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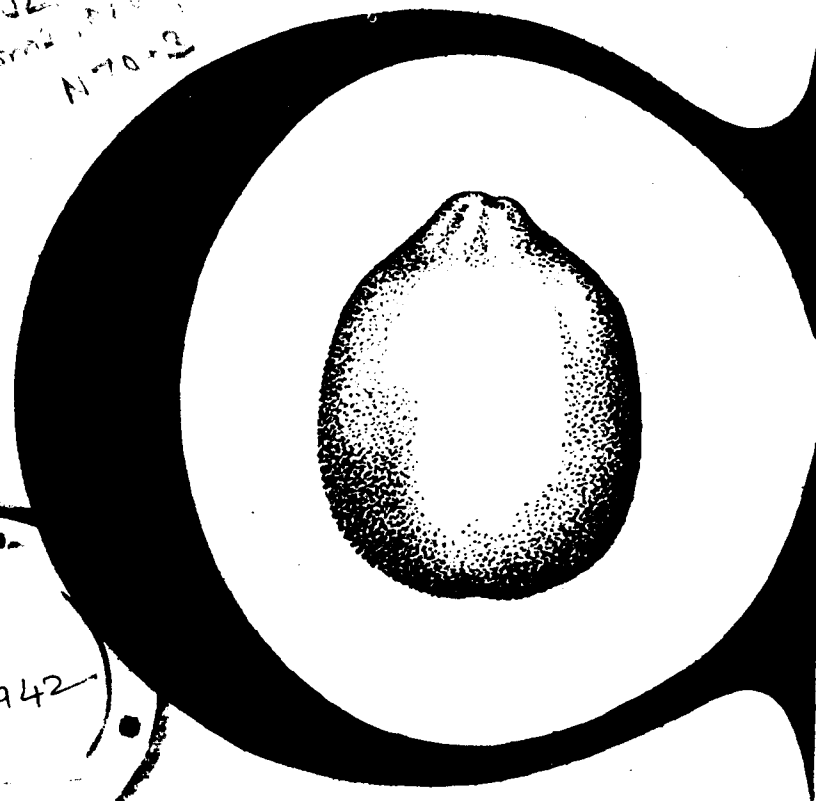
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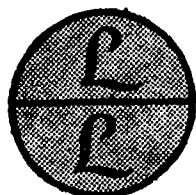
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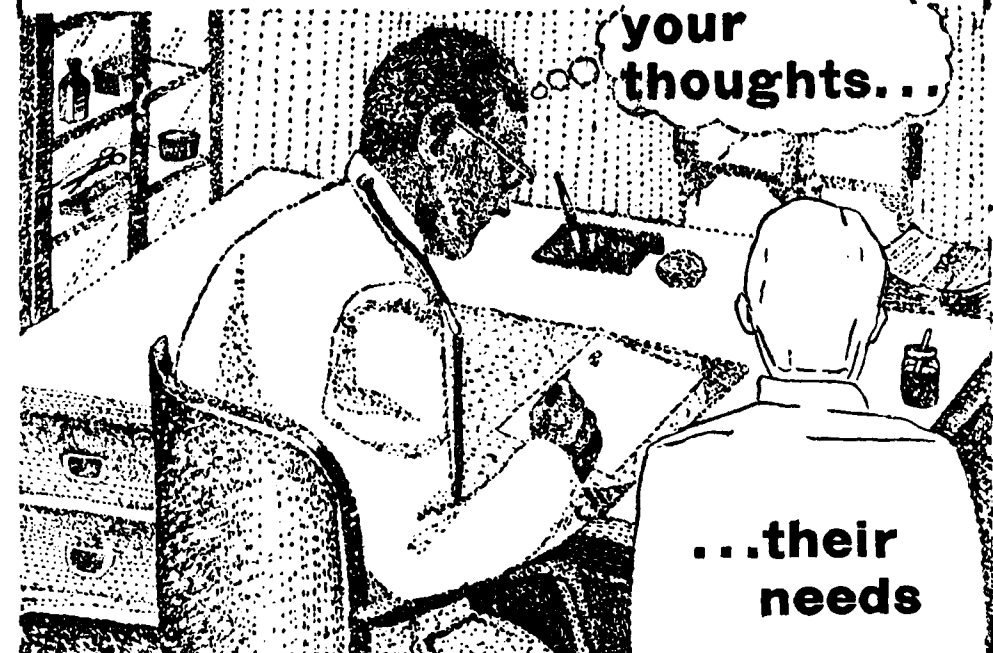
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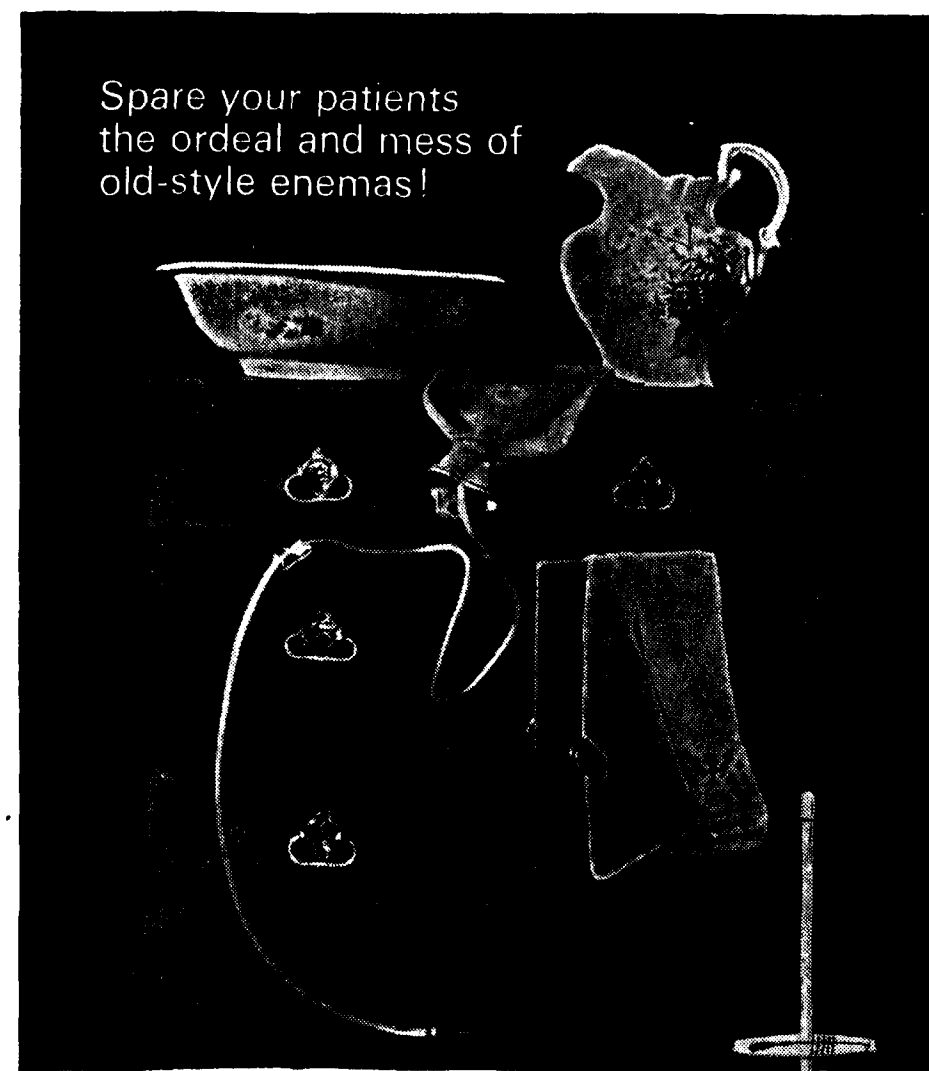
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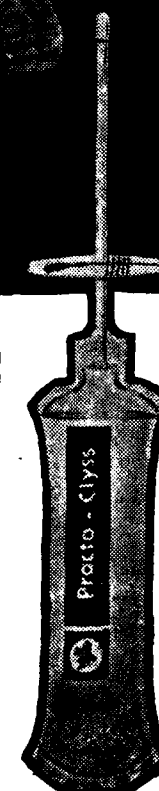


