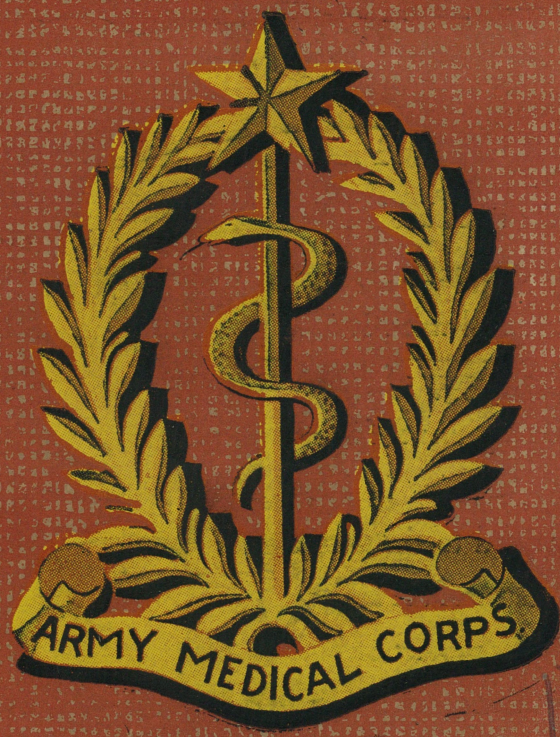


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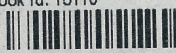
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CONTENTS.

	PAGE
Clarification Reaction for Syphilis, by Major S. O. Waller and Dr. S. Sen, M. B. (Calcutta)	1
✓ Epidemic Hemorrhagic Fever From 406th Med. Gen. Lab. ...	8
Hemopoietic Changes with Chloromycetin Therapy, by Lt.-Col. H. B. Lal & Major L. C. Aggarwal.	11
✓ Preliminary Report on an investigation into the influence of Temperature & Humidity on the Incidence of Dysentery and Diarrhoea, by Major M. C. Sanyal and Mr. P. Krishnaswamy-	17
✓ A Note on Anopheles Varuna, by Major V. P. Jacob and Capt. R. D. Mitra.	22
A case of Foreign Body in the Oesophagus with Post Anesthetic Respiratory Crisis, by Capt K.M. Soparkar. ...	24
Medico-Legal Disability Pensions, by Lt.Col. V. Sivasankaran. ...	28
- Editorial	32
Adm : Notes	35
Letters to the Editor.	37
News Letter from A.M.C. Centre (N) Lucknow	43
Record Office Bulletin (English)	46
Record Office Bulletin (Roman Hindi)	47

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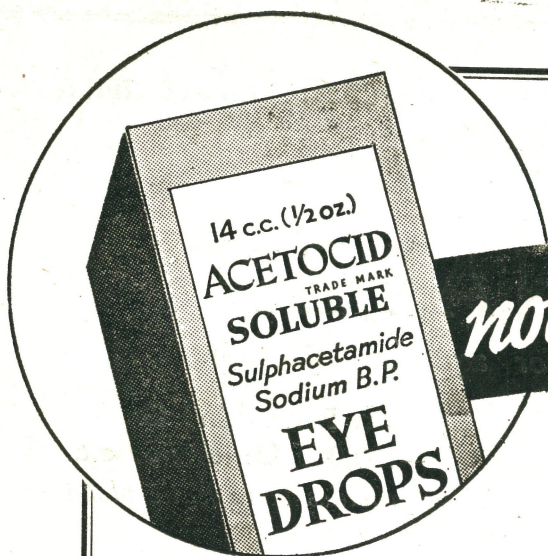
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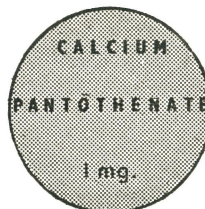
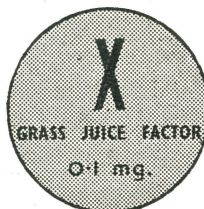
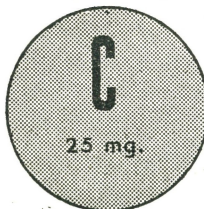
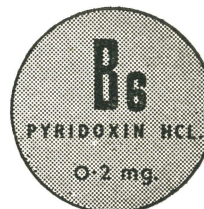
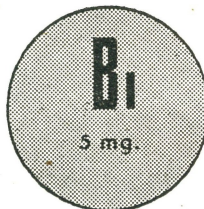
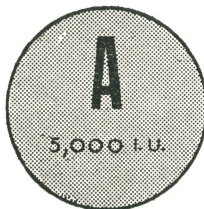
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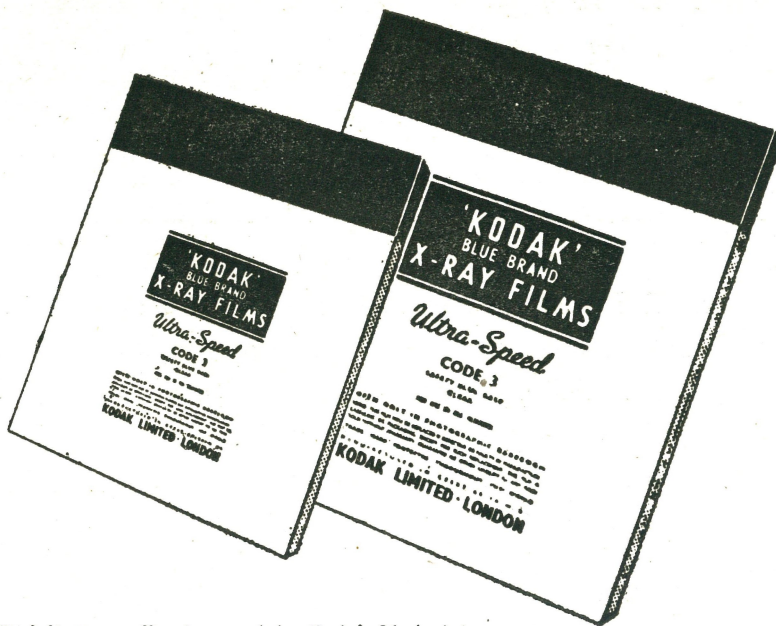
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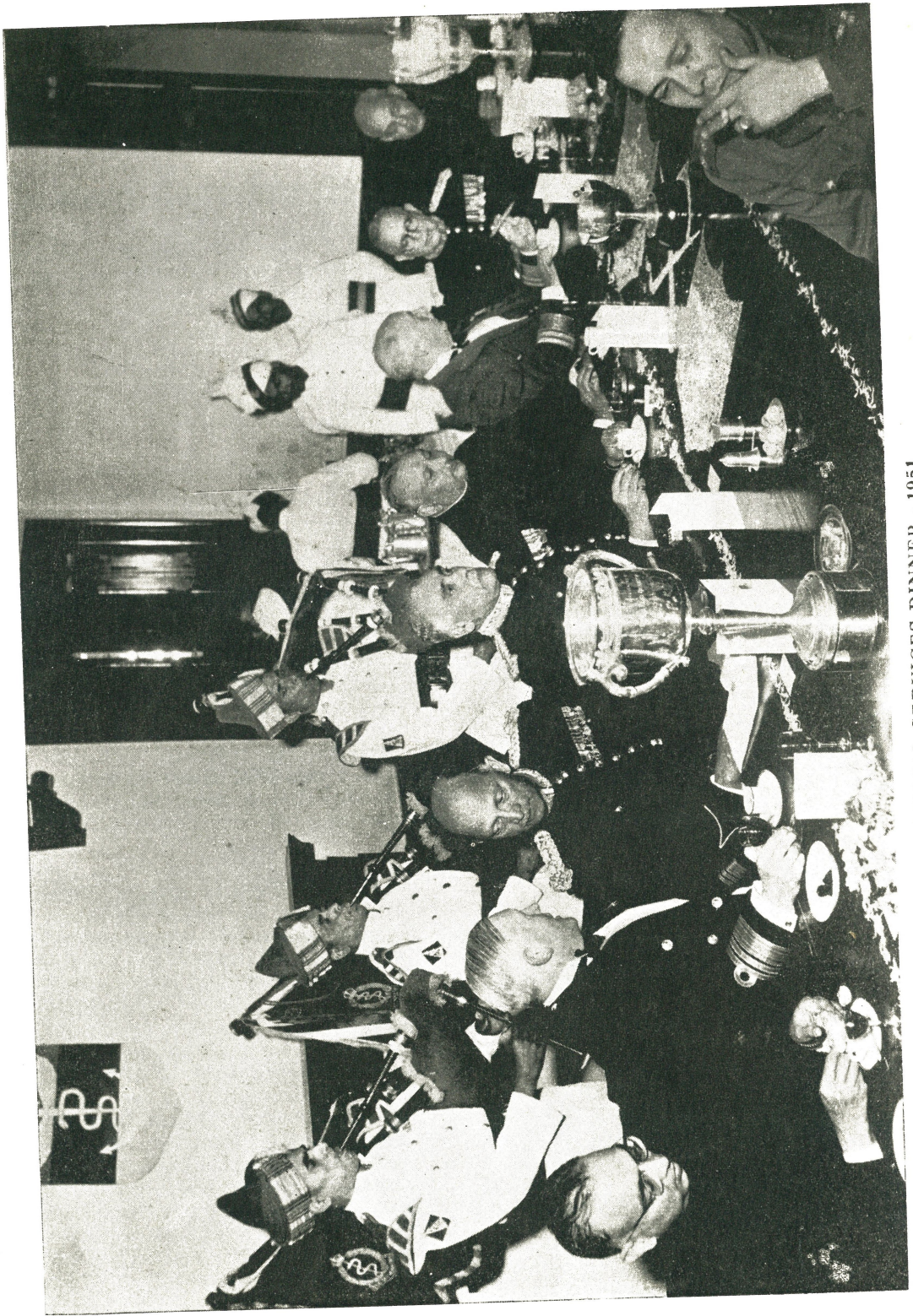
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MEDICAL SERVICES DINNER - 1951

Clarification Reaction for Syphilis

(A modification of Meinicke's Test with F. R. C. Antigen compared with the standard Wassermann and Kahn Reactions in a series of 1500 sera, 50 parasite positive Malaria sera and 50 Leprosy sera).

by

Major S. O. WALLER, M.B.B.S., (Madras), A.M.C.,
Specialist in Pathology, Military Hospital, Calcutta.

and

Dr. S. SEN, M.B. (Calcutta)
Asst. Surgeon Superintendent & Pathologist,
B. I. S. N. Co. Ltd. Calcutta.

Wassermann and Kahn Reactions have been and still continue to be universally employed as the serological test in the diagnosis of Syphilis. Of the various Clarification tests used in the past Meinicke's Clarification Reaction is the only one that gained some foothold in Laboratory procedures. Although originally described by Meinicke in 1922, improved by him in 1932 and finally modified by Ford Robertson and Colquhoun in 1939, it still continues to be relatively unknown.

The practical value of the F. R. C. Test has been adequately borne out in the work of Ford Robertson and Colquhoun (1940), Colquhoun, Kyles and Rannie (1945), Besseman and others (1947) and McMenemy and Whitehead (1949).

Ford Robertson and Colquhoun's modification of Meinicke's Clarification Test is gaining more popularity amongst Laboratory workers all over the World. One of us (Dr. Sen) worked with Ford Robertson and Colquhoun in their Shelley Road Laboratory, Glasgow, in 1949, and was greatly impressed by the simplicity of their technique, the easy reading and interpretation of results. It is considered that this test could with advantage be employed as a diagnostic test of syphilis in our country.

The W. R. and Kahn Tests were performed by the routine methods employed in all Military Laboratories, the biological reagents for which were supplied by the Pathology Department, AFMC Poona. The Clarification Test, which is the main object of this paper to describe, has followed in its entirety, the procedure laid down by Ford Robertson and Colquhoun in their brochure of January 1945, an extract of which is given below :-

Technique

Apparatus :

1. Small test tubes 60 mm x 7 mm internal diameter.
2. Wooden racks to hold 12 such test tubes (3 for each serum in each rack). The racks should have a serial number at each third hole.

Measurement of racks - Base $10\frac{1}{4}$ " x $1\frac{3}{4}$ ", Top 1" wide. Distance between upper surface of base and top 2".

3. Graduated pipettes - (a) Two 1 cc pipettes; one for sera, and one for antigen, (b) One 5 cc pipette for diluted antigen (c) One 10 cc pipette for measuring saline.

4. Six stout test tubes 6" x $\frac{3}{4}$ " for preparing Antigen Saline emulsion.
5. Water bath at 56 degrees centigrade.

Reagents

1. F. R. C. Antigen (100 CCs will suffice for 650 tests). This can be had from the West of Scotland Neuropsychiatric Research Laboratory, 10 Shelley Road, Glasgow, at an approximate cost of £.1 per 100 ccs.
2. A. 3%, 1.5% and 1% solution of Annalar Sodium Chloride.
3. Patients serum, unheated.

Test Proper

1. Pipetting of the sera - Set up the tubes in the racks. With the pipette marked sera deliver 0.3 ccs to the first, 0.2 ccs to the second and 0.1 cc to the third tube. To prevent contamination of any serum by traces of those previously pipetted, rinse the pipette by drawing and blowing the 0.85% saline three times and then finally draining the pipette for a few seconds by holding the tip against a clean piece of filter paper.

2. Preparation of Antigen Suspension and the quantity required for each Test - The Saline Antigen Emulsion is prepared by mixing the proper quantity of antigen with three different concentrations of Annalar Sodium Chloride (3%, 1.5% and 1%) making three different emulsions marked A, B and C. In the test racks are three tubes for each serum and each tube gets 0.5 cc of Antigen emulsion, the first from A, the second from B and the third from C. The amount of Saline and Antigen to be taken for the emulsion is calculated as follows - The quantity of saline of each strength will be half the number of tubes expressed in ccs. The quantity of Antigen will be 1/10th the volume of saline.

Of the six big test tubes, three are marked A, B and C for Saline and three marked a, b and c for Antigen. If there are altogether 20 sera to be tested then 10 ccs of 3% Saline is taken in tube A, 10 ccs of 1.5% Saline is taken in tube B, and 10 ccs of 1% Saline taken in tube C. 1 cc of Antigen is placed in each of the tubes marked a, b and c. The tubes containing Saline are

placed in a water bath and when the temperature of the saline has reached 56°C (this is done by placing the thermometer in an extra tube of saline) the tubes containing Antigen are placed in the Water bath and all left there for exactly 2 minutes. (It is important that the Antigen be heated at 56°C for exactly 2 minutes irrespective of the quantity).

The tubes are then taken out of the bath and the salt solution is poured on to the corresponding Antigen as rapidly as possible, repeating the process three times. The resulting suspension which is white and opaque is pipetted without delay, otherwise it tends to lose its sensitivity for syphilitic serum.

The Antigen emulsions are distributed out of a 5 cc pipette-0.5 cc of A to the first tube, 0.5 ccs of B to the second tube and 0.5 ccs of C to the third.

