers and deodorizing of feathers.

"There are two general sources of exposure to ozone", PHS cautioned. "Ozone is produced by the discharge of high tension electrical current in air or oxygen, such as from electrical equipment, welding operations, ultraviolet light spectrographs and plasma jet operations. Exposure to ozone may also occur from ozone generators developed for use in industrial processes. Examples of this type include ozone produced for use as a disinfecting germicide,

or to control growth of fungus, molds and bacteria in food processing.”

For workers exposed to ozone, medical supervision, including preplacement and periodic medical examinations, is a necessity, PHS declares. All prospective workers should be given a complete preplacement medical exam, including chest x-ray. Those with pre-existing diseases of the lungs or heart, and those highly susceptible to respiratory infections, should not be exposed to ozone. Workers

repeatedly exposed to ozone should have annual checkups, PHS says.

“The injured worker should be removed from exposure immediately,” it states. “He should lie down, remaining at rest until he can be seen by a physician. In cases of acute exposure, the examining physician may hospitalize the worker until the danger of severe lung damage or possible pneumonia has passed.”

## EDITOR'S SECTION

### MEDICAL SERVICE CORPS OFFICERS ACADEMIC ACHIEVEMENT

<u>Name</u>	<u>Duty Station</u>	<u>Degree</u>	<u>Institution</u>
CDR J. W. Wolf (with distinction)	NH, Bethesda	BA, (Social Sc.)	The George Washington University (GWU)
LCDR W. A. Andersen	BuMed, Code 414	MS, (Fin. Mgmt.)	GWU
LCDR J. S. Bailey	NH, St. Albans	BBA	C.W. Post College
LCDR P. J. Collier	NSHA, Bethesda	MS, (Pers. Mgmt.)	GWU
LCDR W. J. Crodick	9th MarAmpBrigade	BS, (Gen. Studies)	GWU
LCDR R. G. Devine	BuMed, Code 462	BA, (Social Sc.)	GWU
LCDR C. A. Holston	NH, Bethesda	MS, (Pers. Mgmt.)	GWU
LCDR F. J. Sickels	DDO, Com 5	BS, (Gen. Studies)	GWU
LT R. R. Bolton	NMS, Bethesda	MBA	GWU
LT J. S. Cannizzaro	NNMC, Bethesda	BA, (Social Sc.)	GWU
LT Harlan D. Foster	5th MarDiv	BBA	GWU
LTJG D. K. Bain	USS REPOSE	BA, (Social Sc.)	GWU

Currently there are 83 Medical Service Corps officers assigned to full-time training which includes 11 doctoral and 12 Master's degree candidates. This semester 165 Medical Service Corps officers are sponsored by BuMed in part-time, off-duty courses of instruction in a degree program. It is estimated that at least 30 more officers are pursuing their studies under other programs. Twenty-six Medical Service Corps officers received academic degrees during the past year. Much of this was accomplished on a part-time, off-duty basis.

A significant number of Supply and Administration officers are within 15-30 semester hours of receiving their baccalaureate degrees. Continued efforts in this area are strongly encouraged.

The following data illustrates a significant increase in average number of Medical Service Corps officer participation in part-time, off-duty courses of instruction. Approximately 98% of these consistently have been officers of the Supply and Administration Section.

<i>FY</i>	<i>Average number enrolled per semester</i>
1959	34
1960	55
1961	60
1962	85
1963	143
1964	154
1965	146
1966	148
1967	165

In evaluating this data, consideration must be given to the fact that a large number of Supply and Administration officers have been assigned to operational billets where enrollment in formal academic programs has not been possible.—MSC Div, BuMed.

### NAVAL RESERVE MEDICAL COMPANY 9-4 BANQUET

Mission of Medical Company 9-4 was accomplished on 28 January 1967. Obstructions afforded by inclement weather conditions at Great Lakes Training Station obviated the attendance of honored guests and military inspectors. Thanks to a host of understanding officers in the area the obstructions were met and overcome. COL Hardy Hay made an excellent and timely presentation of the Vietnam sit-

uation, showing the movie "The Corpsmen", and added great color to the occasion. Many of his remarks were addressed to Ensign Company and their wives. CAPT David Bell, CO of the Training Center, as the Commandant's designee, conducted the flag presentation ceremony with despatch and excellence.—CO, Navresmedco 9-4, Kansas City, Missouri.



*Back row:* RADM Switzer USNR, Mrs. Richard Kiene, CAPT D. Bell, Mrs. Hardy Hay, CAPT Byers USNR, COL Hay, Mrs. Switzer, RADM Kiene USNR, Mrs. Philip Byers.

*Front row:* CDR Joseph Sasano and Mrs. T. Jones.—Lyman Photo, Kansas City, Mo.



## NAVAL HOSPITAL RECEIVES THEIR 5,000TH PATIENT

With the admission March 30th of PFC James D. Glor USMC, the U.S. Naval Hospital, Yokosuka, Japan received the hospital's 5,000th patient from Southeast Asia.

Marking the occasion for both PFC Glor and the hospital was the presentation to the young Marine of a plaque bearing the hospital shield and the best wishes for a speedy recovery from the hospital's

Commanding Officer, CAPT F. P. Ballenger MC USN. Following the presentation PFC Glor enjoyed a steak dinner and shared a large cake with other patients on the ward.

PFC Glor, the son of Mrs. Donald L. Glor of Batavia, New York, entered the Marine Corps in June of 1966.—CO, U.S. Naval Hospital, Yokosuka, Japan.



PFC James D. Glor USMC, arrives at the Fleet Activities, Yokosuka, Japan Heliport March 30th prior to his admission to the Naval Hospital.—Official U.S. Navy Photograph.