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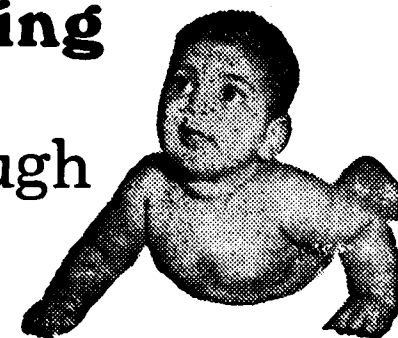
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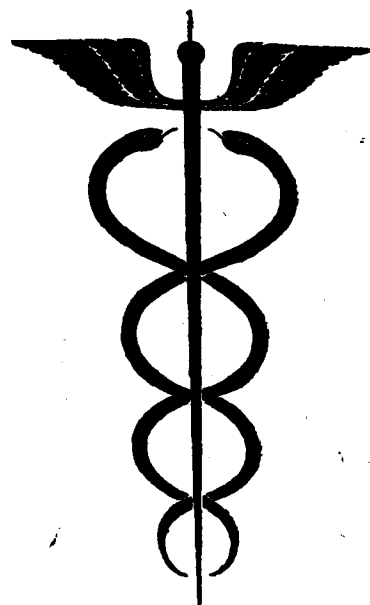
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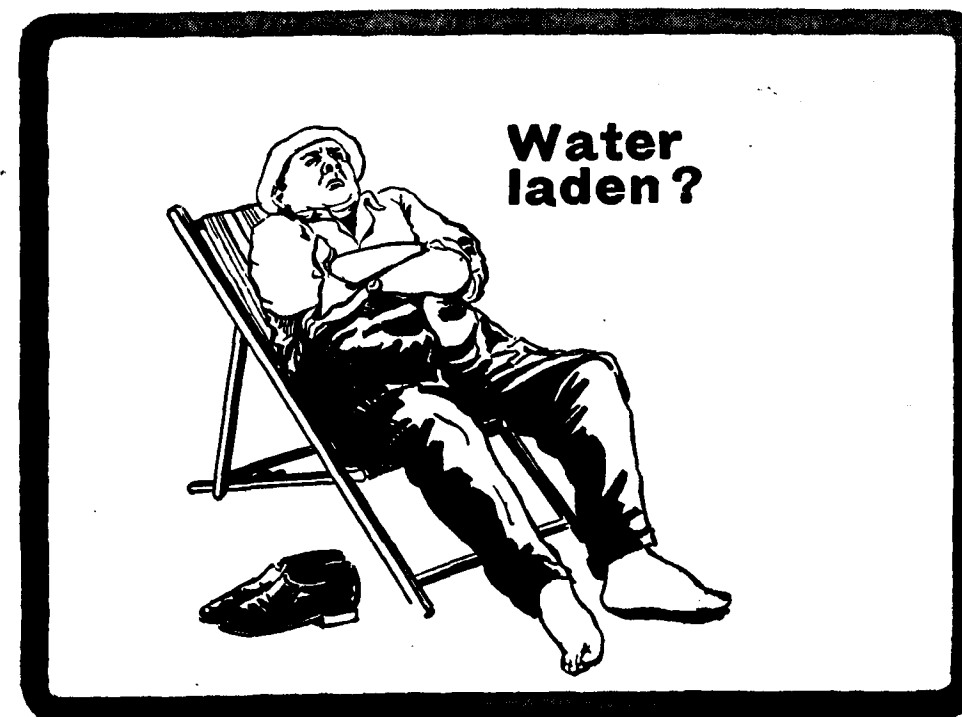
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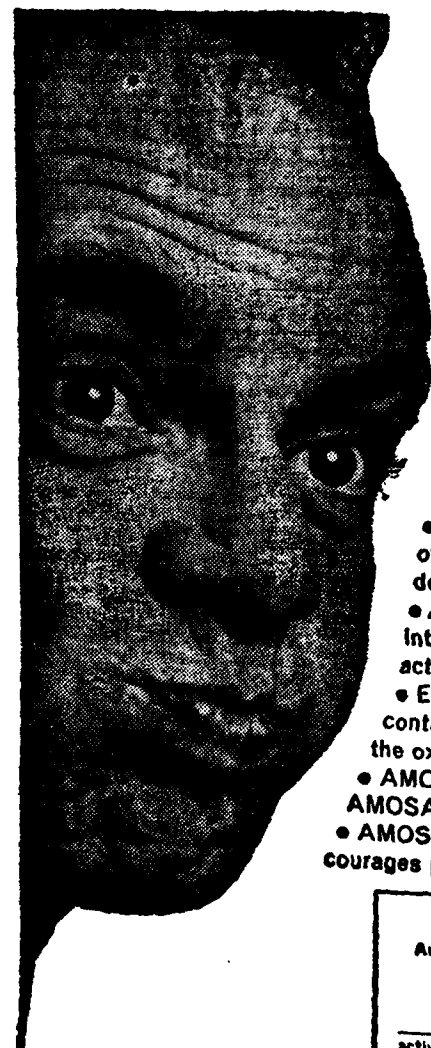
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2. Smith, J.F. et al: Dent. Survey 45:33 (Nov.) 1969. 3. Rice, E. et al
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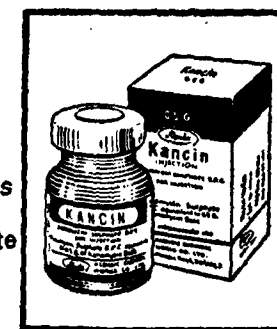
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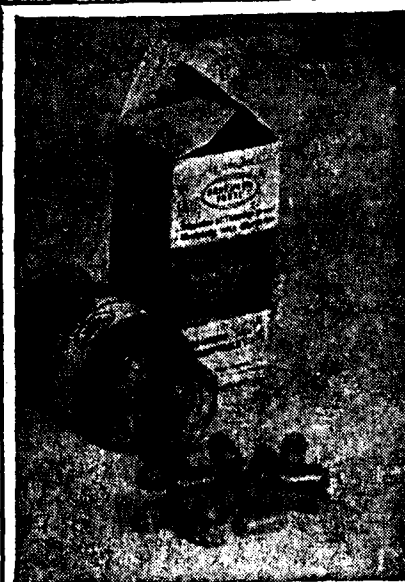
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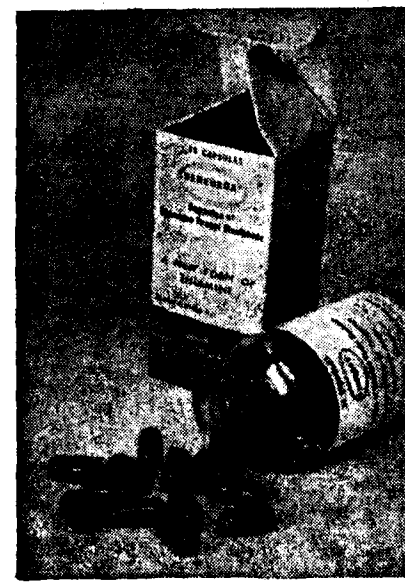
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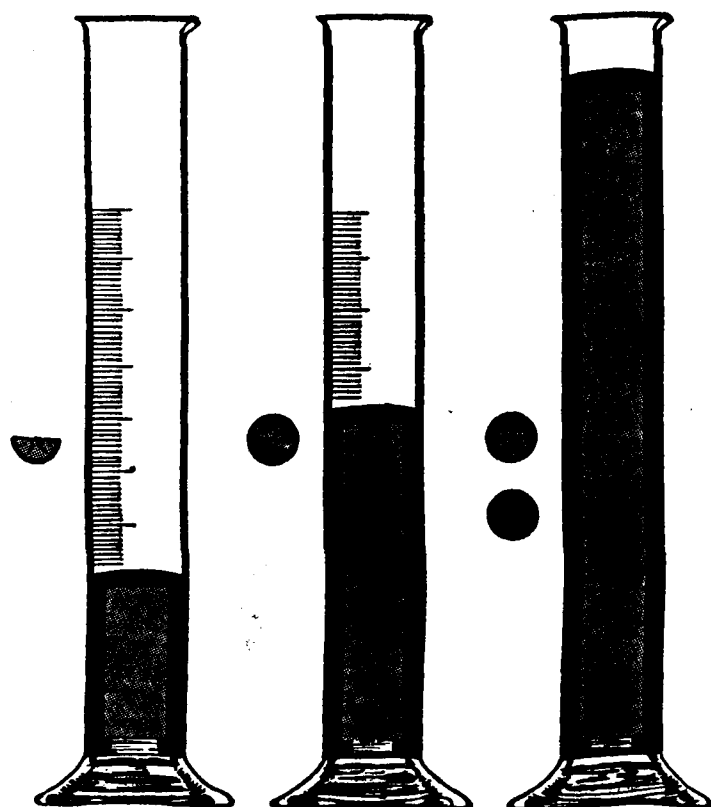
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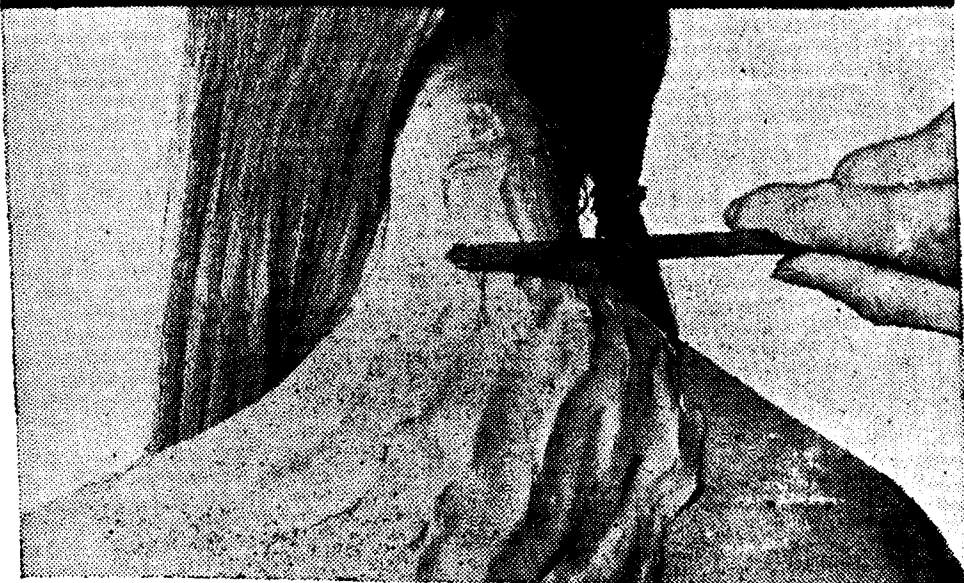
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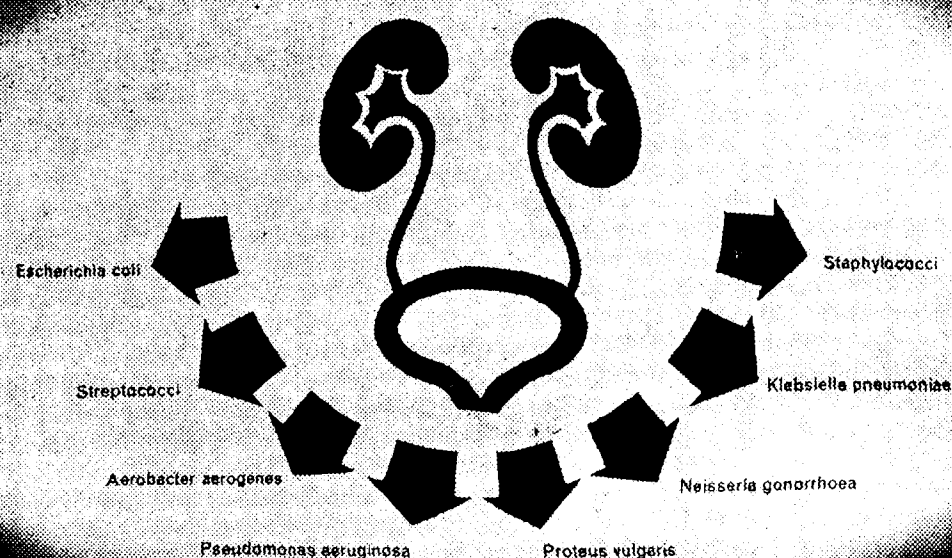
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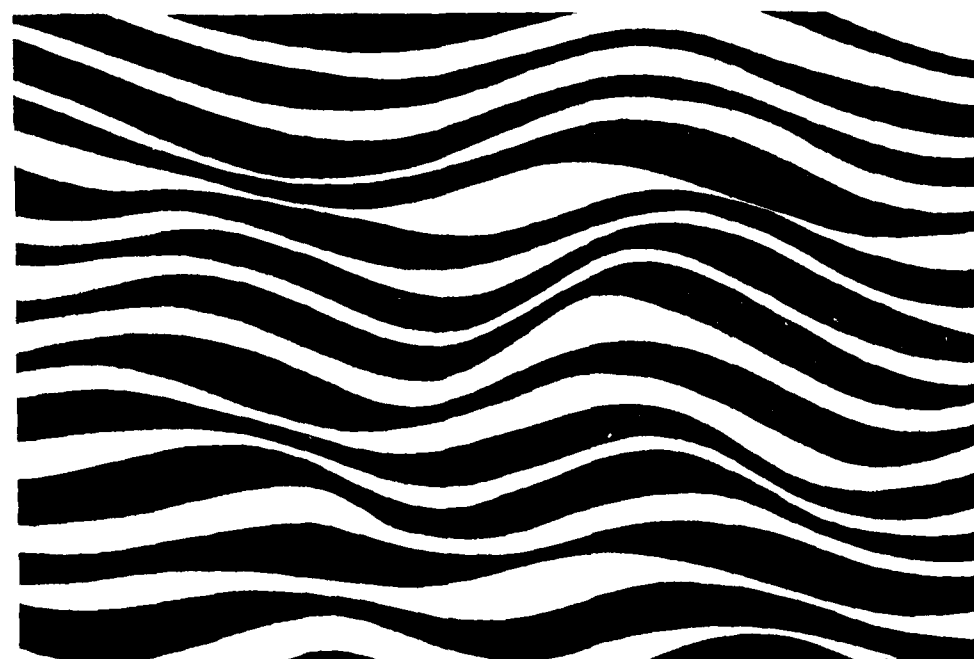