After this each tube is taken out of the rack, held horizontally and shaken well to ensure thorough mixing of Serum and Antigen Emulsion, and then returned to the rack.

Three tubes each containing 0.5 ccs from each of the emulsions marked A, B and C are put up with the tests and constitute the controls. The racks are kept inside a cupboard away from draft at room temperature for 16 to 24 hours after which the results are read.

Reading of Results

The intensity of the reaction is measured by the extent of clarification of the mixture in each tube. Consequently it is necessary to focus attention not only on the supernatant fluid but also on the deposit at the bottom of the tube. Usually a completely clarified tube shows a deposit at the bottom, and an opaque unclarified one shows a small clear button. There are intermediate reactions in which tubes show haziness of various gradations, with large or small buttons, which should be duly recorded. It is customary to set up three control tubes but occasionally these tubes show precipitates. This is generally due to contaminations by salts of heavy metals but in the test proper the high protective power of the serum prevents such interference, and if in the control tubes such reactions occur, they should be ignored.

DEGREES OF CLARIFICATION			SYMBOL	INTERPRETATION	
Tube A	Tube B	Tube C		1	2
1. Partial	Complete or Partial	Complete	+ + + - or - + + + - - -	Very strong	Very Strong
2. Complete	Complete	Complete	+ + +	Strong Positive	
3. Complete	Complete	Partial or None	+ + + or + + -	Moderately Strong Positive	Positive
4. Complete	Partial or None	None	+ + - or + - -	Weak Positive	
5. Partial	None	None	+ - - - - -	Doubtful	
6. None	None	None	- - -	Negative	

Excepted in treated cases partial positive reactions seen in No. 5 are designated doubtful. These are of limited diagnostic significance, but are nevertheless of importance since they always call for further investigation.

Serum for Clarification tests should never be heated; inactivated sera always give positive results. On one occasion we carried out the test with 18 inactivated sera and the results were all positive.

ANALYSIS OF THE RESULTS OF 1500 CASES.

AGREEMENTS	PARTIAL AGREEMENTS	DISAGREEMENTS.
a. WR — Positive } Kahn — Positive } 244 FRC — Positive }	a. WR — Positive } Kahn — Negative } 39 FRC — Positive }	WR — Positive } Kahn — Positive } 4 FRC — Negative }
b. WR — Negative } Kahn — Negative } 1058 FRC — Negative }	WR — Negative } Kahn — Positive } 11 FRC — Negative }	WR — Negative } Kahn — Negative } 107 FRC — Positive }
	WR — Negative } Kahn — Positive } 22 FRC — Positive }	
	WR — Positive } Kahn — Negative } 15 FRC — Negative }	

Of the tests which showed non-verifiable and are considered negative only partial agreement, 58 were proved. The results have been analysed as follows:—

		CORRECT		FALSE	
		Positive	Negative	Positive	Negative
FRC	...	45	13	16	13
WR	...	36	11	18	22
Kahn	...	22	18	11	36

Of the 107 cases in which the F.R.C. Test alone was positive, 67 were treated cases of Syphilis in which the W.R. and Kahn had become negative (9 of these subsequently gave positive W.R. and Kahn reactions), 3 were NYDVS cases which gave positive WR and Kahn Reactions later on and 37 were

non-verifiable but suspected of Syphilis.

*F. R. C. Test with sera of Malaria Patients:—*50 parasite Positive Malaria cases in the febrile stage were tested. All showed the W. R., Kahn and Clarification tests to be negative.

COMPARATIVE RESULTS OF 50 LEPROSY CASES.

Case	Clinical History.	History of V.D.	F.R.C.	W.R.	Kahn.	Remarks.
34 Cases.	Mostly all were Lepromatous Leprosy.	No	—	—	—	—
8 Cases	(a) Lepromatous, no history of Syphilis.	No	+	+	+	
	(b) Flat nose (History of Syphilis).	Yes	+	+	+	
	(c) L3 Cirrhosis, Ascites.	No	+	+	+	
	(d) L3 Uncomplicated	No	+	+	+	
	(e) Bad Lepromatous Case	No	+	+	+	
	(f) Bad Lepromatous Case History of Syphilis.	Yes	+	+	+	
	*(g) Bad Lepromatous Case. History of Syphilis	Yes	+	+	+	
	(h) R3 Flat Nose - History of Syphilis.	Yes	+	+	+	

Note*—This case showed a positive FRC test but negative WR and Kahn on 21-4-50. It was repeated on 26-5-50, 30-5-50 and 2-8-50. On the first and second repetitions, the Kahn was Positive with the FRC, and on the last occasion all three tests were positive.

Case	Clinical History	History of V.D.	F.R.C.	W.R.	Kahn	Remarks
2 Cases	(a) Old L2, two years standing. Responding to NAB. History of Syphilis.	Yes	+	-	+	
	(b) Uncomplicated L3 History of Syphilis.	Yes	+	-	+	
1 Case	(a) LI Flat Nose	No	+	-	-	
2 Cases	(a) Possibly Sarcoid	No	+	+	-	
	(b) Lepromatous	No	+	+	-	
3 Cases	All Lepromatous	No	-	+	-	

In a personal communication to Dr. Sen, Dr. E. Muir, Director of the Purulia Leper Hospital, said that in advanced cases of Leprosy, particularly those which show an abundance of Lepra Bacilli in their lesions, always give false positive W. Rs. which become negative as the case improved and the bacilli diminish in the lesions with anti-Leprosy treatment.

Discussion

There appears to be no single test yet devised which will not give false positive and negative reactions in certain cases. The extent to which these reactions occur have varied from time to time with different tests and with different observers.

With regard to false positive, many conditions have been incriminated. Davis (Medicine - Dec 1944) has stated that sera from cases of Malaria and Vaccination will give 100% positive reactions if tested over considerable periods. The same author states

that 72% of Leprosy, 20% of Malaria and 1% of normal individuals give false positive reactions. Rosenberg (Bull: U. S. Army Med Dept-Jan 1945) carried out various flocculation tests and the standard complement fixation test of Kolmer, with sera from Malaria cases at various stages of the disease, and found that positive reactions varied from 59% in the Mazinni (50% and 28% in the Kahn and Kolmer respectively) to 9% in the Hinton. Similar statistics with the F. R. C. test could not be obtained but in our small series of Malaria and Leprosy, neither in the case of the F.R.C. Test nor W. R. and Kahn Reactions were we in accord with the findings of other observers. Of the Leprosy cases which gave positive FRC Tests, 6 gave a history of Syphilis.

The occurrence of false positive reactions is usually related to the sensitivity of the Antigen, but reduction of sensitivity results in loss of specificity. Both are undesirable in that the former may incriminate an innocent serum, the latter may miss a serum

containing specific reagin. The W.R. is said to be the least sensitive of all tests in the diagnosis of Syphilis. The F.R.C. test is much more sensitive; it appears earlier and disappears later in cases of syphilis than either the W.R. and Kahn. As the principle of the test does not involve specific Antibody-Antigen reaction positive reactions must of necessity require confirmation on clinical grounds. This indication will be brought to bear earlier in the case of the F.R.C. test than in other tests. It is said that 90% of false positives become reversed in 3-6 weeks. A few however continue to be positive and present a difficult problem and there is no test which will settle the issue in such cases.

Ford Robertson and Colquhoun recognise four degrees of positivity in their test. McMenemy and Whitehead however have employed a numerical notation and the results of the tubes are recorded in numerals based upon the following degrees of clarification :-

Complete Clarification 3

Partial Clarification with transparency 2

Partial Clarification without transparency 1

No change.

A reading of 300 is regarded as the minimum level of positivity. A reading of 100 is not unusual in a treated case of syphilis and should not be dismissed unless carefully investigated. According to these authors an F.R.C. reading of 310 or less is more likely to coincide with negatives in the W.R. and Kahn whereas a reading of 320 and over is more likely to coincide with positives.

In retrospect, had we applied the same numerical notation to our series 76.6% of our negative W. Rs and 86% of negative Kahns would have fallen within the group 100 to 300 compared with an average of 62.1% and 47.6% for W.R. and Kahns respectively in McMenemy and Whiteheads cases.

The occurrence of false negatives is of greater moment in the sero-diagnosis of syphilis than false positive reactions. Ford Robertson and Colquhoun found no false negative reactions in a selected series of 385 cases of untreated syphilis. In McMenemy and Whitehead series of 12180 cases 0.16% of sera gave false negative F.R.C. Tests and W.Rs. compared with our figures of 0.86% and 1.4% respectively. False negative reactions do occur and are said to be due to excessive reagins. We had four such cases which exhibited the phenomenon of complete inhibition in the F.R.C. Test.

Conclusions

1. The simplicity of technique and low cost (a factor which should not be ignored) are strong points in favour of this test.
2. It is more sensitive and as reliable as the W.R. and Kahn in the sero-diagnosis of Syphilis.
3. In early syphilis, the F.R.C. Test may be positive long before the W.R. and Kahn and in those undergoing treatment it remains positive after the W. R. and Kahn have become negative. The persistence of the F.R.C. has shown W.R. relapse later on. The F.R.C. Test thus provides a greater safety margin.
4. We have not found this test positive in Malaria. In the case of Leprosy only 14% gave positive F.R.C. Tests.
5. In common with other tests false positive reactions do occur. This must not be confused with early appearance and late disappearance of positivity in cases of syphilis. Such cases should be considered in the light of detailed history and clinical findings.
6. False negative phenomena of inhibition are on record. In our series we had four such instances.
7. The F. R. C. and W. R. form a good combination for the serodiagnosis of Syphilis. The Kahn could then be used as confirmatory test. Wherever the W. R. or Kahn alone is performed we can confidently say

that the F. R. C. Test is a better substitute.

We are grateful to Lt-Col. H. Sen Gupta, AMC, OC Military Hospital Calcutta and to Dr. W. G. Garrow, Surgeon Superintendent B.I.S.N.Co. Ltd for placing facilities at our disposal, to Dr. E. Muir of the Purulia Leper Hospital, for supplying Leprosy sera and giving us clinical details of his cases and to L/Nk/Lab. Asst. M. M. Roy, AMC & Mr. E. W. Parker for technical assistance in carrying out our tests.

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Epidemic Hemorrhagic Fever

From 406th Med Gen Lab

Epidemic hemorrhagic fever is an acute infectious disease first encountered by the Japanese in 1939 during their occupation of Manchuria. The only available descriptions of the disease are in the Japanese Medical literature of the World War II period, plus a brief account appearing in Technical Bulletins, Medical, Nos. 208 and 216. The sources for this latter material probably antedates the work appearing in the Japanese literature.

Inasmuch as information concerning this disease is not readily accessible, the following summation of material extracted from Japanese medical literature and from the Japanese authors is presented.

Epidemic hemorrhagic fever is an acute infectious disease of virus etiology transmitted by a mite, *Laelaps jettmari*, *Litzthum*, characterized by fever, myalgia, hemorrhagic rash, bleeding from lungs, kidneys, and gastrointestinal tract and leukocytosis. The host of the mite and probable disease reservoir is the field rodent, *Apodemus agrarius*. The disease was first recognized in the Songo district of Manchuria during the winter of 1939 and first described by Japanese workers in 1942. In contrast to scrub typhus, no biting marks can be observed on the skin, the mites are not engorged with lymph, and evidence of blood-sucking is lacking. The mode of transmission has not been demonstrated, but the virus is thought to pass from the salivary gland of the mite into the skin puncture during the biting process.

The incubation period is usually from two to three weeks but may range from one

week to a month. Prodromal symptoms of headache, backache begin suddenly with chills and fever rising rapidly to 104°F. The fever usually maintains a level of 102.5-104°F. for three to five days, later gradually returning to normal. In more severe cases a high plateau may be maintained for a week or more. One of the most constant features of this disease is the dissociation between the febrile peak and the fastigium of the disease. After the temperature returns to normal either by lysis or, in more severe cases, by crisis, the other manifestations of disease become more severe, and death, when it occurs, usually takes place one or two days after the temperature falls. The appearance of a generalized hemorrhagic skin eruption associated with mucosal and conjunctival injection and hemorrhages, usually beginning about the third day of disease, is an important feature. It begins as a petechial rash on the neck and face and in the axilla, becoming progressively more widespread and severe. This is associated with a generalized flush described as a "sun-burned" appearance. Headache, nausea and vomiting, severe muscular aches and pains, particularly backache, insomnia and signs of cerebral damage may occur throughout the disease but characteristically become more severe after defervescence. Temporary myopia frequently occurs and paroxysms of hiccups are common. Edema of the face and a blank facial expression are characteristic. The tongue usually has a thin yellow coating. The pulse is relatively slow and blood pressure usually drops just before or after the temperature starts to decline. In more severe cases hematemesis, hemoptysis, hematuria and melena may appear. No organ systems are known to be consistently spared in the hemorrhagic

diathesis characteristic of this disease. Albuminuria is consistently noted immediately before and after the fever begins to decline.

The red blood count and hemoglobin have a tendency to increase during the initial stage of the disease and nucleated erythrocytes frequently appear. With the increase in hemorrhagic rash, the red blood count begins to fall. The white blood cell picture is characterized by a decrease during the initial stage followed by a marked leukocytosis during the severe period; values range from 25,000 to 80,000 cells per cubic millimeter. The differential is characterized by the presence of eosinophiles throughout the entire course of disease and the frequent appearance of nucleated erythrocytes. Thrombocytes decrease from the initial stage. The literature is contradictory on the nature of the Weil-Felix reaction in this disease.

Pathological Picture—The outstanding gross pathological findings in epidemic hemorrhagic fever are the degeneration and hemorrhage found in the kidney. This organ is tense and enlarged to several times its normal weight. The cut surface of the cortex is swollen and grayish-yellow in color. The medulla is dark red and the cortico-medullary demarcation is distinct. Hemorrhage into the medulla is frequent. These renal findings are consistently found and are thought to be peculiar to this disease. Hemorrhages into the parenchyma of the spleen and into the skin and all mucosal and serosal surfaces of the body are almost always present. In addition hemorrhages into the myocardium and into the anterior pituitary have been recorded. Advanced pulmonary congestion (probably hemorrhagic pneumonia) and fatty degeneration of the liver usually occur. Microscopically, the most characteristic lesions are parenchymal degeneration and diffuse capillary damage in every organ.

Etiology—The specific causative agent is a filterable virus capable of passing Chamberland candles L2, L3, L5, L9, and Sitz EK filter. Attempts to isolate rickettsiae by animal inoculation have been unsuccessful. The virus remains potent for at least 81 days by drying and freezing at -70°C in serum. It resembles the viruses of yellow fever and

dengue in its viscerotropism. No immunological relationships have been demonstrated between this and other virus diseases.