### RUFUS J. PEARSON, JR. BECOMES REAR ADMIRAL

Dr. Rufus J. Pearson, Jr., who succeeded Vice Admiral George W. Calver as Attending Physician at the Capitol, Washington, D.C., became Rear Admiral Rufus J. Pearson, Jr. MC USN on 22 March 1967.

Rear Admiral Pearson is a graduate of the Emory University School of Medicine, Atlanta, Georgia. He was commissioned Lieutenant (junior grade) in the Medical Corps of the U.S. Naval Reserve in 1942 and transferred to the U.S. Navy on 21 June 1951.

Previous duty stations have been the Recruiting Station, Jackson, Mississippi; Armed Forces Induction Station, Hattiesburg, Mississippi; Evacuation Hospital, Milford Haven, Wales; Naval Air Technical Training Center, Jacksonville, Florida; Naval Hospitals, Jacksonville, Florida; Beaufort, South Carolina; Bethesda, Maryland; Charleston, South Carolina, and Portsmouth, Virginia. After a course of instruction in cardiology at the Massachusetts General Hospital under Dr. Paul D. White and Dr. Edward Bland he was chief of the Cardiology Section at the Naval Hospital, Bethesda where he aided in instituting the Cardiovascular Laboratory and the residency



RADM Rufus J. Pearson, Jr. MC USN

training program in Cardiology. His last duty, prior to his assignment to the Office of the Attending Physician at the U.S. Capitol, was as Professional Assistant to the Commanding Officer and Chief of Medicine at the Naval Hospital, Bethesda.

Rear Admiral and Mrs. Pearson (formerly Emily Kimmelman of Atlanta, Georgia) have two children, Virginia Randolph Pearson and Rufus J. Pearson III.

#### LETTER FROM GRANDSON OF FORMER SURGEON GENERAL JONATHAN M. FOLTZ

"My physician, Dr. Samuel M. Hauck, has just given me his copy of the February 24th Medical News Letter which has a photograph and a very good short biography of my grandfather, Surgeon General Jonathan M. Foltz on the cover.

"Would it be possible for me to get a few copies of the Medical News Letter to send to other

members of the family. One of them, a physician, has just returned from a tour of duty with the army in Berlin. Another is a nurse with the S.S. Hope in Colombia, South America.

"The old boy is a sort of legend in the family because his determination so frequently got him into trouble. Such as his confrontation with the captain of the Frigate Raritan in 1846 off the coast of Mexico who would not send a foraging party ashore to bring back fresh vegetables, limes and lemons needed to combat the scurvy which eventually incapacitated so many of the crew that there were not enough able-bodied seamen to keep the ship in action. I treasure, of course, the "testimonial" to him from 233 "Petty Officers, seamen and marines" of the Raritan."

*This letter is published with permission of COL F. S. Foltz in the hope that relatives of other Surgeons General will be stimulated to send us biographical material which may not be included in the sketches which are available to us.—Editor.*

#### RESERVE NURSE CORPS SYMPOSIUM

The annual Military Symposium for Reserve Nurse Corps Officers shall be conducted at the Naval Medical School, NNMC, Bethesda, Maryland during the period of 31 July to 11 August 1967. This year's program is planned to assist the Nurse Corps officer in understanding medical developments and nursing implications in current military operations. Reservists desiring to attend this course should submit their applications to the Commandant of the Naval District in which they reside. Quotas are limited so interested personnel should submit request early. For further information consult the catalog of Active Duty for Training, NavPers 93661.—Reserve Sec, BuMed.

## KEY WEST HIGH SCHOOL CONCHETTES VISIT NAVAL HOSPITAL, BETHESDA



—Official U.S. Navy Photograph

A happy and smiling patient, PFC Stephen K. Smith USMC, is obviously enjoying himself as he is surrounded by five pretty members of the Key West High School Conchettes in front of the Naval Hospi-

tal, Bethesda, Maryland, following their performance of a routine to the tune of "Beguine" which was dedicated especially to PVT Smith, a native of Florida.

### VIETNAM MEDICAL RESEARCH CONFERENCE AT NAMRU-2

Military medical research problems were discussed at a recently concluded two and a half day symposium held at NAMRU-2, Taipei, Taiwan. Attending the conference were Commanders of six Medical Research Laboratories, directly or indirectly involved in health problems of U.S. personnel in Vietnam. The conference, the first of its kind to be held in the Far East, was convened for the purpose of discussing coordination of research effort, possible areas of collaboration, and means of exchanging information in regard to biomedical research, disease surveillance and preventive medicine in Vietnam.

Discussions centered on infectious diseases with particular emphasis on means of identifying febrile illnesses and malaria which together account for more casualties than enemy action.

Attending the conference, which was hosted by CAPT R. H. Watten MC USN, Commanding Officer at NAMRU-2, were COL Paul Musgrave MC USAF, Commanding Officer of the 5th Epidemiological Flight, Manila; COL Stafano Vivona MC USA, Director of United States Army Medical Component SEATO Research Laboratory, Bangkok; LCOL Joseph Metzger MC USA, Commanding Officer of 406th Medical General Laboratory, Camp Zama, Japan; LCOL Garrison Rapmund MC USA, Officer in Charge, United States Army Medical Research Unit, Kuala Lumpur; LCOL Harry Dangerfield MC USA, Director of the U.S. Army Medical Research Team, Saigon; LCDR Thomas Byrd MC USN, Officer in Charge, U.S. Navy Preventive Medicine Unit, NSA Station Hospital, DaNang; and LT Stephen Berman MC USNR, Medical Officer, PMU, DaNang.—Public Affairs Office, BuMed.



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