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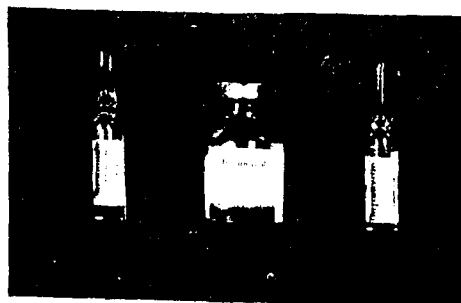
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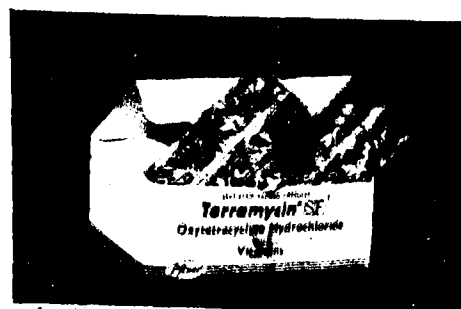
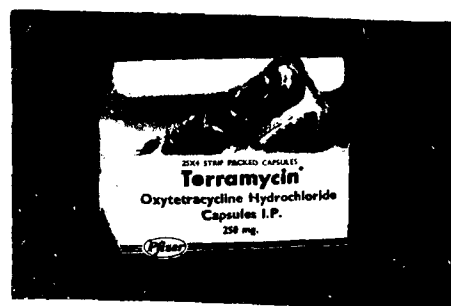
—Welch, H., et al., Dept. of Health, Education, Food and Drug Administration, Washington, D.C.