Experimental Infections and Host Range—

The host range of this virus is thought to be narrow, involving only the field rodent, *Apodemus agrarius*, the mite *Laelaps jettmari* Litzthum, man and the horse. The rodent infection is felt to be an inapparent disease. In November, 1942, 40 *A. agrarius* were collected in the Songo district of Northern Manchuria and 203 *Laelaps jettmari* were collected from these rodents. An emulsion was prepared from the mites and 1 cc was injected subcutaneously into the thigh of a monkey. After 19 days a moderate infection with a fever of 39.4°C was noted. A second monkey was inoculated with blood from the first monkey during its febrile period. After an incubation period of 12 days fever and albuminuria appeared and at autopsy the kidneys showed the typical pathological findings seen in epidemic hemorrhagic fever. The infectivity of serum is highest during the initial or fastigial period of fever. The infectivity is lost when the temperature returns to normal. An *A. agrarius* was observed for 25 days after intraperitoneal inoculation of one-half cc of infected serum. It developed no detectable disease and the viscera appeared normal at autopsy. Liver, spleen and kidneys were emulsified with ten parts of Ringer's solution and 1 cc of this emulsion was injected subcutaneously into a monkey. After an incubation period of 11 days, fever of 40.2°C and moderate clinical disease was noted. A second monkey developed the infection after inoculation of blood from the first monkey, thus demonstrating the occurrence of inapparent infection in the host rodent. Several species of fleas and other blood-sucking insects were originally suspected of being capable of transmitting the disease but animal experimentation with other arthropods yielded negative results.

Diagnosis—A diagnosis of epidemic hemorrhagic fever may be suspected in individuals having been in an endemic or suspected endemic area who demonstrate an acute onset of chills and fever, relatively slow pulse, flushed skin, conjunctival injection and vomiting during the early stages followed by the

appearance of a hemorrhage rash beginning on the neck and axilla. Visual disturbances, hiccups, albuminuria, and leukocytosis with the presence of eosinophils and nucleated erythrocytes, are helpful in aiding in the diagnosis. The later appearance of gross hematuria, hemoptysis, hematemesis and melena superimposed upon the general background of an acute infectious disease as described above lead one to strongly suspect this disease. Lastly the tendency to show no improvement even after the temperature falls to normal, frequently with death occurring in the afebrile stage, is characteristic.

The Japanese state that the following diseases must be considered in differential diagnosis; typhus, food poisoning, scarlet fever, influenza, epidemic cerebrospinal meningitis, plague, relapsing fever, typhoid fever, and pneumonia.

Prognosis is poor when bradycardia and hypotension appear in the initial stages of the disease. The appearance of central nervous system symptoms, gross bleeding from lung, gut, or kidneys, and the appearance of anuria are likewise unfavourable signs. Intractible hiccups not infrequently appear in cases with fatal termination.

Epidemiology — Epidemic hemorrhagic fever is known to occur in Northern and North-Eastern Manchuria. The presence of this disease in Northern Korea and Siberia has not yet been demonstrated. The geographical range of the mite is not definitely known to include Korea but *A. agrarius* is a common field rodent found throughout the Korean Peninsula. Hence, it might be anti-

ipated that the disease is at least enzootic in Korea. In North-Eastern Manchuria it is especially prevalent along the river banks where the ground is damp and overgrown with grass. This type of terrain is apparently the habitat of *Apodemus agrarius*. However, wooded areas are known to be inhabited by this species. The greatest incidence occurs in May, June, and again October and November, but outbreaks are known to have occurred throughout the year. Outbreaks usually occur at the same time each year in any given district. Outbreaks have occurred frequently among Japanese troops and particularly among those handling horses. Horses are known to be susceptible but the mode of horse to man transmission is not known. Japanese troops in Manchuria experienced numerous outbreaks of this disease, and if light infections are included, as high as 80% of the troops in the epidemic area were infected during one period. The death rate is generally highest early in a given epidemic. Usually fatality rates are fifteen percent, although rates of forty to fifty percent have occurred in some epidemics.

Control Measures — The prevention of this disease can best be attained by the application of control measures aimed at the mite and the rodent, much as in scrub typhus. These consist of the use of insecticides and repellents both on the skin and clothing, and of the clearing of the terrain of epidemic areas for rodent eradications; Rat-proofing of buildings is also desirable. During an epidemic early recognition is important in order that mite and rodent infested areas can be quickly identified and the appropriate measures taken.

Hemopoietic Changes with Chloromycetin Therapy

by
 Lt.Col. H. B. LAL, AMC.
 Major L. C. AGGARWAL, A 1C.

The last word on therapeutic and toxic effects of the antibiotics has not yet been written. It would be surprising that such effective antagonists that can render the enzymes in the disease producing organisms totally ineffective, were without any side effects on the human body. One such complication of the administration of chloromycetin is a marked fall in the total leucocyte count occurring simultaneously with the control of fever and improvement in the clinical condition of the patient. At times fall is not only precipitous but also to a level which would not only be deemed dangerous, but may even be indicative of aplasia of the bone marrow. Volini et al have described three cases of severe reversible granulocytopenia with some arrest of erythroid and granulocytic maturation in the marrow during chloramphenicol treatment occurring about the seventh day. In another of their cases severe anaemia resulted from the therapy. They state that the maturation arrest of the bone marrow occurred without any effect on the platelet count or any alteration in the monocyte or lymphocyte counts. A fatal case of aplastic anaemia following the therapy has been reported by Rich et al.

In order to assess the complications accompanying the antibiotic, it had been made a regular practice to watch all our cases from the clinical and haematological angles during the therapy. It must be

admitted that the number of cases treated by us with this drug has been small, that is, only 4 cases in March, April and May 1951.

In these cases bone marrow and blood haematological studies were made before administration of chloromycetin and at different stages of the therapy and finally at the end of the same. The series consisted of two cases of Brucellosis, one of typhus and one of typhoid. The treatment consisted of an initial dose of 0.75 gm followed by 0.5 gm every 4 hours for the next 48 hours; this being further reduced to 0.5 gm every 6 hours for the remaining part of the course. A total of 18 gms was used in cases of Brucellosis, 15 gms in case of typhoid and only 9 gms for the typhus patient.

Case I. P. A. Age 30 yrs Brucellosis 12.3.51. Admitted with intermittent fever, pain in the right sterno-clavicular joint and excessive sweating. Was also previously in hospital from 7.11.50 to 2.2.51 disease Brucellosis. No abnormal physical signs were discovered except a slightly tender right sterno clavicular joint. Irregular intermittent temperature persisted during period of investigations, and completely settled by lysis on the 5th day of chloromycetin therapy.

17.3.51: Blood for Brucella agglutination positive 1 in 1280. Blood culture for Brucella-negative

18.3.51: Started on chloromycetin.

Haematological reports were as follows:—

Date	Chloromycetin in gms	TWC	Neutrophils	Lymph	M	Eos	Hb gms	TRBC
18-3-51	Preliminary	12,800	70	22	3	5	14.5	5.25
19-3-51	3.75	10,400	73	21	2	4	14.5	5.15
23-3-51	11.75	7,600	48	46	3	3	14.5	5.25
26-3-51	17.75	6,500	59	31.5	3	6.5	—	—
27-3-51	12 hrs after stoppage of drug	10,600	67	28	2	3	—	—

Case II. J. M. Age. 37 yrs Brucellosis

25.4.51 : Fever of 3 weeks duration of a remittent type, precipitated by T.A.B. injection. Fever associated with frequent chills and profuse sweating, and ranged between 100° F and 104° F. Spleen that was just palpable on admission gradually

enlarged to two inches below costal margin. Fever subsided by lysis on 5th day of treatment.

30.5.51 : Blood for Brucella agglutination positive 1-2560. Blood culture for Brucella - negative.

1.6.51 : Started on chloromycetin.

Haematological reports were as follows:—

Date	Chloromycetin in gms	TWC	Neutrophiles	Lymph	M	Eos	Hb gms	TRBC	Remarks
30-4-51	Preliminary	5,500	59	38	3	—	13.5	4.32	—
2-5-51	3.75	4,700	25	70	4	1	—	—	—
3-5-51	6.75	4,600	17	78	4	1	—	—	—
4-5-51	8.75	4,380	30	67	1	2	—	—	Dose reduced
5-5-51	10.75	5,100	46	51	2	1	—	—	—
6-5-51	12.75	5,200	48	47	4	1	—	—	—
7-5-51	14.75	6,800	50	45	4	1	—	—	—
8-5-51	16.75	6,975	53	43	3	1	—	—	—
9-5-51	18.00	4,800	29.5	65.5	4	1	—	—	—
11-5-51	28 hours after stoppage of drug	6,850	41	58	1	—	14.0	4.8	—

Case III. S.S. Age 30 yrs. Typhus

7.5.51 : Fever of 7 days duration of a continuous type with an irritable cough and well marked toxæmia and prostration. Signs of pneumonia at right base detected. Blood count showed total W.B.C 8200 per cmm with 68% neutrophiles. BSR 44 mm in the 1st hour.

Placed on penicillin, 300,000 units daily till 12.5.51 without any effect on temperature,

toxæmia or lung signs. XRays showed hyperæmia of both lungs with pleural thickening of Rt base, and an area of segmental pneumonitis at periphery of Rt lower zone.

12.5.51: Blood for Weil Felix Reaction showed a titre of 1-640. Started on chloromycetin.

Fever responded within 24 hrs, and patient remained afebrile since.

Case II. J. M. Age. 37 yrs Brucellosis

25.4.51 : Fever of 3 weeks duration of a remittent type, precipitated by T.A.B. injection. Fever associated with frequent chills and profuse sweating, and ranged between 100° F and 104°F. Spleen that was just palpable on admission gradually

enlarged to two inches below costal margin. Fever subsided by lysis on 5th day of treatment.

30.5.51 : Blood for Brucella agglutination positive 1-2560. Blood culture for Brucella - negative.

1.6.51 : Started on chloromycetin.

Haematological reports were as follows:—

Date	Chloromycetin in gms	TWC	Neutrophiles	Lymph	M	Eos	Hb gms	TRBC	Remarks
30-4-51	Preliminary	5,500	59	38	3	—	13.5	4.32	—
2-5-51	3.75	4,700	25	70	4	1	—	—	—
3-5-51	6.75	4,600	17	78	4	1	—	—	—
4-5-51	8.75	4,380	30	67	1	2	—	—	Dose reduced
5-5-51	10.75	5,100	46	51	2	1	—	—	—
6-5-51	12.75	5,200	48	47	4	1	—	—	—
7-5-51	14.75	6,800	50	45	4	1	—	—	—
8-5-51	16.75	6,975	53	43	3	1	—	—	—
9-5-51	18.00	4,800	29.5	65.5	4	1	—	—	—
11-5-51	28 hours after stoppage of drug	6,850	41	58	1	—	14.0	4.8	—

Case III. S.S. Age 30 yrs. Typhus

7.5.51 : Fever of 7 days duration of a continuous type with an irritable cough and well marked toxæmia and prostration. Signs of pneumonia at right base detected. Blood count showed total W.B.C 8200 per cmm with 68% neutrophiles. BSR 44 mm in the 1st hour.

Placed on penicillin, 300,000 units daily till 12.5.51 without any effect on temperature,

toxæmia or lung signs. X Rays showed hyperæmia of both lungs with pleural thickening of Rt base, and an area of segmental pneumonitis at periphery of Rt lower zone.

12.5.51: Blood for Weil Felix Reaction showed a titre of 1-640. Started on chloromycetin.

Fever responded within 24 hrs, and patient remained afebrile since.

Haematological reports were as follows:—

Date	Chloromycetin in gms	TWC	Neutrophiles	Lymph	M	Eos	Hb gms	TRBC
12-5-51	Preliminary	8,400	68	24	3	5	13.5	4.84
13-5-51	2.75	8,100	65	28	1	6	—	—
14-5-51	5.75	7,000	41	31	2	26	13.5	4.78
15-5-51	8.75	8,000	49	35	1	15	—	—
16-5-51	—	5,700	39	46	2	13	13.5	4.77
17-5-51	—	6,050	21	69	3	7	14.0	4.80
18-5-51	—	5,650	51	41	2	6	14.5	4.81

Case IV M.S. Age 25 yrs.

Inoculated with T.A.B vaccine on 14.9.50.

e.g. 84 per minute with temp of 103°F. The toxæmia gradually increased in severity. Tongue coated and abdomen slightly tumid.

7.5.51 : Admitted with a history of remittent continuous fever of 7 days' duration, and marked constipation. The fever maintained a level of 100°-104° F with a relatively slow pulse

13.5.51 : B.typhosum isolated in blood culture.

17.5.51 : Started on chloromycetin. Was totally afebrile on the 5th day, with no further relapse.

Haematological reports were as follows:—

Date	Chloromycetin in gms	TWC	Neutrophiles	Lymph	M	Eos	Hb gms	TRBC	Remarks
17-5-51	Preliminary	4,950	46	52	1	1	14.5	4.53	—
18-5-51	3.00	5,100	50	47	1	2	—	—	—
19-5-51	6.00	3,300	55	44	0.5	0.5	14.5	4.62	—
20-5-51	9.00	3,250	50	47	1	2	—	—	—
21-5-51	11.00	3,870	70	25	3	2	—	—	Dose reduced
22-5-51	13.00	4,100	57	38	4	1	—	—	—
23-5-51	15.00	4,600	61	33	2	4	—	—	—
24-5-51	24 hrs after stoppage of drug	4,300	49	45	2	4	13.0	4.38	—
25-5-51	48 hrs after stoppage of drug	4,900	50	46	2	2	13.5	4.26	—

To establish the basis of the neutrophil leucopenia that was apparent on all the cases, the patients were subjected to sternal puncture. It is a matter of regret that the smears in case No. 2 did not prove to be successful. The bone marrow smears showed a marked fall in the total number of nucleated cells, accompanied by a similar fall in that of segmented (mature) neutrophils. There was no appreciable fall in the metamyelocyte count, though on the other hand there was

a noticeable increase in their number in case No. 3, along with an increase in that of eosinophilic metamyelocytes. Normoblasts part of the erythroid series showed an increase in all cases, which being relative to the fall in the white cell series perhaps was without significance, particularly in view of the fact that no change in the erythrocyte count occurred in the peripheral blood. The myelograms of three of the cases were as follows:—

MYELOGRAM

CASE No. 1 (P.A.)

CASE No. 3 (S.S.)

CASE No. 4 (M.S.)