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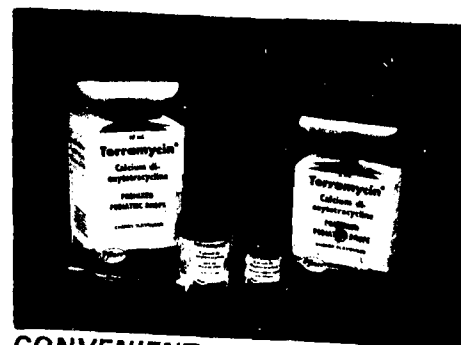
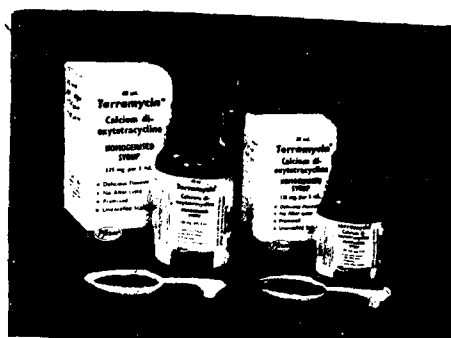


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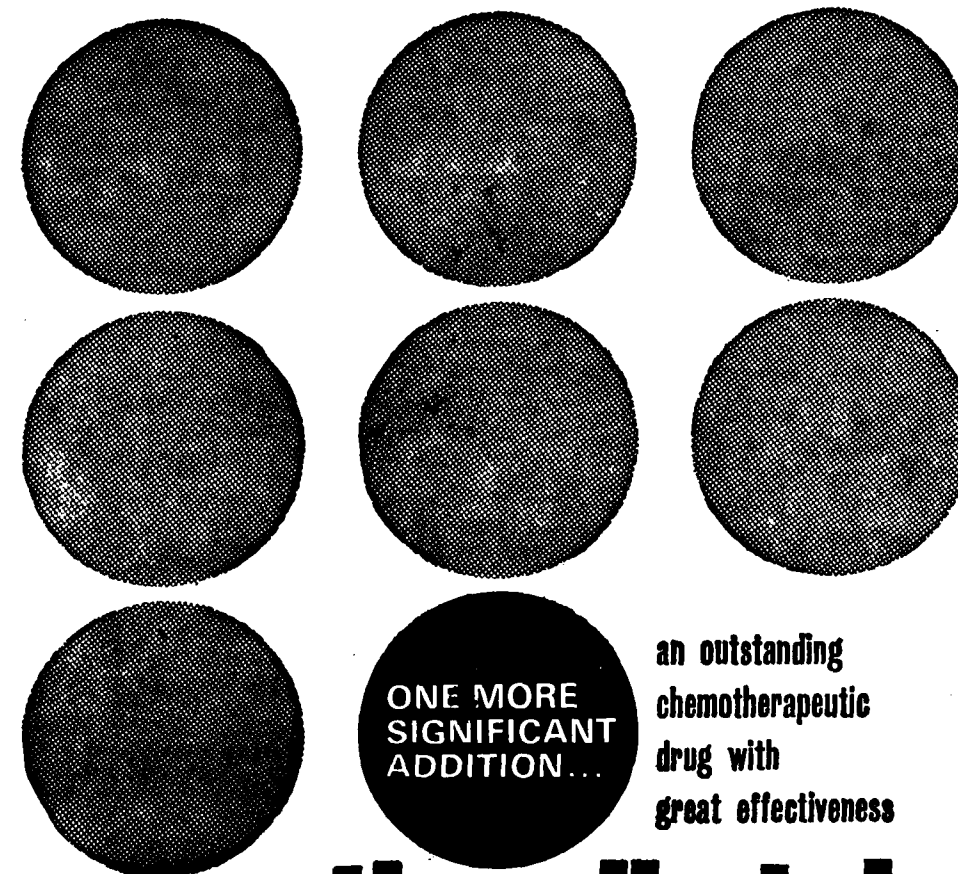


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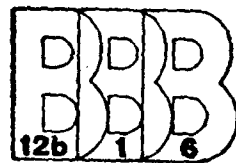
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No. 3

Original Articles

A STUDY OF NEEDLE BIOPSY MATERIAL OF THE PARIETAL PLEURA*

In the Aetiological Diagnosis of Pleural Effusion

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PLEURAL effusion often presents considerable diagnostic difficulties from the aetiological point of view. The exact aetiological diagnosis is important for immediate as well as for long term treatment of patients. In some cases, effusion is the primary feature of an illness and a thorough investigation including chemical, cytological and bacteriological analysis of the pleural fluid fails to establish an aetiology. Carr *et al* (1955) and Wilson *et al* (1947) reported that 17 to 40 per cent of cases of pleurisy with effusion could not be accurately diagnosed with all the existing laboratory tests and so this group is classed as 'idiopathic effusion.'

Various workers studied these cases to ascertain the aetiology by using different procedures, of which surgical biopsy of the pleura is one. Sutlif, Hughes and Rice (1954) were the first to perform surgical biopsy of the pleura. Stead *et al* (1955), Small and others (1955) took up the work subsequently. All of them advocated the routine use of surgical biopsy of the pleura in cases of pleural effusion of unknown aetiology.

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Surgical biopsy of the pleura requires the help of a thoracic surgeon and it cannot be done in the wards. Moreover, it is often associated with post-operative complications. To make it easier De Francis *et al* (1955) adopted a simple technique of pleural biopsy by a Vim-Silverman needle. Mestiz *et al* (1957), Anjara *et al* (1960) and Mathur *et al* (1961) also stressed the importance of needle biopsy in cases of pleural effusion.

This study is designed to evaluate the place of needle biopsy of the parietal pleura in the diagnosis of the aetiology of pleural effusion in patients admitted into the Assam Medical College Hospital, Dibrugarh.

Material and methods.—The material consists of 26 patients showing clinical and radiological evidence of pleural effusion admitted into the different medical wards of the Assam Medical College Hospital. After full clinical and laboratory investigations, 20 patients were diagnosed as having idiopathic effusion, four as malignant effusion, and two as empyema. Aspirated fluid in all the patients was subjected to physical, chemical and cytological examinations. Centrifuged deposit of the fluid was screened for A.F.B. and malignant cells. Sputum and gastric wash were examined for A.F.B. by the smear and concentration methods. Sputum was also studied for malignant cells by the Papanicolaou method when there was a suspicion.

Blood examination for haemoglobin, T.C., D.L.C., E.S.R., B.T., C.T. and Mantoux test were also performed as a routine.

Biopsy of the parietal pleura by a Vim-Silverman needle was done in every case. A small cylinder of tissue about 1 to 2 mm. in diameter and 2 to 3 mm. in length was obtained and preserved in 10 per cent formal saline. Sections were cut from this tissue and stained with Haematoxylin and Eosin stain for histopathological study. Serial sections were made when necessary.

There were 22 males and 4 females, whose ages ranged from 18 to 70 years.

TABLE I
Showing the incidence of pleural effusion in different age groups

Age groups in yrs.	0 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	71 to 80	Total
No. of patients	0	6	7	6	4	2	1	—	26

14 patients had pleural effusion on the right side and 12 had it on the left. (see Table II, page 151).

Protein fluids:—The aspirated fluid, in 15 patients contained 4 to 4.9 g.% of protein; 5 to 5.9 grammes % in eight and 6 to 6.9% in three of the patients.

Character of the fluid:—The fluid was clear or pale yellow in 20; hæmorrhagic in 4 and purulent in 2 of the patients.

TABLE II
Showing the E.S.R. in mm/1st hour in the 26 patients

E.S.R.	0 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	71 to 80	81 to 90	91 to 100	Over 100
No. of patients	0	0	0	1	3	4	1	2	3	1	11

Cytology:—Malignant cells and A.F.B. were not spotted either in the pleural fluid or in the sputum in any case. The gastric contents also did not show A.F.B.