	18-3-51 Preliminary	21-3-51 after 8 gms	27-3-51 after stoppage	12-5-51 Preliminary	16-5-51 after 9 gms	17-5-51 Preliminary	22-5-51 after 13 gms
A. Granular White Cell Series							
1. Premyelocytes ...	Nil	Nil	Nil	Nil	1.00	0.20	0.30
2. Neutromyelocytes ...	1.00	1.00	0.50	6.15	5.00	4.00	6.60
3. Neutrophil metamyelocyte and band forms	30.00	27.00	25.50	19.00	29.00	24.00	23.60
4. Neutrophil segmented	46.00	39.75	46.00	49.00	35.25	36.25	27.30
5. Eosinophilic myelocytes ...	Nil	Nil	Nil	Nil	Nil	Nil	Nil
6. Eosinophilic metamyelocyte and band forms	Nil	Nil	Nil	Nil	2.00	Nil	0.30
7. Eosinophilic segmented ...	1.30	0.25	Nil	2.00	2.00	0.40	2.00
B. Nongranular White Cell Series							
8. Lymphocytes ...	2.00	3.00	3.00	6.15	2.50	4.00	5.00
9. Plasma cells ...	Nil	Nil	Nil	0.20	0.25	0.25	Nil
10. Monocytes ...	0.60	0.25	Nil	1.50	Nil	1.50	0.60
C. Red Cell Series							
11. Proerythroblasts ...	0.60	1.50	1.00	0.50	Nil	0.40	0.60
12. Megaloblasts ...	Nil	Nil	Nil	Nil	Nil	Nil	Nil
13. Early and intermediate normoblasts ...	Nil	Nil	Nil	1.50	1.00	2.50	4.00
14. Mature normoblasts	18.50	27.00	24.00	14.00	22.00	26.50	29.70
15. Total nucleated cell count ...	115,400	110,500	46,500	Not done	Not done	133,000	74,250

Discussion

It is a constant observation that cases e.g. typhus, typhoid and Brucellosis, treated with chloromycetin, show a leucopenia of marked degree. Observation over our cases treated with the drug have substantiated the fact of marked haematological and bone marrow changes. While this fact agrees with the observations made by Volini et al, it certainly differs from them in the fact that the fall in the leucocyte count is simultaneous with administration of the drug, and seems to be in keeping with the heaviness of the dosage employed; while they maintain that the fall occurs after about seven days of administration. On the other hand it has been noticed that even reduction of the dosage allow a recovery partial or otherwise of the leucocytic level, as occurred in case 2 and 4. However it must be acceded that the low leucocytic count obtained, may last for a short period, after the stoppage of the administration of the drug e.g. case 3. It was further observed that the drug has no effect on eosinophil cells either in the bone marrow or in the peripheral blood, in fact there was observed a very definite rise in the number of eosinophil cells in both sites, in one of the cases (No. 3)

There is also an increase in the percentage of the mature normoblasts in the bone marrow smears. Since there was no diminution of the erythrocytes in the peripheral blood, it must be presumed that the rise is relative due to a decrease in the cells of the leucocytic series, rather than any stoppage in the further maturation of the normoblasts.

Volini et al maintains that there is a definite maturation arrest of the white cells from the metamyelocyte stage to the mature segmented cells. The arrest seemed in our cases to particularly apply to the neutrophil cells only, since it was noticed that the phenomenon was immediate, it is felt that the effect of the drug is direct on the bone marrow itself, instead of through a deprivation of any biological factors synthesized in the intestinal tract. As such withdrawal of the drug partial or complete, is accompanied by

a proportionate recovery of the bone marrow, which is reflected in the peripheral blood, even though in case I there was still a marked fall, shown in total cells of the bone marrow, while the neutrophiles in the peripheral blood had already shown a rapid rise, after the drug was stopped.

The significance of this fall in the neutrophil series of cells in the marrow and the peripheral blood has to be considered from the point of view of the possibility of a permanent damage to the bone marrow, considering that prolonged course of the drug is now recommended in cases of typhoid and Brucellosis. Further with a fall of the leucocytic count to a dangerously low level, the likelihood of secondary invasion by organisms of the gram positive series has to be considered. The spontaneous occurrence of new bacterial infections during antibiotic therapy was reported by Weinstein and by Appelbaum and Leff. But the quick recovery of the bone marrow and the peripheral blood, certainly offsets any possibility of aplasia of the bone marrow, and the mild but definitely antibiotic effect on the organisms mentioned, makes it unlikely, that any harm can occur to the patient or his defence ring broken, but left unguarded, before the recovery of the bone marrow can occur.

Summary

1. Blood counts and bone marrow smears of 2 cases of Brucellosis and one each of typhoid and typhus, before, during, and after the administration of chloromycetin are described.

2. It is felt that the maturation arrest of the neutrophil series of cells in the bone marrow and fall of leucocytes of the same series, are simultaneous and proportionate with the administration of the drug, and definitely transitory, and that the drug does not cause any permanent damage to either of them.

3. It is also concluded that the precipitous fall of the leucocyte count does not carry any added risk to the patient.

An opportunity is taken to express our gratitude to Col. T. R. Pahwa for the permission to carry out the observations, and for his invigorating and helpful criticism.

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Preliminary Report on an Investigation into the Influence of Temperature and Humidity on the Incidence of Dysentery and Diarrhoea

by

Major M. C. SANYAL, AMC, Hygiene Department, A.F.M.C.,
and

Mr. P. KRISHNA SWAMY, Research Officer, A.F.M.C.

1. Introduction.

It is acknowledged that the Fly is the principal agent in the transmission of Dysentery and Diarrhoea from man to man. When the fly cannot be implicated water-borne routes have been incriminated and transmission by carriers.

But certain work quoted below, indicates that the susceptibility of man to intestinal infections may have a seasonal variation, this variability being brought about by changes in Temperature and Humidity.

In 1929 Arnold¹ in confirming Salle's work that a rise in body temperature was followed by a decrease in total gastric secretion, in total and free acid and in pepsin, also showed that in animals kept in a warm humid room there was a change in the enteric flora—the faecal flora of the large intestine ascending into the lumen of the duodenum. He found that with an alteration in the acid base balance in the gastric tract towards the alkaline side, there was an appearance of a typical colonic flora in the duodenum. His results indicated that the acid of the stomach has a bacteriostatic effect on the bacteria ingested into the stomach and duodenum and that this effect disappeared with the reduced activity of the stomach induced by an exposure of the animal to a hot humid environment.

In another series of experiments Arnold and Brody (1927)² showed that bacteria injected directly into the duodenum of a dog kept in a warm humid room appeared in the caecum, but not if the dog was kept in a cool room.

Later Work by Kleigler and Olitzki (1931)³ and by Robertson and Weld (1932)⁴ showed that in conditions of high temperature and high humidity, there was a higher fatality rate in rats infected with *S. enteritidis*.

Finally in 1936 Kleigler⁵ working on human volunteers found that there was a change in the intestinal flora in correlation with the seasonal changes in temperature and humidity and that these seasonal changes were closely linked with the dysentery and diarrhoea incidence.

2. Details of Investigation.

It is felt that if Kleigler's assumption is correct that at certain seasons the human body becomes more susceptible to intestinal infection then, it should be possible to show a significant degree of correlation between temperature and humidity on the one hand and the incidence of dysentery and diarrhoea on the other.

Accordingly, hospital admissions for dysentery and diarrhoea were abstracted

from the A and D books of the M. H. Poona, for 1948 expressed as weekly rates/1000 and tabulated against the weekly means of temperature and humidity for Poona (Table I).

Graph I shows a histogram of the weekly admission rates for dysentery and diarrhoea plotted against the weekly means of temperature and humidity.

3. Statistical Analysis.

A linear regression equation of the form $y = b_0 + b_1x_1 + b_2x_2$ was fitted, where y represents the weekly incidence of dysentery and

diarrhoea, x_1 and x_2 represent the mean weekly temperature and mean humidity respectively and b_0 , b_1 and b_2 constants to be determined.

The usual statistical methods were used in estimating the constants b_0 , b_1 and b_2 (Fisher⁶). The equation, on estimating the constants, came out as

$$y = -2.34 + .03339x_1 + .006405x_2$$

An analysis of variance was done to test the fitness of the regression equation (Fisher⁷).

Variance due to	Degs. of freedom	Sum of squares	Mean square	$\frac{1}{2}$ loge (Mean square)
Regression formula	2	2.02	1.01	.0050
Deviation	49	12.60	0.2571	-0.6791

$$\text{Value of } z = .0050 - (-0.6791) = 0.6841$$

Significant values of z for degrees of freedom 2 and 49 are :

$$0.58 \text{ (5\% level) and,} \\ 0.82 \text{ (1\% level).}$$

The observed value is significant at 5% level but not significant at 1% level. The value of the Multiple correlation co-efficient R , which measures in a sense the extent to which y depends upon the combined variation of the two variates x_1 and x_2 , can easily be calculated from the above table, even though it is not necessary for the test of significance :

$$R = \frac{2.02}{14.62} = 0.37$$

The results show that the data do not disprove the hypothesis that the incidence of dysentery and diarrhoea increases with a rise in temperature and humidity, and that there is a linear relationship to a limited extent.

4. Discussion.

The Statistical analysis shows that there is a significant degree of correlation between the dysentery and diarrhoea rates on the one hand and the mean temperatures and humidities on the other. This correlation is, however, to only a limited extent.

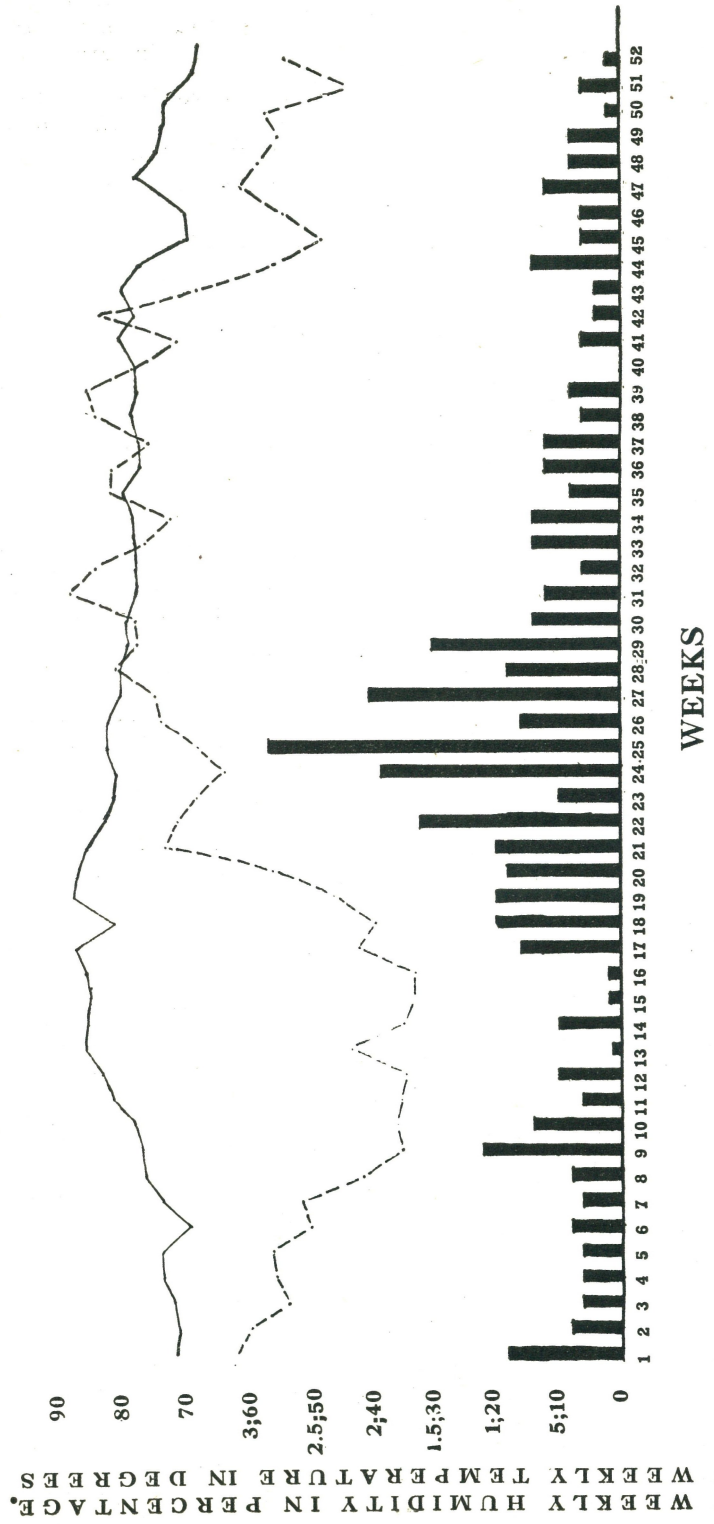
From the Graph it is apparent that there is a marked seasonal incidence in the rates of admission to hospital for dysentery and diarrhoea, the peak being reached between

the 24th-28th weeks (June-July). It is also to be noted that a rise in the incidence commences in the 17th week (May) when the humidity also commences to rise. From our own observations and from work published by Manifold⁸ (1928), it is known that fly incidence curve resembles the curve for dysentery and diarrhoea particularly in the manner in which the two peaks coincide. There are however, certain differences between the two incidence which are worthy of note.

- (a) The rise in the dysentery and diarrhoea rate commences in the 17th week (May) when the fly incidence is low. The annual increase in the fly incidence does not commence till much later, about the 24th week (late June) after the monsoon breaks in Poona.
- (b) The fly population drops suddenly in the middle of August to a low figure, and the dysentery and diarrhoea rates also fall, but less suddenly.
- (c) The decrease in the fly population occurs at a time when the mean temperature and humidity, remain optimal for their development and survival and continues to remain so for some weeks longer.

A possible explanation for the differences between the two curves may be that with a rise in the temperature and humidity the

GRAPH I.



MEAN WEEKLY HUMIDITY IN PERCENTAGES.
 MEAN WEEKLY TEMPERATURE IN DEGREES.

■ DYSENTERY & DIARRHOEA RATES PER 1000.
 — MEAN WEEKLY TEMPERATURE
 - - - MEAN WEEKLY HUMIDITY

WEEKS

human being becomes more susceptible to intestinal infections, resulting in an initial rise in the disease rates in which transmission is by carriers. The subsequent peak occurs when the transmission agent - the fly - increases enormously in numbers and at the same time as man becomes more susceptible to intestinal infection.

The cause for the sudden drop in the fly population in August is obscure. Manifold in his original paper, is also unable to account for it. A probable reason for it may be that at this season the relative humidity during the day begins to fall, and by 1700 hrs it is below the optimal lower limit for the fly, although at 0800 hrs it may be adequately high. This difference in the relative humidity between 0800 hrs and 1700 hrs probably accounts for the corresponding fall in the dysentery and diarrhoea rates after August, when there occurs a decline in the comparative activity of the fly coupled with a decreased human susceptibility to infection.

It is however, felt that the investigation should be extended to other stations which show greater extremes in temperature and humidity than Poona, e.g. Delhi and Calcutta.

5. Summary.

- (a) A hypothesis is postulated that the incidence of dysentery and diarrhoea increases with a rise in temperature and humidity.
- (b) The hypothesis is tested statistically, and the result is significant, and the existence of a linear relationship to a limited extent is shown.

- (c) It also seems that there is a seasonal variation in man's susceptibility to intestinal infections.
- (d) It is proposed to extend the investigation to other stations showing greater extremes of temperature and humidity than Poona.

6. Acknowledgements.

Our thanks are due to O.C. M.H. Poona for permission to abstract the relevant figures from the hospital A & D books and to the Librarian of the Royal Society of Medicine for tracing references.

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TABLE I.