Discussion.—Twenty-six patients who had pleural biopsy were studied, sixty per cent of them who were initially labelled

TABLE III
Showing the histological findings of pleural biopsy in the 26 patients

Result	No. of patients
Tuberculosis	12 (46.1%)
Malignancy	1 (3.8%)
Non-specific	6 (23%)
Acute inflammation	1 (3.8%)
Inadequate tissue	6 (23%)

as idiopathic effusion, Group I proved on needle biopsy to be

due to tuberculosis showing caseation, giant cell, epithelioid cell and round cell infiltration in the pleura (see Fig. I and II). De Francis *et al* (1955) performed pleural biopsy on six patients of whom 2 showed tuberculosis in the pleura. Weiss *et al* (1957) found 12 with caseating tuber-

cle in 22 patients with pleural effusion studied by them

Mestiz and Polard (1958) had positive results in 80 per cent of tuberculous and 60 per cent of malignant effusion in biopsy material. Joshi *et al* 1961 reported 9 with tuberculous caseous lesions in 35 cases with idiopathic pleural effusion. Reddy and Indira (1963) reported the results of needle biopsy of pleural effusion in 62 patients. Seventy per cent of the



FIG. I. Pleural biopsy (high power) showing Langhans' type of giant cell and lymphocytes—Tuberculous pleurisy—(x 215)

interpretable lesions proved to be of tuberculous origin. Mishra and Sarma (1958, reported on 36 patients with idiopathic

pleural effusion. Only four of them showed evidence of tuberculosis in the pleura. They thought that the low percentage of positive results might be due to the previous administration of anti-tuberculous drugs. From the above, it will be seen that the percentage of positive results varies from 11 to 80 per cent. In our present study 60 per cent of the patients showed tuberculous infiltration in the pleura. Needle biopsy alone helped in arriving at the earliest diagnosis in the majority of cases where other conventional diagnostic methods failed.

TABLE IV

Showing the correlation between the initial and the final diagnosis

Clinical diagnosis	Pleural material findings					
	No. of patients	T. B.	Malig-nancy	Non-specific	Inflam-mation	Inadequate tissue
Idiopathic effusion (Group I)	20	12	—	4	—	4
Malignancy effusion (Group II)	4	—	1	1	—	2
Empyema (Group III)	2	—	—	1	1	—
Total No. of patients	26	12	1	6	1	6

There are two views about idiopathic pleural effusion: (1) Effusion may be due to allergic reaction caused by sensitisation

of the pleura by the tuberculo-protein. (2) It may be due to a direct infection of the pleura both visceral and parietal. The second view is supported by the high percentage of positive results in our study.

Twenty per cent of the patients with idiopathic effusion showed non-specific tissue reaction in the pleura. This does not exclude tuberculosis as the aetiology.

Because occasionally pleura may have changes of non-specific pleuritis around an area of tuberculous infiltration (Donohoe, 1957). It may be that a repeat biopsy at some other site would have shown more positive results for tuberculous infiltration in the pleura.

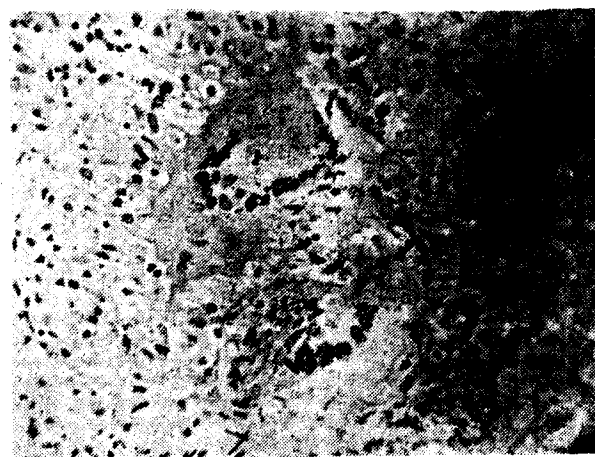


FIG. II. (High power) showing two giant cells, epithelioid cells and lymphocytes—Tuberculous pleurisy—(H & E x 215)

Haemorrhagic effusion (Group II):—The effusion in the four patients in this group may have been due to malignant growths in the lungs, pleura or other organs. One of these four showed non-specific pleurisy (see Fig. III, below) and another showed malignant changes in the pleura (see Fig. IV, below).

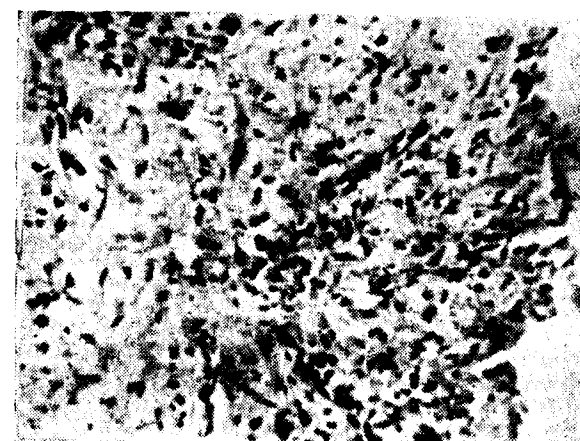


FIG. III. High power showing collagenous fibrous tissue, fibroblasts and lymphocytes—non-specific pleurisy.—(H & E x 215)

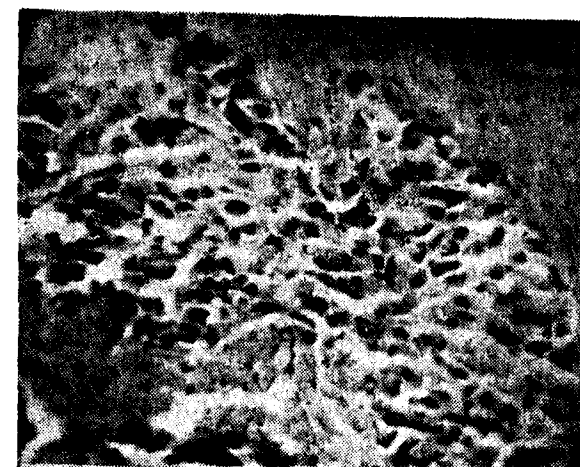


FIG. IV. High power showing carcinomatous cells showing anaplastic character, nuclear hyperchromatism and mitotic figure—Carcinomatous involvement of the pleura—(H & E x 215).

Mestiz *et al* (1958) established the diagnosis in 60 per cent of suspected cases of malignant effusion, by pleural biopsy. Benzamin *et al* (1962) found specific malignancy in 59 per cent of his patients with neoplastic effusion. The positive results in this series is low as compared to those of other workers, because the parietal pleura may be involved by direct extension or by lymphatic spread from a malignant growth of the lungs; it may not involve the entire parietal pleura. So the biopsy needle may not take out an island of malignant tissue if it is localised. Donohoe *et al* (1957) emphasized that malignancy may be present yet the pleura may show non-specific changes.

Empyema (Group III):—Two patients were studied. One showed an acute inflammatory reaction and the other showed chronic inflammation (non-specific) in the pleura. Mishra and Sarma (1958) studied 3 patients with empyema. All showed signs of chronic inflammation in the pleura. Joshi *et al* (1961) studied 3 patients with empyema. They found thickened pleura in 1 and a chronic inflammation in two. The mere finding of

acute or chronic inflammation does not give a precise clue to the aetiology. Needle biopsy in such cases may be helpful when combined with other diagnostic methods and cultures of the pleural fluid.

Summary.—Pleural biopsy material from 26 patients with pleural effusion was studied.

(1) Of twenty cases of idiopathic pleural effusion diagnosed clinically, 12 showed tuberculous lesions in the pleura providing early aetiological diagnosis. Four showed non-specific tissue reaction.

(2) Of 4 cases with malignant effusion one showed malignant change. Another showed non-specific reaction in the pleura.

(3) Of two cases of empyema, one showed acute and the other chronic inflammation.

(4) Non-specific pleuritis was found in six of the 26 patients. This finding does not eliminate the possibility of underlying tuberculosis or malignancy as only a small portion of the pleura was obtained by needle biopsy.

Acknowledgement. We are grateful to the Principal cum Superintendent Assam Medical College and Hospital, Dibrugarh, for according permission to us to utilize the hospital records and for permitting us to publish this paper. We also thank Dr. B. D. Baruah, M.B., B.S., Ph.D., Professor and Head of the Department of Pathology and Bacteriology, Assam Medical College, Dibrugarh, for his kind advice and guidance and for affording all facilities to carry out the laboratory tests in his department.

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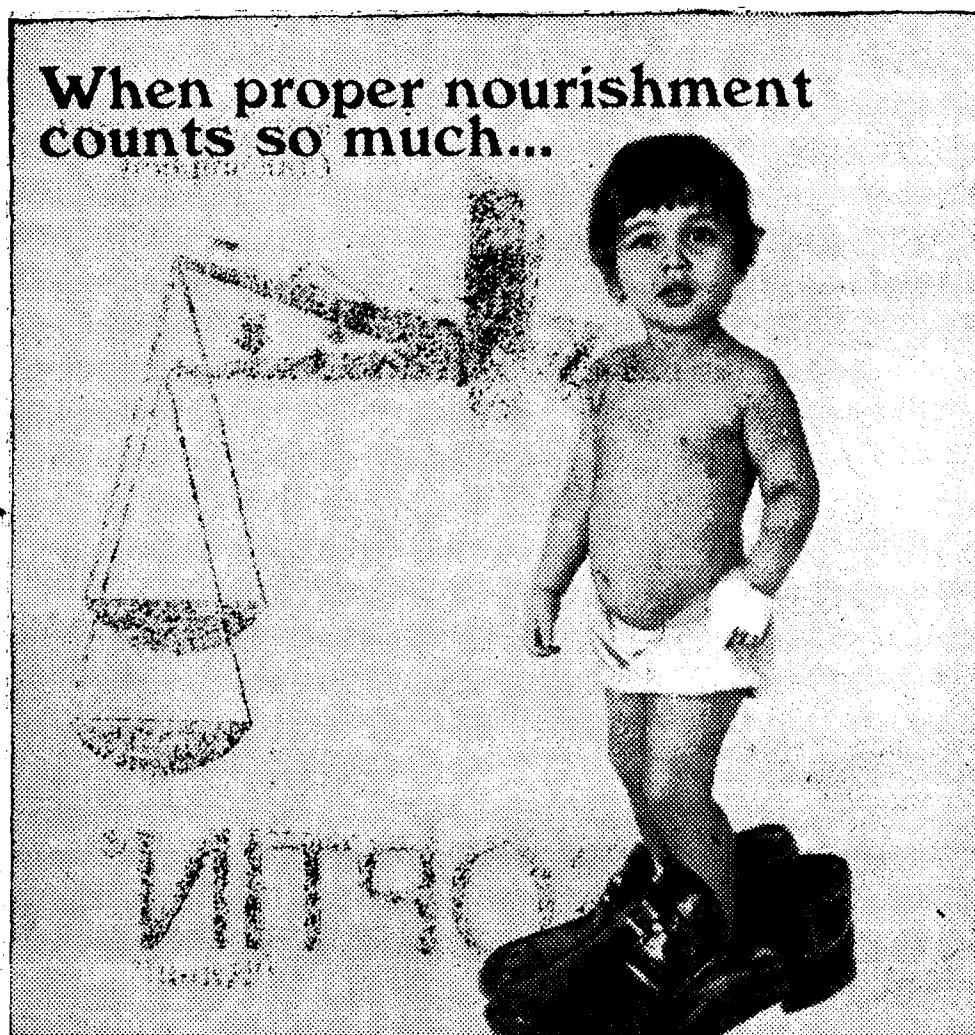
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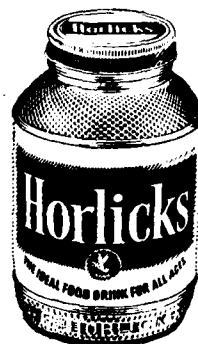
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CORTICOSTEROIDS IN THE MANAGEMENT OF ACUTE GLOMERULONEPHRITIS*

M. J. MEHTA, M.D., D. Paed., *Asst. Prof. in Paediatrics,*

AND

S. H. PATEL, M.B.C.P. (Lond.), D.O.H. (Lond.), D.T.M. & H. (Eng.),
Hony. Prof. in Paediatrics,

[Dept. of Paediatrics, B.J. Medical College, Ahmedabad]

AT present, there is no specific treatment for acute glomerulonephritis. Steroids have been used in the hope of depressing the inflammatory reaction and preventing subsequent scarring. Steroids are also known to depress immunologic responsiveness. But their use in acute glomerulonephritis is of doubtful value.

Material and methods.—Fifty children under the age of 12 years, with oedema, proteinuria, haematuria, with or without hypertension and a clinical diagnosis of acute glomerulonephritis were admitted to the Civil Hospital, Ahmedabad. The following investigations were made on all of them:—(1) Mid-stream urine for proteinuria; centrifuged deposit for microscopic haematuria, leucocytes and casts, and all specimens were cultured; (2) Erythrocyte Sedimentation Rate; (3) Haemoglobin; (4) blood-urea, serum cholesterol, serum protein and (5) throat swab culture (before commencing treatment).

The patients were divided in three groups for the purpose of treatment:—

Group I:—34 received antibiotics with no steroids.

Group II:—Ten had antibiotics with steroids in the form of prednisolone 1–2 mg. per kg. per day, till good clinical response was obtained and gradually tapered off over a period of 3 months.

Group III:—Six children received antibiotics with steroids in the above dosage when proteinuria and haematuria persisted for 4 weeks and continued for 3 months—(as for Group II).

[*Note:*—Steroids were not given to children with hypertension, cardiac failure and encephalopathy.]

The patients were discharged when oedema disappeared, blood-pressure dropped to normal level and the urinary findings were nearly normal. All these patients were followed-up for one year.

Results.—Of the 50 patients, 44 were cured (33 in *Group I*, 9 in *Group II* and 2 in *Group III*) at the end of one year. Two died in the acute stage (one each from *Groups I* and *II*). The comparison of responses between the follow-up of 50 cases is shown in Table I, p. 156.

* Specially contributed to the 'ANTISEPTIC.'

TABLE I

Showing the comparison of responses between the follow-up of 50 cases

	Total cases 50	Group I 34	Group II 10	Group III 6
	No.	No.	No.	No.
• Urine cleared in 15 days.	17 or 34%	11 or 32.5%	6 or 60%	—
1 month	13 or 26%	13 or 38.2%	—	—
2 months	13 or 26%	8 or 23.6%	3 or 30%	2 or 33%
3 months	1 or 2%	1 or 2.7%	—	—
Urine abnormal at the end of year	4 or 8%	—	—	4 or 67%
Progressed to chronic nephrosis	3 or 6%	—	—	3 or 50%
Nephrosis	—	—	—	1 or 17%
Expired in acute stage.	2 or 4%	1 or 2.7%	1 or 10%	—

* Absence of proteinuria and casts; Occasional R.B.Cs. on microscopic examination.

In *Groups I and II*, no child progressed to chronic nephritis or nephrosis while in *Group III*, two progressed to chronic nephritis and one to nephrosis.

Discussion.—Farnsworth⁸ noted rapid clinical recovery with a fall in blood urea and serum cholesterol in 2 patients with acute⁴ glomerulonephritis treated with A.C.T.H.

Iseri and Madar administered A. C. T. H. to patients with persistent hæmaturia over four weeks and reported improvement. However, six of their cases improved spontaneously. Roy⁶ reported beneficial effect of prednisolone on heavy hæmaturia. Burnett *et al*² reported a case of nephritis which deteriorated after treatment with cortisones. Thorn⁷ states that there is no significant alteration in the course of the disease after giving corticosteroids. Mitchel and Walters⁵ reported that hæmaturia had increased in nephritis during cortisone and A.C.T.H. administration. Adam *et al*¹ tried large doses of A.C.T.H. and prednisolone in three cases of acute glomerulonephritis with rapidly advancing azotæmia and severe oliguria; all died with no alteration of their course which could be attributed to steroids.

In our series, *Group I* showed a cure rate of (97.3%) as compared to that of *Group II* (90%) and *Group III* (33%). In *Group II*, 60% showed improvement in urinary findings as compared to that *Group I* (32.5%) in first 15 days. Two cases in *Group III* when frank hæmaturia persisted for 4 weeks, found much improvement after steroids therapy and hæmaturia was cleared in 45 days and 48 days. However, acute glomerulonephritis is known for spontaneous remission. In 4 cases, no beneficial effect was observed and the disease progressed to chronic nephritis in 3,

and to nephrosis in one case. The mortality in our present series is 4%; there is no significant difference between the deaths that occurred during active stage.

In general however, there appeared to be no significant alteration in the course of the disease brought about by the use of steroids in the present series.

Summary.—In this study of fifty patients divided into three different groups different treatments were used. *Group I* had antibiotics alone. *Group II* had antibiotics and steroids. For *Group III* antibiotics and steroids were given when proteinuria and hæmaturia had persisted for four weeks. The efficacy of treatment was assessed on the basis of the disappearance of œdema, control of hypertension and normal urinary finding. All the patients were followed for one year. This trial clearly brought out that there is no significant alteration in the course of the disease by the use of steroid therapy in the present series.