Weekly.	Weekly Dysentery and Diarrhoea rates/1000.	Weekly mean Temps.	Weekly mean Humidities.
	y	xl	x2
1	0.9	71	62
2	0.4	70	60
3	0.3	71	53
4	0.3	73	55
5	0.3	73	56
6	0.4	69	50
7	0.3	73	51

Weekly.	Weekly Dysentery and Diarrhoea. rates/1000.	Weekly mean Temps.	Weekly mean Humidities.
	y	x1	x2
8	0.4	76	41
9	1.1	76	35
10	0.7	78	35
11	0.3	81	35
12	0.5	83	34
13	0.1	85	43
14	0.5	85	34
15	0.1	85	33
16	0.1	85	33
17	0.8	87	42
18	1.0	81	39
19	1.0	87	46
20	0.9	86	56
21	1.0	85	72
22	1.6	32	70
23	0.5	81	67
24	1.9	81	63
25	2.8	82	67
26	0.8	82	73
27	2.0	79	74
28	0.9	79	80
29	1.5	78	76
30	0.7	78	77
31	0.6	77	88
32	0.3	77	84
33	0.7	77	76
34	0.7	77	72
35	0.4	79	81
36	0.6	76	81
37	0.6	77	75
38	0.3	77	84
39	0.4	77	85
40	0	77	77
41	0.3	80	70
42	0.2	78	83
43	0.2	79	67
44	0.7	77	54
45	0.3	68	48
46	0.3	69	53
47	0.6	77	60
48	0.4	73	52
49	0.4	72	54
50	0.1	72	56
51	0.3	68	43
52	0.1	67	53
53	7.6	1497	1323
MEANS	.63	77.56	59.75

A NOTE ON ANOPHELES VARUNA

by

V. P. JACOB, Major, A.M.C.

and

R. D. MITRA, M.Sc., Capt. M.L.I.

From Armed Forces Medical College, Poona

Anopheles varuna Iyengar 1924 is not listed by Covell and Puri (1936) or Barber and Rice (1937) as one of the species prevalent in Poona. It has now been found in Poona from the villages of Pashan * and Vithalwadi. +

A. varuna is a proved vector of malaria "in certain areas though it appears to be innocuous in others" (Covell, 1944) and its breeding, resting and feeding habits are known to differ widely in different places. Although the number of specimens so far obtained are not enough to fully understand its afore mentioned habits, yet it is proposed to mention those briefly as observed here so far.

Nature of Breeding Place.

Larvae of *A. varuna* were obtained from Vithalwadi in a crater like rocky pool through which a hill stream flows. This pool is situated close to the bank of river Mutha at a higher level than the river. It has a bottom of mud and is about 18" deep; *A. fluviatilis*, *A. culicifacies*, *A. annularis*, *A. splendidus*, *A. stephensi* and other aquatic insects usually breed in it. The cool, clear water in this sun-lit pool is acidic in reaction and has a lower organic pollution as compared to water contained in numerous stagnant rocky pools close by where *A. culicifacies* and *A. subpictus* breed regularly and *A. stephensi* and *Aedes* occasionally.

The edges of this breeding place of *A. varuna* is grassy and contains in addition to submerged or floating blue green algae, the following water plants: *Paspolidium germinatum*, Staff., *Vallisneria spiralis*, Linn., *Maniera curicifolia*, Mich. and *Frimbristylis dichotoma*, Vohl. The near by rock pools on the other hand do not possess grassy edges or plants except brownish algae scum.

The nature of this breeding place of *A. varuna* differs from its breeding places in areas where it is known to be a vector. In those places it breeds in road side storm water collections (Iyengar, 1924) rural ponds containing Macro-phytoplankton in nearly all strata, ditches, inundated fallow lands (Mitra, 1943) or paddy fields with water temperature below 42°C (Sen, 1948).

Adult Habits.

In Vizagapatam *A. varuna* consisted of 65 per cent of the total catch in cattle sheds in one area between February and August but only 4.5 per cent of the whole year's catch in another; it is purely a cattle feeder and prefers to rest in sheds made of Palmyra thatch (Senior-White, 1941). In Poona *A. varuna* is caught from bed rooms (Table I) which have mud floor, stone wall plastered with mud and roof of tiles about 8' high. Cow sheds usually contain a very large population of all kinds of mosquitoes and provide far greater ease for their ingress as compared to bed rooms which usually have a single door. Cow sheds and bed rooms are equidistant from the breeding places.

* Pashan is 6 miles NE of Poona.

+ Vithalwadi is 7 miles SW of Poona.

Summary.

1. *A. varuna* is recorded in Poona for the first time. It breeds in clear flowing water having grassy edges and rests in houses.

2. A difference in the resting and breeding places is noticed here from those observed in deltaic Bengal etc.

3. This difference as noticed during the preliminary observations, if subsequently confirmed, is likely to lend support to the hypothesis of existence of two biotypes (Senior-White et al., 1945) or biological races (Covell, 1944) of this species - one a dangerous vector the other an innocuous form.

Acknowledgement.

The authors express their sincere thanks to the Economic Botanist, Bombay, Asst. Economic Botanist, College of Agriculture, Poona for identification of water plants; to Dr. A. K. Chatterjee, Armed Forces Medical College, Poona for testing samples of water.

The authors are grateful to Brigadier B. M. Rao and Lt-Col. T. D. Chablani for providing facilities for this investigation.

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TABLE I.

Date.	Locality.	Place		Found in association with.
		House	Cowshed	
21-4-5	Vithalwadi	Bedroom	—	<i>A. culicifacies</i> . <i>A. fluviatilis</i> .
25-4-51	Pashan	„	—	<i>A. culicifacies</i> . <i>A. fluviatilis</i> . <i>A. stephensi</i> . <i>A. splendidus</i> . <i>A. turkhudi</i>

A Case of Foreign Body in the Oesophagus with Post Anaesthetic Respiratory Crisis

by

Captain K. M. SOPARKAR, M.D., F.C.P.S., A.M.C.

No. 8657 Bhag Singh aged 28 years while eating his evening meal in the unit lines felt that he swallowed a piece of bone from the mutton curry he was eating. He reported sick to the hospital M. I. Room at 2200 hours, complaining of pain in the centre of the throat. The pain was sticking in character; there was difficulty in deglutition and he could not drink water without experiencing pain. He was admitted to the hospital and X-Ray pictures were taken of the cervical and upper dorsal regions. Radiographs showed an opaque body nearly one inch long with the sharp upper end lying longitudinally at the level of the body of the seventh cervical vertebra. Shadow of the trachea was clearly visible anterior to the foreign body.

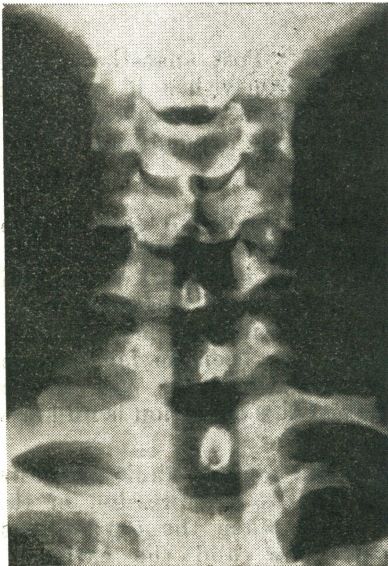
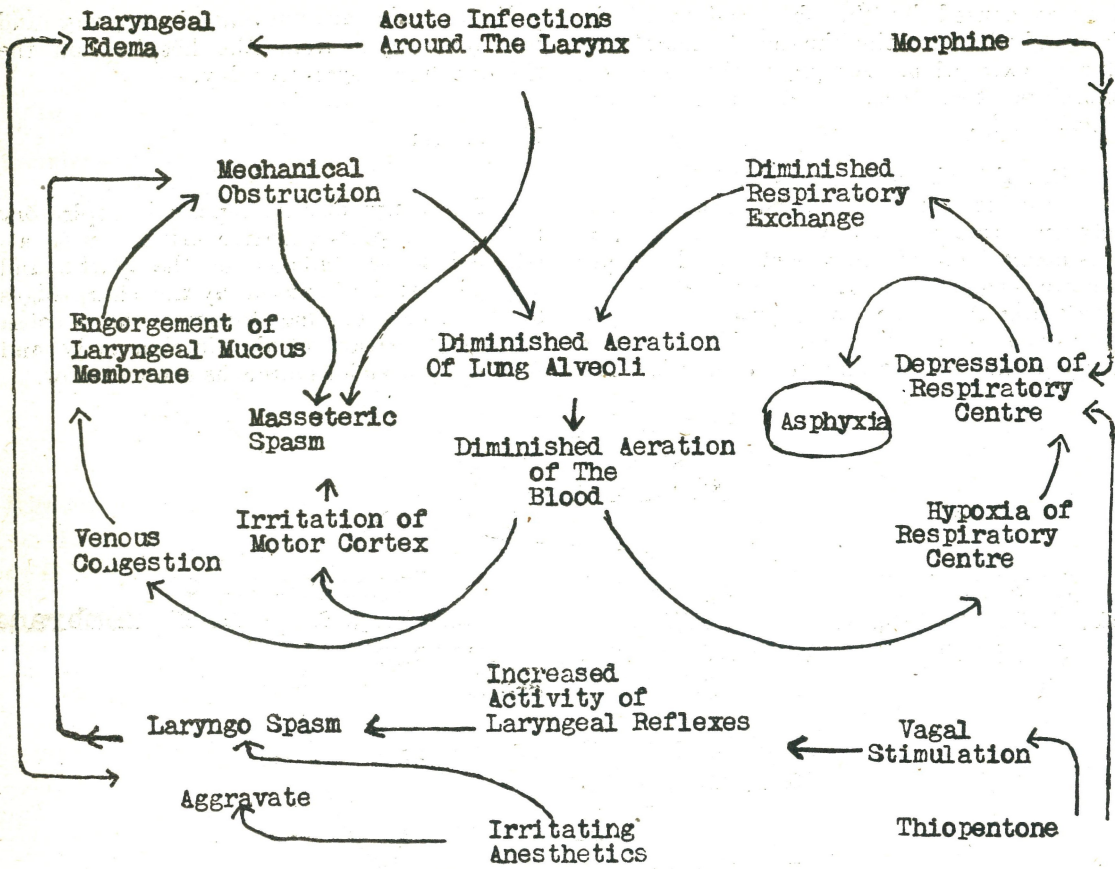
It was clear from the X-Ray pictures that a piece of bone was stuck in the Oesophagus about one and half to two inches below the crico-pharyngeal constriction. Considering the sharp edges of the piece and also its size it was decided to extract it with the help of an Oesophagoscope without delay.

Operation :

Morphia gr. $\frac{1}{4}$ and Atropine gr. $\frac{1}{100}$ were administered half an hour before the operation. A 10% cocaine spray having failed and due to the nervousness of the patient it was decided to extract the foreign body under intravenous pentothal and gas oxygen anesthesia. Accordingly 0.5 grm. of pentothal was administered for induction and when the patient was under, the endotracheal tube was passed into the trachea and anesthesia continued with gas, Oxygen and Trilene.

With the help of the Oesophagoscope the foreign body was visualized lying longitudinally in the oesophagus and its mucous membrane was found collapsed over the piece of bone and the sharp edges were stuck against it. The piece was then manipulated, rotated and extracted along with the Oesophagoscope after two previous attempts had failed. While this manouvering was going on the patient's respiration had become apnoeic in character once or twice but not seriously long enough to interfere with the surgical procedure. The operation time was thirty minutes. After removal of the foreign body the endo-tracheal tube was pulled out and the patient was returned to bed. Immediately after, his breathing became suddenly shallow and stopped, and for a few seconds there was no radical pulse. Two c. cm. Nikethamide was injected intramuscularly and the patient was quickly taken to the Operation theatre. An endo-tracheal tube was passed and oxygen administered through Boyle's apparatus at the rate of four litres per minute. Breathing then became regular and normal. Oxygen was continued for about half an hour and the endo-tracheal tube was then removed. The patient continued to breathe normally for further 45 minutes when he was returned to bed. Soon after his respiration again became shallow and stopped. The same procedure as mentioned above brought the respiration phase again to normal. The cause of this repeated respiratory failure was thought to be due to some obstruction in the air passage.

When the pharyngoscope was passed, moderate edema of the glottis was noticed. The respiratory failure was attributed to the



Anteroposterior skiagram shows the foreign body at the level of the 7th C. V.



Skiagram lateral view shows the foreign body at the level of the 7th C. V.

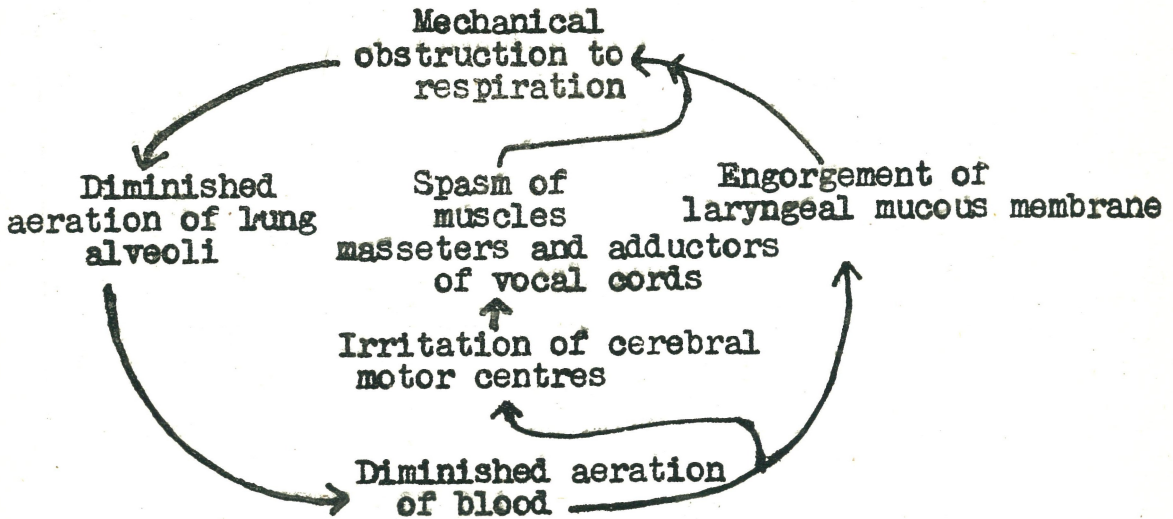
trauma caused by the sharp edges of the foreign body lacerating the mucous membrane during extraction. A high tracheotomy was therefore considered and carried out immediately.

Breathing became normal and the patient also regained consciousness. A continuous oxygen administration with carbon dioxide was maintained at the rate of four litres per minute and the breathing continued normal. Thereafter the patient's respiration stopped only once for a few seconds. The tracheotomy wound was closed after 72 hours. The

patient made an uneventful recovery and was discharged from the hospital on the thirteenth postoperative day.