Acknowledgement.—We are thankful to the Dean, B. J. Medical College, Ahmedabad for according permission to publish this paper.

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THE PILL AND B. P.

What is the effect of an oral contraceptive on blood pressure, and are some formulations more likely to raise blood pressure than others? What is the right course of action should the blood pressure go up while any woman is taking a contraceptive pill?

An increase in blood pressure in women using oral contraceptives has been shown by several workers but the frequency with which this change occurs is not known. In general, the rise is more marked in the systolic than in the diastolic pressure. Pre-existing hypertension may be aggravated, but this is by no means invariable. On stopping oral contraceptives the raised blood pressure usually falls, but not always. Changing to a different formulation may then have little or no effect on the blood pressure—or may again lead to an increase. The available data do not provide any definite distinction between different formulations as regards their hypertensive effects.

It is not yet clear what causes the apparent small increase in systolic pressure in the majority of oral contraceptive users or the more marked increase in both systolic and diastolic pressure which occurs in a small minority of these women. Changes in the renin-angiotensin-aldosterone system may be involved but the evidence for this is not yet clear. Minor rises of systolic blood pressure do not contraindicate continued use of oral contraceptives but a major rise, especially if involving the diastolic pressure too, suggests counselling a change to an alternative method of birth control. If the patient declines this advice, or if the alternatives are unacceptable for other reasons, the concomitant use of a hypotensive drug should be considered.—(*Brit. Med. Jour.*, 2-9-1972).

GONOCOCCAL OPHTHALMIA

The specific aetiological agent of gonococcal ophthalmia was first described by Neisser in 1879 and the successful prophylaxis of silver nitrate 2 per cent was introduced by Crede in 1887. He reduced the frequency of gonococcal ophthalmia in his clinic from 10 per cent to 0.5 per cent. Because of the adoption of this prophylactic procedure in practically every newborn nursery this infection has almost disappeared. For this reason and because of secondary chemical conjunctivitis, silver nitrate was discontinued.

During the six-year period from 1 January, 1966 to 31 December, 1971, 32,978 infants were born alive in the National Maternity Hospital of whom 20 were diagnosed as suffering from gonococcal ophthalmia—an incidence of 0.6 per 1000 live births. Each infant presented with marked inflammation and oedema of the eyelids plus a copious purulent discharge. The clinical picture appeared as early as the second day in two cases, between the third and sixth day in seventeen and as late as the tenth day in the remaining case. Laboratory diagnosis was based on a gram stain of a smear from a freshly taken eye swab. In each case intracellular gram negative diplococci showing the morphological characteristics of *N. gonorrhoea* were present. An attempt to culture the organism was made in every case—without success. The diagnosis, however was substantiated by a positive smear from a cervical swab taken from each mother.

Treatment:—Rapid resolution of the infection was achieved by a combination of systemic penicillin—250,000 units twice daily by intramuscular injection and local instillation of penicillin eye drops (2,500 units per ml.) hourly for the first twenty hours and at four hourly intervals from then on. Therapy was continued for a ten day period in every case.—(O'Brien G. Niall and O'Connell Eugene, *Jour. Irish. Med. Assoc.* 22-7-1972).

EFFICACY OF PERTUSSIS VACCINES: A BRIGHTER HORIZON

A study of pertussis infections in 186 children under 11 years of age in the Manchester region during 1969—71 suggests that recently manufactured vaccines have been more effective than those made before 1967. The earlier vaccines were effective mainly against the serotypes of *Bordetella pertussis* possessing antigen 2, while those made from 1967 are more nearly equal in their effectiveness against the different serotypes. A booster dose of the earlier vaccines did not prevent infection with type 1, 3 organisms, but we obtained a positive culture from only one child who had received four doses of recent vaccine.

Simultaneous infection of a child with two or more serotypes was frequently seen. The predominant serotypes in a patient were usually types 1, 3; less often it was type 1, 2, 3 or types 1, 2; it was never types 1. A change of serotype sometimes occurs during the course of the illness and is probably directed by the vaccination status of the patient in relation to the serotype of the initial infection.

Our findings emphasize the need for vaccines to contain adequate amounts of all three pertussis agglutinogens, and for satisfactory immunization schedules to be used in their administration.—(Preston N. W. and Stanbridge T. N., *Brit. Med. Jour.*, 3 : 448-451, 1972).

HERBAL REMEDY

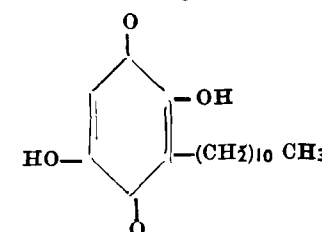
FOR TAPE WORM INFESTATION*

B. VAIJANATH, M.D., B.S., Medical Officer,

Civil Dispensary, Gurmitkal, Dist. Gulbarga

Herb used.—Pulvis of fruits of Vidanga, *Embelia ribes*, (E Robusta Beris) Chitra Tandul in Sanskrit, Vaiwadanga in all Indian languages.

Chemistry:—*Embelia ribes* is a plant belonging to the natural order myrsinaceae. In 1888 Scot isolated "Embelin" from this plant. These berries contain Embelin 2.5—3.1% quercitol 1%, fatty ingredients 5.2%, volatile oil, resinoid, and "Alkaloid" Chrystembine. This compound has the formula of C₁₈, H₂₈, O₄ with following structural configuration.



2.5 dihydroxy-3 lauryl-pasa Benzoquinone or Embelin.

Material and methods.—34 patients formed the subjects of this study.

TABLE I

Showing the age and sex incidence

Age	3 to 14 years		15 to 45 years		46 to 60 years		Total
Sex	M	F	M	F	M	F	
No. of cases	9	8	3	11	—	3	34

The youngest child was 3 years old and the oldest woman was 60 years of age and two of them were enceinte.

Method of administration.—A fine powder of dried *Vaiwadanga* berries was made. It was mixed with curds and given to the patients orally. For children the mixture was administered through Ryle's tube. This was administered at 6 A.M. on an empty stomach. The patients were asked to take their food after 3 hours. In between they are permitted to take water or curds only. The worms were passed by the patients 3 hours after the meals. That is 6 hours after the drug was taken. Purgatives were not used.

Dose:—200 mg. powder per kg. body weight was used with 200 ml. of curds. It is a tasteless mixture.

* Specially contributed to the 'ANTISEPTIC.'

25 of the 34 patients passed live worms, six hours after the administration of the drug. Nine patients passed them in bits on the next morning.

Specimens:—In two cases we could find Scolex. Four of the specimens were sent to the Medical College of Gulbarga, and the rest preserved in this dispensary. The neck breadth of the worm was one mm. and the body was 1 cm. The length of the worm measured from 3 to 8.7 metres.

TABLE II

Showing the length of the worms passed by the patients

Length of worms 3 to 4 metres	Length of worms 4 to 6 metres	Length of worms 6 to 8.7 metres
No. of patients 5	10	10

Follow up:—We followed-up the cases for 3 months. None of them passed any segments. The stool was examined three times at intervals of one month, and we did not find any eggs of the tape worm.

Side-effects:—Ten of the 34 patients, complained of body-ache after passing the tape worm.

Advantage over Mepacrine:—1. Easily available and cheaper than Mepacrine.

2. There was no vomiting sensation in any of the patients.
3. Drug can be administered orally.
4. No purgative is necessary.

Acknowledgement.—I wish to thank Pharmacist Sri. K. M. Mohib Kouser and Sri Sharnappa wardboy for their help in my clinical trials.

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A CLINICAL EVALUATION OF EPICILLIN (DEXACILLIN) IN THE TREATMENT OF URINARY TRACT INFECTIONS

Epicillin, chemically designated as—6—(D—2—amino—2—I, 4—cyclohexadienyl) acetamido penicillanic acid, is a new semi-synthetic penicillin structurally related to ampicillin. It is an amphoteric substance which is inactivated by penicillinase, yet is stable in the presence of gastric acid. Following absorption it is reversibly bound to human serum proteins to the extent of only 10 per cent—30 per cent. (Basch *et al*, 1971).