Discussion :

The cause of this repeated respiratory failure and post-operative crisis can be attributed to the edema of the glottis and laryngeal regions caused by the sharp edges of the bone cutting through the mucosa during extraction of the foreign body and setting up a vicious circle as shown below.



The anesthetic agents could not be blamed for this condition as only gas oxygen and trilene were used with pentothal for induction. Thiopentone may some times give rise to masseteric and laryngeal spasm if the endotracheal intubation is not carried out promptly before the operation. The trilene used was of standard quality and purity and though no chemical tests were carried out, therapeutic test had been entirely satisfactory as the same re-agent was used for several patients following.

Maitra in a personal communication has described a similar case of post anaesthetic respiratory crisis in which the patient died 42 hours after operation. Hunter has described nine cases of post anaesthetic respiratory crisis all of which ended in death and has ascribed this to what he calls a new

condition of "Post anaesthetic encephalopathy". Necropsy has in a few cases revealed thrombosis of cerebral arterioles and softening of brain in small patches in various areas.

Whether the above case is also one of "Post anaesthetic encephalopathy" due to anoxemia from laryngeal vasospasm but recovered after timely treatment with oxygen and carbon dioxide is a moot point, as only nine cases have been so far recorded since 1946 in the literature and the essential pathology of this condition is un-known.

Once the vicious circle was established it would lead to a depression of the respiratory centre when the oxygen tension was sufficiently low and the carbon dioxide content increased in the blood due to stop-

page of respiration, the respiratory centre was stimulated to sufficient activity and patient breathed again. This is illustrated by the diagram facing page 24.

Summary :

- (1) A case of post anaesthetic respiratory crisis after general anaesthesia has been described.
- (2) The probable factors in the causation of this condition are described and evaluated.
- (3) Attention is drawn to a new condition of "Post anaesthetic encephalopathy" after general anaesthesia.

Acknowledgement :

I am extremely grateful to Lt. Col. A. K. Maitra, A.M.C. for allowing me to

report this case and for the valuable help and suggestions given from time to time in the preparation of this paper.

Thanks are also due to Col. H. S. Ahluwalia, O. C. 92 General Hospital for valuable help from time to time.

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Medico Legal – Disability Pensions

by

Lt-Col. V. SIVASANKARAN.

“Aggravation Passed Away.”

Disability compensation does not depend upon whether the disease in question is attributable to or aggravated by military service, for, it is the same in either case as it depends only on the degree of disablement by the disease. However, the duration of the award of a disability pension may be different because, if the disease is attributable to war service, disability pension continues so long as any disablement from the disease remains. If, however, the disease is aggravated by war service, then disability compensation continues only so long as it remains aggravated thereby. If the aggravation passes away so that the man is no worse than he would have been apart from military service, the pension ceases even though some disablement may remain, because that disablement is not due to military service. Thus recollecting this aspect as per my last article, there are two questions in every case to be answered. First, when did the disease arise? And secondly, what were the causes of its origin. If the disease existed before military service, it cannot be attributable to military service, but it may be aggravated by it. If it arose during military service and if service factors were one of the causes of its origin, then it is attributable to military service. But if military service was not a cause of its arising, it cannot be attributable to service, but may be aggravated by it. It is often difficult to say when a disease started. The usual question is whether the disease arose before military service, and in order to assert it, inferences from pre-service symptoms, X-Rays etc. would be useful. For example, in a case of Osteo-Arthritis – a disease in which

the symptoms may appear long after the commencement of injurious process, it would be quite correct to say that the disease was not attributable to service, but was aggravated by it. The difference must always be borne in mind between symptoms of a disease which may appear at a late stage and the disease itself which commenced with the injurious process leading to the symptoms.

Medical Boards are called upon on various occasions to state in a case considered as aggravated by service whether the effects of aggravation persist or have passed away. If there is evidence from which it can be stated that a disease which is pursuing its normal progressive course renders an individual no worse than he would have suffered in any event, apart altogether from military service, then aggravation would be considered to have passed away. To cite a case, BARNETT V. the Minister of Pensions, Mr. Barnett was enlisted on 14th October 1940 in the R.A.F. and rendered service till 6th November, 1941, when he was discharged physically unfit for any form of Air Force service in consequence of Bilateral Otitis Media. It was accepted by the Minister of Pensions that the disability ‘Otitis Media’ had been aggravated by exposure and stress and strain of Air Force service, and a pension was awarded to the individual, the assessment for the disability being 40% until 27th September, 1944. The Minister of Pensions refused to make any further award and decided that the aggravation of the appellant’s disability by Air Force service had ceased to persist on 27th September, 1944. The appellant appealed against this decision. A Medical Board was convened on 27th November, 1945, when it was found that all

systems were normal, but the right ear had profuse discharge with C.S.O.M. and, could not hear spoken voice at one foot. In the left ear, there was some catarrh, little or no discharge, and he could hear spoken voice at 4 yards. Together however, conversation during examination was carried on without any difficulty whatever, and ordinary conversational voice was not over 6 feet. The individual stated that his deafness was going worse; that he was a grocer's assistant before the war, but could not do that work now. It was held that the present degree of disablement might be regarded as the result of the natural progress of a chronic condition which existed prior to service, the effects of aggravation by service having ceased to persist. The case came before the High Court of Justice, Kings Bench Division, Denning J. As in this case he had slight defective hearing on enlistment, following typhoid fever in infancy, and in view of the fact that Otitis Media was a progressive disability; common to all walks of life, the point at issue was whether the condition from which he suffered in November 1945 was really just a progression of the disease he had before he joined the service or whether there remains aggravation by war service. It was noticed that the man after discharge had not been incapacitated for work at all, and a conversation during the examination by a Medical Board was carried on without any difficulty. It was decided that a condition from which he suffered after September 1944, was no worse than he would have suffered in any event, apart altogether from military service, and that the military service factors by that time had passed away altogether and did not affect his then condition. His disability pension ceased.

It was also held that where the evidence shows that a disability which is naturally progressive existed before military service and after military service is worse, a claim to pension in respect thereof is rightly rejected if the amount of the disability suffered after military service was no more than would have been suffered in any event apart from service. This one was a case of Fibrositis in which one Mr. Baker was called up for service on 26.3.42 in category A-1, and was invalided out of service on 1.6.43 with a disability

'Fibrositis'. At the time of discharge, his general condition was fair, skin healthy except that he had generalised fibrositis all over the body with no clinical signs of disability. He had suffered from Fibrositis prior to joining the Forces and he claimed that it had been worsened by army life and what was localized in the chest, became later generalized all over the body. A disability pension of 20% was awarded on account of Fibrositis having been aggravated by military service upto 5.7.45, when aggravation was deemed to have passed away, though it was found that the effect on function found by the Medical Board in the year 1943 was slight, whereas the effect on his function was moderate as found by the Medical Board in 1945, i.e. that there was a bigger effect in 1945 than in 1943. It was held that the aggravation by military service had passed away on the following grounds:— Because this is an illness or a disease which is naturally progressive, and the condition found in 1945 was no more than he would have suffered in any event apart altogether from military service. There may be other instances in which a disease may have existed before enlistment in the Army and aggravated by military service, but ameliorated by treatment so that the condition is what it was before military service and is in no way worse than it would have been if there had been no military service. In such cases also, aggravation due to military service would be considered as having passed away.

Capacity for work is not the basis of whether the aggravation of disablement has passed away or not, because a person may work whilst his complaint is aggravated, but the fact that he is able to work in that way provides evidence which we can take into account in deciding whether the disablement has reached the condition which it would have reached even if it had not been aggravated by military service. For example, myocardial degeneration cannot be held as attributable to service where medical evidence shows it to be a degenerative process due to interferences with the nutrition of the heart muscles. However, where aggravation is conceded before it can be said to have passed away medical evidence must show that the claimant is no worse of than he would have been with this progressive disease,

apart from service. In this case, Mr. Mathison was discharged from the army on 14th November '41 after nearly five years service in consequence of Myocardial Degeneration—the condition in respect of which the Minister conceded aggravation by military service. The disability pension on the basis of aggravation was sanctioned till 6th June 1946 when the Ministry Resurvey Medical Board showed that the clinical finding—Blood pressure and Electro-cardiogram—were normal for his age. Aggravation was considered to have passed away in view of the fact that the disease was a progressive degenerative one, occurring usually in persons of advancing years and the individual who had been suffering from giddiness, palpitation and breathlessness in 1944 had improved considerably in 1946 and that was what was to be expected in a man of his age and history at the time when the Resurvey Medical Board saw him even if he had not served in the Forces.

The Resurvey Medical Board, viz. I.A. F.M. 1291 in respect of officers, contains two questions pertaining to the above issue in cases where a disability was originally considered as aggravated by service. These questions viz.—

- (a) Has the condition improved to such an extent that aggravation no longer persists?
- (b) If not, have effects of aggravation ceased to operate to increase disablement? —

could suitably be answered in the light of what has been stated above.

Thus, to sum up, in considering whether aggravation by service has passed away, it is very material that the Medical Board should consider the condition of the individual as at the original Medical Board, i.e. on the date of discharge from the Forces, and compare it with the man's present condition. Even if the medical evidence is substantially the same as that of the first board, nevertheless there may still be properly a finding that aggravation has passed away because there may be little or no incapacity at the date of review or at any rate no more incapacity than the individual had before enlistment; or if the

disability was progressive, a stage had been reached when even apart from military service, the condition would have been the same. In order to assess the state of a disease, it is necessary to look not only into the clinical findings, but all other factors which indicate the state of health—capacity to do work, hours of work lost during post discharge employment. If the net result is, that on the date of review he is no worse than he would have been if he had not served, then aggravation may be found to have passed away.

Unforseen complications of service treatment.

In a case of a disease aggravated by military service where an operation is followed by complications, the test of attributability or aggravation by military service of the sequelae is—

- (a) where the disease would, in any event, apart from military service, sooner or later, have necessitated an operation; in which case the complications would only be accelerated by military service and being only accelerated, the proper finding would be one of aggravation of the original disease. But —
- (b) where the disease, but for military service, might not have necessitated an operation at all so that aggravation by military service is really the cause of the operation, the complications which follow directly on the operation are attributable to service.

Quoting an instance, Mr. Pilbeam suffered from Duodenal Ulcer while serving with the R.A.F. from 29-12-41 to 12-7-42, when due to tours of duty with consequent irregularity of meals, he alleged, he developed Duodenal Ulcer. Furthermore, he stated that his duties in Iceland from 12-7-42 to 10-7-43 were associated with irregular meal time with night duties in aerodromes and unloading at the docks at all hours of the day and night irrespective of the meal hours. He was enlisted in the Army on 31st October, 1941, and gave history of stomach trouble for over nearly 20 years prior to enlistment. He was discharged on 26th April, 1944, in consequence of Duodenal Ulcer, Phlebitis left leg

and deafness left ear. The case was that on 9th September 1943, on account of sudden severe pain in the upper abdomen, due to perforation of the Duodenal Ulcer, an operation was performed. Following the operation an incisional Hernia developed. This was an unfortunate complication arising out of the life saving measure which was performed with every skill and attention. It was held that Duodenal Ulcer was aggravated by Air Force service and pension at the appropriate rate was awarded. Mr. Pilbeam stated that his disability was attributable to military service. But it was held that since duodenal ulcer was merely the culminating effect of a pathological process which had been progressing for several years, and in this case the evidence clearly demonstrated that such process antedated his enlistment in the army, it could not be held as attributable. It was also held that Hernia was an unfortunate complication of the operation for duodenal ulcer and not the result of service compulsions. It was also held that Phlebitis of left leg, following the operation, which was a life saving measure, could not be regarded as brought about by compulsions of service. The man appealed before the High Court of Justice. It was held by Denning J. that the necessity for an operation could not have arisen at all but for the operation by military service compulsions, of the duodenal ulcer which had perforated; that the complication

which followed directly on the operation was, therefore attributable to military service, because the aggravation of the original disease was the cause of the complications Phlebitis and Hernia; that there would have been no necessity for operation but for military service. Incisional Hernia and Phlebitis were thus considered to be separate diseases from the original duodenal ulcer and appropriate awards were given.

In another case of an individual suffering from Hydro Nephrosis, for which an operation of nephrectomy was done, it was contended by the appellant that nephrectomy was a separate disability, apart from the original Hydro Nephrosis, because the Ministry of Pensions had conceded that Hydro Nephrosis had been aggravated by military service. It was held however that treatment for a disease, is different from the disease, and that the right approach was to see what would have happened to the individual apart from military service; that in any case he would have had nephrectomy for his Hydro Nephrosis, and therefore, the disability was one of Hydro Nephrosis with its sequelae and not nephrectomy; that nephrectomy and Hydro Nephrosis cannot be separated. Aggravation by military service having been conceded, a disability pension was conceded only up to the date of his nephrectomy, from which operation the patient rallied uneventfully.

Editorial

MEDICAL SERVICES DINNER.

The unification of the three branches of the Medical Services was nowhere more clearly demonstrated than at the First Medical Services Dinner held at Delhi Gymkhana on the 27th December 1951, where the Chiefs of the three Services, the Deputy Defence Minister, and the Defence Secretary joined in paying tribute to the efficiency of the Integrated Medical Service.

The Dinner was a new innovation. It is true that I.M.S. Officers, used to hold an Annual Dinner in London once a year, but the function was confined to a few retired officers and such of the serving officers as happened to be present in U.K. On this occasion, it was so timed that practically all the senior officers of the Corps, including those seconded to the Navy and Air Force and a large number of other officers were present in the Capital. Opportunity was taken to invite the Hon'ble Defence Minister, the three Chiefs, the Deputy Defence Minister, the Defence Secretary and a good number of retired and serving civilian officers of the I.M.S. present in the Station. Except the Defence Minister who was unavoidably away from Delhi, all others were able to grace the occasion.

It was indeed a large, distinguished and representative gathering at which a total of 129 sat down to Dinner.

The A.M.C. Pipe Band was in attendance.

At the conclusion of the Dinner, the toast to the President of the Republic was drunk with the playing of the 'Jana Gana Mana' by the Pipe Band.

General THAPAR, our D.G., then got up to drink the toast of 'Our Guests'. He is known for his wit and humour but on that night he surpassed himself and rose to scintillating heights. We may be able to recapitulate something of what he spoke but find ourselves unable to capture the spirit in which he said it. It will be conceded by the most puritan amongst us that on such occasions it is the spirit that counts.

He began by pointing out that it was a unique occasion where medical officers of the three services had met in a common function. Old I.M.S. Dinners in London were mainly attended by retired officers settled in U.K. and the I.M.S. Dinners in India were confined to the officers locally stationed. This was, however, the first Dinner when medical officers of the



BEFORE DINNER

From left to right :

**Maj-Gen. D. N. Chakravarti, Lt-Gen. D. R. Thapar, Gen. K. M. Cariappa,
Shri H. M. Patel & Maj-Gen. K. R. Sahgal.**

In the background :

Col. Barkat Narain, Col. H. S. Ahluwalia, M. C., & Col. Jaswant Singh.



AT DINNER



BEFORE DINNER

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AT DINNER



AT DINNER

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three Fighting Services from all over India had assembled and together with them we had our colleagues from the civil cadres of the I.M.S. and also retired officers.

He emphasised that the gathering had become more momentous on account of the array of distinguished guests. He explained that our Hon'ble Minister for Defence could not come as he was busy with elections and he was sure that all present wished him luck in his campaign. However, we had Maj-Gen HIMATSINHJI who, besides being a Politician of eminence, was also an old soldier and knew all the tricks of the trade and always helped us. Our Defence Secretary also, he revealed, made our fights his own and removed all financial obstacles from our way. He was sure the Navy would call him a 'Mine Sweeper'. He disclosed, amidst general applause, that the Defence Secretary had got us 15 annual vacancies for study leave abroad.

The function was thrice blessed by the august presence of our three Cs-in-C. General THAPAR said that he could not eulogize them as it was against military discipline but he thought he could get round the difficulty by stating a fact that the efficiency and improvements in our military hospital were a living monument to the personal interest taken by General CARIAPPA. His abiding interest in our Corps had provided us with a slogan in our drive for recruitment of the Nursing Officers. "Join the M.N.S. and enjoy tea with Cariappa." He remarked, amidst laughter, that if the other Chiefs followed the example

set by General Cariappa, the medicals would be crowded out.

He wound up by saying that lengthy speeches after dinner inhibited gastric secretion and to counter this effect he asked us all to stand up to 'Drink to our Guests.'

General Cariappa, our popular Chief, the Senior Guest at the function, then replied to the toast on behalf of the guests. He spoke of the excellent work done by the Medical Services and praised the cameraderie among the Medicals of all three Fighting Services in spite of their serving in different uniforms. He praised the high standard of professional efficiency in hospitals and field medical units and wished us all success for the future.

Maj-Gen HIMATSINHJI, Deputy Defence Minister, then spoke, congratulating the Medical Services for their efficiency, which was reflected in the spectacularly low sickness rate in the Indian Army. In his opinion, this was, to a great extent due to our good luck in having at the helm of affairs, Uncle Thapar and Uncle Sharma, who guided our destinies.

Vice Admiral PIZEY C-in-C Indian Navy then gave a short and witty speech in which he confessed to being somewhat confused at first by the implications of 'Integration' whereby an Officer could be referred to as a 'Lt-Colonel' and 'Commander' almost simultaneously and could change from one to the other like a chameleon with apparent ease. However, he agreed, that once he got used to the system he had nothing but praise for it.

Air Marshall GIBBS C-in-C Indian Air Force spoke on behalf of his Service. He stated that he had nothing but admiration for the young and growing Air Force and its Medical Service and was proud to have been called upon to serve India as their C-in-C. He pledged himself to looking after its efficient growth and welfare during his tenure of office.

Mr. H. M. PATEL, our Defence Secretary, in a short speech, wished the Integrated Medical Services and their newly inaugurated Annual Dinner success.

Colonel AMIR CHAND, that doyen of the I.M.S., spoke on behalf of the ex-I.M.S. officers - retired as well as serving in the Civil. He was glad that officers who had been our comrades in the past were remembered on such occasion and wished the function and the Integrated Medical Services all success.

After Dinner the Chiefs and other guests watched the band play on the lawn of the Club. The Commanders in Chief Navy and Air Force were

intrigued to see their ex-DsMS in Generals' uniform. The Army Chief, as is his wont, lost himself amongst the junior officers of the three services.

The function ended, perhaps a bit too soon at midnight, and everybody dispersed with the expressed hope that the Medical Services Dinner, will, in future, be a regular Annual Function.

* * * *

The unification of the Medical branches of the three Services of which this Dinner was a symbol is an event of which all of us are proud. The soldiers, sailors and the airmen of our Armed Forces, have a right to ask of the Integrated Medical Services professional skill of the highest order and it will be our utmost endeavour never to fail them. Our strength to serve lies in our Cohesion.

We congratulate the organizers and fervently hope that the Medical Services Dinner will be celebrated annually and that its inner meaning will be reflected in the feeling of oneness amongst the Medical officers of the three Services.

Adm: Notes

Study Leave

Since the issue of our last Journal, the following AMC officers have proceeded on Study Leave to the U. K. :—

1. MR—196 Lt. Col. A. K. Barat
2. MR—235 Major R. S. Hoon
3. MR—465 Capt. C. R. Suryanarayana
4. MR—503 Capt. Mohd Abdul Majid.

The following officers have returned from U. K. after completing their period of Study Leave.

1. MR—193 Lt. Col. S. Kaul
2. MR—251 Major Kirpal Singh
3. MR—294 Major S. Dass

OBITUARY

We regret to announce the death of M-13641 Capt. D. H. ROBERTSON, AMC (Ex IMD/BC) on 3-11-51 at 148 G.H. from Cerebral Haemorrhage.

Capt. Robertson was 49 years of age at the time of his death. He had a very good career in the Army as a 'Pathologist'.



T. C. F.

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Letters to the Editor

Sir,

Sulphonamide Anuria.

In the April 1951 issue of the A.M.C. Journal, there was an interesting article called "Treatment of Uraemia by Extra-Renal Dialysis". We have also treated a case of Sulphonamide Anuria. As there are so few such cases on record we are sending these notes for publication.

Case: 443372 Rect. Ishwar Singh, Age 23 years was admitted on 3-11-50 for an inflammatory condition and was put on a course of Sulphonamide.

On 6-11-50 at 0400 hours he vomited once, complained of pain in the loins and had haematuria. He was given I. V. Glucose saline drip and Mist Alkali 4 hourly. At 1000 hrs. he passed 8 ozs of urine mixed with blood. This specimen of urine was lighter in colour than the first one. I. V. drip was continued thinking the urine would clear, but as the patient did not pass urine till 1600 hours, Sodi Sulph 4% by drip method was commenced.

On 7-11-50 his general condition was fair but he had not passed any urine. Sodi Sulph by drip method was continued and 2% Soda Bicarb was introduced into the Stomach/Duodenum by continuous drip method through a Ryle's tube. By evening his eyelids and face were puffy and slight oedema of the feet was noted. The enteral and parenteral drip were continued at a slower rate.

On 8-11-50 morning, puffiness had increased and the abdomen was distended. Both the drips were stopped and an enema was given with poor result. Patient was

dozing off and on and fine tremors of the fingers were noted. After a few hours, patient had developed generalised oedema, probably owing to the further absorption of fluid from the stomach and intestine and he was on the verge of coma. It was then that we decided to do a pyelostomy.

At 1500 hours under spinal Nupercaine, (R) Kidney and Ureter were exposed by a Lumbar incision. The Pelvis and Ureter were very much distended and the latter looked like a vein. Kidney showed moderate enlargement. A nick was made into the pelvis and blood-stained urine gushed out. A catheter was passed into the pelvis and it was irrigated; the returning fluid looked clear. Below the nick, the ureter felt absolutely solid, even a probe could not be passed into the lumen. The catheter was retained in the pelvis and brought out through the external wound. Straw-coloured urine was found to be dribbling through the catheter while the wound was being closed.

From the time the catheter was inserted till the next morning quantity of urine drained was 115 ozs. The puffiness of the face and the eyelids had almost disappeared. Nothing remarkable was noted from the day of the operation till 12-11-50 when patient again had haematuria, the urine being of a tarry red colour, 80 c.c. in quantity. From then onwards, he passed a good quantity of urine per urethra, the colour of the urine gradually becoming lighter. Drainage per lumbar wound was also satisfactory but less in quantity. On 15-11-50 pt. passed a pint of clear urine in the morning. The catheter was being pulled out gradually and was completely removed from the lumbar wound on 22-12-50.

Discussion :

In the previous article it was stated that shunting of glomerular circulation and tubular degeneration are the cause of Anuria and not blockage. But in our case mechanical obstruction was the only cause found. There could not have been shunting of the circulation or tubular degeneration. If so the urine would not have dribbled at the moment of the insertion of the catheter into the pelvis of the Kidney. In both cases haematuria recurred on the 7th day after absolute anuria. In our case we could state that the pelvis being opened up, gave the ureters time to get rid of the crystals and blood clots causing the blockage and regain their normal function of excretion. It is also worth mentioning that even when the patient passed tarry red urine per urethra, that from the pelvis of the ureter was of normal straw colour. This also shows that the whole pathology was in the ureter below the level of the pelvis.

Major A. C. Bose, A. M. C.

Capt. T. G. C. Panikkar, A.M.C

Physiological and Pathological Variations in Blood Sugar Curves and Diagnosis of Mild Diabetes

Sir,

The article "Physiological and Pathological variations in Blood Sugar curves and diagnosis of Mild Diabetes" by Lt. Col. Inder Singh in the October 1951 issue of the Army Medical Corps Journal is likely to give an erroneous impression about a very complex subject and especially so if the readers of the journal do not have the references quoted by the author of the article ready at hand. References from well known authorities when viewed apart from their context are apt to give an entirely misleading picture.

To quote Lawrence "To the majority of cases who ask why they developed diabetes I have to answer that I do not know" (Lawrence 1). Diabetes Mellitus is defined by Joslin as "a hereditary disease characterised by an increase of sugar in the

blood and the excretion of sugar in the urine; it is dependent upon the loss or decrease of the insulin secreted by the islands of Langerhans of the pancreas and is functionally interrelated with other endocrine glands particularly the pituitary, but also the adrenal and thyroid and the liver".

The author of the article has restricted "True Diabetes" to hypoinsulinism, whereas cases of relative deficiency of insulin are not "True Diabetes" and "that matters a lot in the patients' future outlook in Life". But to quote Haussay Long and others fully which has evidently been missed by the author of the article. "Diabetes Mellitus used to be considered as due to lesions of the islets of Langerhans resulting in deficient output of insulin; within recent years the conception of its etiology has been widened to include *any* (italics mine) disturbance in the normal balance of regulating endocrine factors that will result in the symptom complex"... "This wider conception of the disease differentiates it from hypoinsulinism in that while all cases of the latter are diabetes, *all diabetes do not exhibit hypoinsulinism*". (Cameron I) (*Italics mine*).

For the future well being of a patient and not to give him false assurances it is important that one should have a "wider conception" of the disease, because an important factor in islet destruction is a continuous hyperglycaemia and both experimental and clinical studies has shown that if this hyperglycaemia can be detected and treated, whether by diet and/or insulin the progress of the disease can be stopped or minimised. It is known that hyperglycaemia can be initiated by extra pancreatic factors and human diabetes may well begin this way. It is not at all certain that severe insulin deficient diabetes is primarily due to an inherent pancreatic weakness. It may well have begun with hyperglycaemia due to extra pancreatic factor (Lawrence 2).

It is important to note in the experiments of Watson quoted by the author that the diabetic tendency is only arrested and to maintain normal carbohydrate metabolism subsequently there must be continued

restriction of diet. To quote Lawrence immediately after as has been done by the author that "If these (i.e. Blood sugar tests) are normal then the original diagnosis of Diabetes is untenable" is to beg the question, since Watson has not claimed that the diabetic state is cured but only arrested and dietetic treatment is to be continued. Further Lawrence states that although the diabetic tendency is only discernable by Blood Sugar tests—"but it persists" (Lawrence 3).

It is a *sine-qua-non* that a case of Glycosuria not to say of symptomless diabetes should be thoroughly investigated because there is no doubt that the disease is usually established long before symptoms develop (Lawrence 4) and also because it is of the utmost importance to prove or disprove the presence of Diabetes Mellitus or any tendency to it early, and institute therapy, otherwise it is invariably progressive. In this investigation the co-operation of the patient is essential as false readings can be very misleading and can only injure the patient in the long run.

The dose of glucose given for a Glucose Tolerance test should not be a controversial point, since it is the usual practice to give 50 gms, which is the amount considered sufficient to put the power of body and particularly of the Liver to deal with or "tolerate" sugar to a searching test. (Lawrence 5). Even by the formulæ quoted from Stitt the dose of 1 gram per kilo body weight works out for an individual of 120 lbs to just over 50 grams and the average weight in the Armed Forces (excluding the Boy's Battalion) is near or above that.

In the tabulation of Pseudo-diabetic curves the author has misquoted Lawrence (6) in saying "mild toxic and infective conditions such as common cold" Lawrence only states "Toxic and Septic conditions" without the "Mild" and "such as common cold", and if Harrison is to be quoted then it is "Mild infections such as a cold in the head, probably have a slight effect on the Blood-sugar curve though it is difficult to prove this" (Harrison 1). Further Lawrence states "accidents and infectious diseases, such as

Influenza and scarlet fever, frequently seem to be causal factors, but probably their effect is often merely to develop or draw attention to a latent and unnoticed diabetes" (Lawrence 7). Infections and even common cold intensifies the disease process and increases enormously the demand for insulin, but it is improbable that it initiates diabetes in these patients.

However, as far as infections are concerned in the causation of Diabetes Mellitus, in certain very rare cases there may be a doubt as to whether the onset of Diabetes Mellitus can be accelerated by severe infections involving pancreas, endocrine glands and biliary tract leaving permanent damage to the structures, provided that the onset of the diabetes occurs in immediate time relationship with the above condition.

The author has mentioned the effect of emotion on the fasting Blood sugar curve and quoted Harrison but he has missed adding that in Harrison's experience it is exceptional for emotion to effect Blood sugar significantly (Harrison 2).

For the diagnosis of Diabetes Mellitus a thorough physical examination and a Glucose Tolerance test is essential. The mild diabetic curve has certain factors. It may commence with a normal fasting level, but reaches its maximum later than normal, rises too high (Hyperglycæmia) and is delayed in its return to a normal figure (Lawrence 8). This type of curve has been described as "High and spread". The Glucose Tolerance curve should not be read in isolated bits. This will obviate any question of accusing the patient of having had insulin before the test.

The author of the article seems to be obsessed with the idea of a lower category in cases of hyperglycæmia. With the exception of cases with oxyhyperglycæmic glucose curve and cases of renal glycosuria where a clean bill of health can be given, it will be seen that other conditions mentioned by the author will require a lower category and treatment dietetic or otherwise at least temporarily; for example:—

Simple Obesity, Hyperthyroidism, Hypopituitarism, Hepatic "Diabetes," Addison's

disease, Adrenal Cortical tumour and apart from the fact that hyperglycaemia associated with these conditions may well bring about "True Diabetes Mellitus" some of these conditions are just as serious or even worse than Diabetes Mellitus, where there is immediate grave risk to life. At least Diabetes Mellitus can be controlled like hunger is controlled with food and the outlook is not so dismal.

It is essential that one should cultivate a broad outlook on this subject of Hyperglycaemia—an outlook which injures neither the state nor the individual. Cases which show Hyperglycaemia will have to be reviewed again and again till a definite label can be given. This may be either a frank Diabetes Mellitus or some other conditions mentioned above. There will be some border line cases where hyperthyroidism or hyperpituitarism cannot be pin pointed, yet there is hyperglycaemia. We know that this hyperglycaemia will in the long run be injurious to the islets of Langerhans and it is essential to place such an individual in a lower category at least temporarily, since these cases require treatment and medical control. To give an impression to such individuals, that they have only hyperglycaemia and not Diabetes Mellitus and therefore need not worry is to give them a false picture of the whole question. No individual can eat his cake and also have it.

There are a number of other controversial points where the author of the article has presented only one side of the picture. To show the other side would only lengthen this letter.

Yours faithfully,

C. C. KAPILA,

Colonel.

Poona.

Dated 11 Jan. 1952

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Sir,

I may be allowed to make a few observations on the article, "Physiological and Pathological variations in blood sugar curves and diagnosis of mild diabetes", which appeared in the Oct. '51 issue of your esteemed Journal.

This article seems to me to propound a wrong type of logic, i.e. that, which stresses on the abnormal and the rare, and keeps the common in the background.

It is a sound rule to regard all cases showing a diabetic type of response after a properly done glucose tolerance test as diabetics, unless definitely proved otherwise.

Every body agrees that hyperglycoemia does not invariably indicate diabetes mellitus.

Rare causes, that may give rise to hyperglycoemia do exist and some of these do give rise to a diabetic type of curve. But in spite of all these possibilities, diabetes still remains the most possible cause.

Moreover, people who show a pseudo-diabetic type of curve, are possibly fit for lower category duties only for the period they exhibit the curve, and so no harm is done by medical men putting them in their proper place, till a definite diagnosis is established. Health and life are of much greater value to most people, rather than placement in a high category.

Mention has been made in the article on the occurrence of curve in diabetes. A para from page 87 of Laurence's Diabetic life is quoted below. "No complete and prolonged cure of true diabetes has ever been substantiated. I meet a few patients and hear of many more, who have been cured; but investigation shows that either they never had true diabetes or have improved so much from treatment, usually the reduction of obesity, that the diabetic tendency is only discernible by blood sugar tests—but it persists".

The occurrence of symptomless diabetes has been questioned in the article. Symptomless diabetes is a commonly observed condition, and usually the disease is long established before symptoms appear. Lack of symptoms and a normal fasting blood sugar, are not inconsistent with mild diabetes.

A few lines about glucose tolerance curves will not be out of place. The points to note in the normal curves are a fasting venous blood sugar level between 60-120 mg per 100 c.c., (60-100 mg per 100 c.c. in our country); peak level within the first hour; which rarely exceeds 170 mg per 100 c.c.; the time to return to normal is $1\frac{1}{2}$ to 2 hours; there is no glycosuria, the renal threshold for sugar being about 180 mg percent.

In a diabetic type of curve, the fasting blood sugar is raised above normal in all but very mild cases; there is usually a gradual rise, lasting for an hour or more to a peak level which is 80 mg or more above the

fasting level, and there is a delayed return to normal and the renal threshold for glucose is usually exceeded by the peak level, so that glycosuria occurs during the test.

Pseudodiabetic curve is a well recognised condition and may be obtained in,

- (1) Old age - (age must be really old)
- (2) Other endocrine disorders
 - (a) Hyperthyroidism - A small percentage of patients with hyperthyroidism have a raised blood sugar level. Under the influence of excess of thyroid hormone, the liver becomes hypersensitive to impulses from sympathetic nerves, which promotes conversion of glycogen to glucose. The blood sugar rises rapidly to a peak, seldom exceeding 200 mg and fall more quickly than in the diabetic type of curve.
 - (b) Hyper-pituitarism - Cushing's syndrome, whether due to a lesion of the pituitary or the adrenal cortex is always associated with decreased glucose-tolerance.
- (3) Toxic and septic conditions—Pyogenic infections, especially carbuncles and furunculosis. Usually the blood sugar falls more quickly than in the diabetic type of response. Curves become normal when the skin condition improves. (We are doing routine blood sugar tests in a number of average non-diabetic hospital cases, and have not come across common cold as a cause of diabetic type of curve.)
- (4) Previous carbohydrate restriction.
- (5) High fat feeding and obesity—curve becomes normal when the patient's weight is reduced.
- (6) Emotional disturbance can cause temporary hyperglycoemia.
- (7) Pheochromocytoma.
- (8) Intracranial lesions, specially those involving the hypothalamus and 4th ventricle.

A thorough clinical examination, and repetition of the glucose tolerance test with care will clinch the issue.

Special mention must be made of liver disease, in which condition abnormal responses are obtained in the glucose tolerance test. This is a common enough cause for confusion: the reduced glucose tolerance does not indicate a deficiency of insulin, but a disturbance originating in the liver in its capacity to synthesize glucose.

A glucose-phosphorus tolerance test is of help in differential diagnosis.

Under normal condition in the course of standard I. V. glucose tolerance test, the serum inorganic phosphorus level falls to from 60 to 90% (av. 75%) of the fasting level by the end of the first hour after beginning of glucose administration. (Standard dose of 0.5 gm of glucose/K.gm given over a thirty minute period.) In hyperglycoemia due to liver disease, the average fall of serum inorganic phosphorus is to 63% of the fasting level, and in diabetes only to 88%. In both

these groups the decline is more prolonged than in normal.

Although blood sugar test at one hour after an ordinary mixed meal is extremely valuable and often avoid the necessity for a formal tolerance test, the value so obtained is not strictly comparable to that at the same interval after a known amount of glucose, which is readily absorbable, without digestion.

Renal glycosuria; The view of most authorities is that it gives precisely a normal type of curve, and is asymptomatic. Rarely it is severe enough to be confused with a diabetes case.

A case of glycosuria, with or without symptoms, who on proper glucose tolerance test shows a diabetic type of curve, is more likely to be a case of diabetes than anything else.

Yours faithfully,
B. B. Bhattacharjya,
Lt. Col. A.M.C.
Poona.

News Letter - A.M.C. Centre North Lucknow

I Training.

Training has gone on as usual except that in addition to Boys and Recruits Training, there have come for training to the Centre, ex-service men on short service engagement, who are being put through an accelerated course of training.

Two batches of SSRC Officers have been put through four weeks (each) course in Basic Military training. A third batch of SSRC Officers is expected to report for training w.e.f. 1st DEC 51.

A ten weeks' Junior/Intermediate Cadre Course for NCOs has been going on since the 15th of Oct 51. 92 A.M.C NCOs are undergoing this course.

II Visits/Inspections.

Major-General A.N. SHARMA DMS Army Inspected this Centre in October. On the evening of 23 Oct 1951 a buffet supper in his honour was arranged at the AMC Officers' Mess which was largely attended. On the morning of 24.10.51 a ceremonial parade was held at the Centre parade ground when the DMS after inspecting the parade gave a very encouraging talk to Officers and men.

The DMS then went round the various sub-units and departments of the Centre, including the Centre Farm where the General performed the opening ceremony of the Farm irrigation project. This huge project has been designed and successfully completed by the unit personnel without any outside help. The DMS named the newly acquired Diesel Field Marshall Tractor as "SHRADHA" which represents the spirit behind the Grow More Food effort of this Centre.

The Col Commandant Lt-General D. R THAPAR, CIE, OBE, inspected this Centre on 21 Nov. 51. To celebrate the occasion, a regimental guest-night was held in the Officers' Mess on 21 Nov 51. In an after dinner speech the Col Commandant expressed pride and satisfaction at the way the Corps was progressing and especially the good work being done all round by the younger Officers and especially towards the maintenance of the Spirit and traditions of the Corps. After the dinner there was a dance display by the Boys Coy of the Highland Fling and khukri dances round a Bon fire on the lawns which was highly appreciated by all.

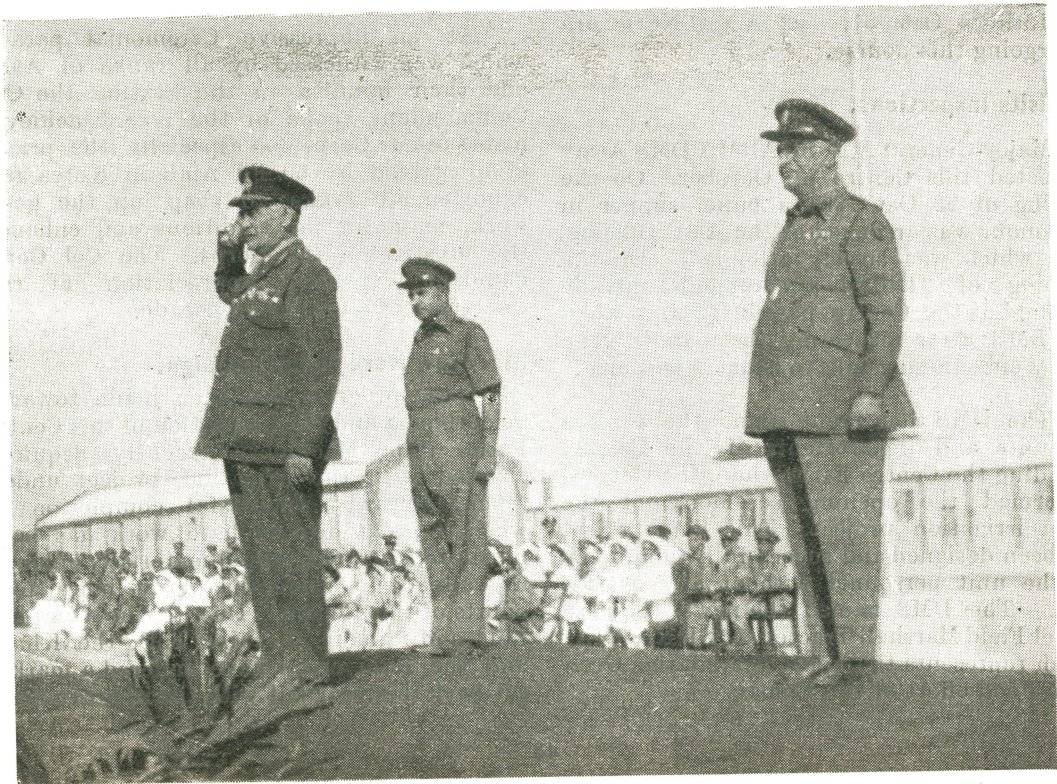
At an impressive Ceremonial parade which was witnessed by all ranks of AMC and their families in the Station the Col Commandant spoke of the recent achievements of our Corps and especially the praise of all gained by 60 Fd Amb in Korea and exhorted all ranks to keep up the good work, maintain the traditions and enhance the prestige of the Corps. The Col Commandant expressed appreciation at the smartness of all ranks on parade.

III Grow More Food Campaign.

Great progress has been made towards modernising and Mechanisation of this Centre Farm. The Machinery recently acquired coupled with the irrigation project undertaken, towards successful completion of which a great deal of hard work has been put in by all ranks, would materially enhance the already considerable grow more food efforts of this Centre. Due to the complete failure of rains in the area both the Kharif and the Rabi crops have suffered a marked set-back this year but with the improvements



THE D. M. S. ADDRESSING THE PARADE



THE COLONEL COMMANDANT TAKING THE SALUTE AT THE CEREMONIAL PARADE

now in hand, it is hoped conditions for the future will be markedly improved.

The Centre has already been awarded the first prize (of Rs. 1000/-/-) for the most outstanding work in grow more food campaign in the Army. A congratulatory message from C-in-C Army received recently in this connection reads as follows :—

“I congratulate you and all ranks under your Command on your Centre having been selected as the unit which has done the most outstanding work in the “Grow More Food Campaign” during the year 1950/51, in the Army. The Cash prize of Rs. 1000/- offered by the Ministry of Food and Agriculture for this, has been rightly awarded to your Centre.

Please tell all your officers, JCOs, men and non-combatants of your unit how

pleased I am with their excellent efforts. I hope that your unit will continue this good work and will put up an even better show next year.”

IV Sports.

The Centre Hockey Team started the hockey season this year entering the Dewa Fair Hockey Tournament, during the month of October. Some of the well-known hockey teams of U.P. participated in the tournament. The Centre team qualified for the semi-final by defeating M.Y.A the holders of local League Championship and reached the final by winning against Military 11, Barabanki, but unfortunately lost in the final to Government Press Allahabad by one goal. The team were however winners of the Station tournament. The Centre Boys Boxing Team came out runners up in the Sub Area Boxing Tournament.

Record Office Bulletin

Mustering out Pension : J.C.Os.

The question of grant of Mustering Out Concessions to JCOs who, on discharge during the release period, had completed the prescribed period of service in the particular rank (24 years in the case of Jemadar and 28 in that of Subedar) was under consideration at Army HQ.

It has been decided at Army HQ that M.O. Concessions will NOT be admissible to these JCOs on the grounds that as they had already become due for retirement under Rule 238 RAI, they could not be regarded as released on account of reduction in establishment and further, that there has not been any premature loss of career in their case.

60 Indian Field Ambulance

At the request of the U.S. Defence Department, the C-in-C United Nations Command has organised a group of United Nations Service men from the U.N. Forces in Korea to visit the United States in connection with U.N. Day ceremonies in Washington on 24 October '51.

60 Indian Field Ambulance have despatched No. 6136 Havildar Muthukrishnan and No. 6733341 Nursing Orderly Kushal to represent India.

Mustering out Pension: J.C.Os.

Army Headquarters men un JCOs ko jo apne release waqt me discharge hone par apni rank men puri naukri yani 24 sal Jemadar aur 28 sal Subedar ki hasiyat se, kar chuke the mustering out concession dene ke sawal par vichar kiya ja raha tha.

Abhi Army Headquarters ne yeh faisla kar diya hai kih kionkih yeh JCOs pahile hi RAI Rule 238 ke mutabiq apni naukri puri kar chuke the aur establishment men koi kami hone ki wajah se nahin release hue aur na pension jane se unki naukri ke jivan par koi nuksan dene wala usar para hai, mustering out concession ke haq dar nahin hain.

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DIETARY SUPPLEMENT

THREPTIN

THE PALATABLE

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IN CRISP AND DELICIOUS GRANULES

CONTENTS PER OZ.

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Thiamin.....	1 mg.
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IX-P 245



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A potent antibiotic compound derived from streptomycin by reduction with hydrogen.

WHEN IS IT INDICATED?

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HOW DOES IT ACT?

The antibacterial activity of Dihydrostreptomycin usually parallels that of streptomycin in tuberculosis. Resistant strains of organisms appear to develop as rapidly as with streptomycin.

WHAT ARE ITS ADVANTAGES?

Dihydrostreptomycin is significantly less neurotoxic than streptomycin and hence can be given in larger doses and for more prolonged periods. In addition, patients showing allergic reactions to streptomycin have been able to continue with the dihydro form.

HOW IS IT ADMINISTERED?

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WHAT IS THE DOSAGE?

Daily doses of 2 grams of Dihydrostreptomycin Squibb may be given safely for periods equal to those in which streptomycin has been restricted to 1 gram a day, provided there is no renal dysfunction. Average dosage—1 to 2 grams daily in divided doses every 12 hours.

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