The results of a trial of the new semi-synthetic penicillin, epicillin in a series of 43 cases of symptomatic and asymptomatic urinary tract infection resulted in eradication of the pathogen in 33 cases (76 per cent). Three patients developed an allergic drug rash which subsided with the termination of therapy.—(Kelly, D. G. *et al*, *Jour. Irish Med. Assn.*, 8-7-1972).

CLOFIBRATE IN HYPERCHOLESTEROLEMIA*

(A Short Term Study)

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OLIVER* in 1962 first reported the hypolipidæmic action of Clofibrate. Since then the hypolipidæmic action of this drug and its efficacy in the prevention and treatment of ischæmic heart disease has been reported by many other authors 2,3,4,5,6,10,11. The drug was recently introduced in our country. This report details the hypolipidæmic effect of Clofibrate observed in 15 patients with ischæmic heart disease and hypercholesterolaemia over a period of eighteen months.

Material and methods.—Fifteen patients with hypercholesterolaemia and ischæmic heart disease were studied. Fourteen were males and one was a female. Ten had clinical and electrocardiographic evidence of myocardial infarction and five had clinical and electrocardiographic evidence of angina pectoris. Six had hypertension and two had diabetes mellitus in addition. Five hypertensives had evidence of retinopathy. One diabetic had hard retinal exudates, circular hæmorrhages and microaneurysms in both eyes.

TABLE I—Result

No.	Age and sex	Diagnosis	Initial cholesterol level mg. %	Final cholesterol level mg. %
1	56 M	Myocardial Infarction (M.I.)	420	245
2	65 M	M.I. Hypertension	325	
3	62 M	M.I.	290	210
4	40 M	M.I. Hypertension	352	240
5	68 M	M.I. Diabetes mellitus Hypertension	428	220
6	40 M	Angina	416	230
7	51 M	M.I.	312	205
8	59 M	M.I. Hypertension	280	180
9	64 M	M.I.	296	210
10	61 M	M.I. Hypertension	286	240
11	49 M	Angina	334	235
12	53 M	Angina	396	230
13	38 M	Angina Hypertension	278	215
14	59 M	M.I. Diabetes mellitus	416	240
15	50 F	Angina	298	210

* Specially contributed to the 'ANTISEPTIC.'

In all these cases fasting serum cholesterol level was estimated initially, at six-weekly intervals on two occasions and at three monthly intervals subsequently for eighteen months.

All the patients were given 1.5 g. of Clofibrate initially and the dose was adjusted up to 2 g. depending upon the therapeutic response. All these cases had in addition measures like weight reduction, substitution of fatty food articles with food low in fat and articles containing unsaturated fatty acids. Besides this they also had regular graduated physical exercises, reduction in the number of cigarettes smoked and also anti-anginal, antihypertensive and antidiabetic measures as required.

Discussion.—How Clofibrate acts is not yet fully understood⁶. When taken it gets hydrolyzed, combines with albumin and gets distributed in the body. The mode of lipid lowering has been attributed to actions like inhibition of cholesterol biosynthesis, peripheral removal of lipoproteins, limiting the free fatty acid mobilization, reducing the fatty acid secretion by the liver and to increased thyroxine activity in the liver.⁶ The net result is a reduction of serum levels of triglyceride-rich lipoproteins and to a lesser extent cholesterol rich low density lipoproteins. In this study the reduction of cholesterol level at the end of eighteen months was 38.33%. This reduction in the cholesterol level is considerably higher than the figures previously reported^{2,11,12} by others. This is due to various additional measures like reduction in fat intake, fat substitution, weight reduction and regular physical exercises. Four patients who lost considerable weight largely abstained from fatty foods and took regular walking exercises were able to reduce the dose of Clofibrate to 0.5 g. daily and maintain the levels of cholesterol below the normal limits. The dosage level had to be maintained at 1 g. per day in four, 1.5 g. in three and 2.0 g. in another four. Any attempt to reduce the Clofibrate below the optimum maintenance dosage resulted in the cholesterol level going up to pretreatment levels.

Only one patient complained of polyphagia and weight gain. The other adverse effects^{6,7,8,9,11} like gastro-intestinal upsets, skin rash, muscle pains, elevated muscle enzyme levels, vertigo, has not been noted in any of the patients. Clofibrate enhances the anti-coagulant activity when anti-coagulants were used in conjunction with this drug. The dosage of anticoagulants should be reduced to half or one third and adjusted depending upon the prothrombin time. None of the patients in this study were on anticoagulants. The two diabetic patients who were well controlled with oral tolbutamide therapy did not experience any hypoglycaemic effects. Case No. 14 a long-standing diabetic with diabetic retinopathy showed considerable clearing

of the hard exudates in the retina at the end of eighteen months. None of the patients developed congestive failure. There was no mortality during the period of study.

At present Clofibrate is the most potent and safe drug available to treat hyperlipaemia. The only disadvantage is that it is very costly and only a few can afford long term therapy. Other measures like weight reduction, low fat diet, fat substitution with unsaturated fatty acids, regular physical activity will allow considerable reduction in the maintenance dose of the drug.

Summary.—15 patients with hyperlipaemia were treated with Clofibrate for a period of eighteen months. A significant reduction in the serum cholesterol levels was noted with little or no adverse effects.

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CHLORAMPHENICOL COMBINED WITH AMPICILLIN IN TREATMENT OF TYPHOID

The study reported here was designed to find out whether treatment of typhoid fever with chloramphenicol combined with ampicillin, when compared with treatment with chloramphenicol alone, shortened the febrile period of the disease, diminished the incidence of febrile relapses, and lessened the number of patients who became carriers.

The dose of chloramphenicol given to adults in both groups (mean weight 70 kg.) was 4 g/24 hrs. by mouth in four divided doses at six hourly intervals. Children aged under 12 were given doses proportional to their body weight. Chloramphenicol was continued in all adults until they had received a total of 30 g. and in all children under 12 until they had received a total of 24 g.

The dose of ampicillin in addition to chloramphenicol given to patients in group B was 4 g/24 hrs. intramuscularly in four divided doses at six-hour intervals in adults and a dose proportional to body weight in children aged under 12. Ampicillin was continued for at least seven days in all cases and always until two days after defervescence.

Five out of 100 patients with typhoid fever, matched for age, stage of illness, and degree of fever, were treated with chloramphenicol and the other 50 were treated with chloramphenicol combined with ampicillin. The febrile period was shortened by up to 29% in patients treated with the

combined drugs, as compared with those given only chloramphenicol. Moreover, no patient on combined therapy had a febrile relapse, whereas two relapses occurred among patients treated with chloramphenicol only. We conclude that chloramphenicol and ampicillin together are better than chloramphenicol alone in the treatment of typhoid fever.—(De Ritis, F. *et al*, *Brit. Med. Jour.*, 4 : 17-8-1972).

ACUTE INVERSION OF THE UTERUS AND ITS MANAGEMENT

A case of acute puerperal inversion of the uterus is described. The case is published because of its rarity, and because of the importance of prompt diagnosis and management in preventing maternal death. Reports in the literature place the incidence of this complication at from 1 : 6000 to 1 : 400,000.

The usual symptoms described are shock, haemorrhage, pain, and sometimes the sensation of a mass in the vagina. Shock is often out of all proportion to blood loss, and this alone should make one suspicious that inversion of the uterus has occurred. Abdominal palpation even in moderate degree of inversion, may not be diagnostic. Palpation is often difficult because of abdominal tenderness, and the uterus as a whole may still occupy a surprisingly high position.

Review of the literature suggests the following as a guide to management:—

(1) If the cervix has not contracted, and the patient is not severely shocked, immediate replacement of the inverted uterus is the correct procedure. This can usually be achieved by manual pressure on either the apex or the neck of the inverted organ. If the placenta is still attached, it is preferable to attempt replacement before separating the placenta. There are only two indications for removing the placenta:—namely (a) to reduce the bulk of the inverted uterus in order to achieve replacement; and (b) when all but a portion of the placenta has separated.

(2) In the presence of severe shock, measures should be instituted to treat the shock before replacement of the uterus is attempted. Some authors advocate correcting a third-degree inversion (protrusion of the uterus through the vaginal introitus) into a second-degree inversion before commencing resuscitation. Packing of the vagina and uterus replacement is favoured by many American authors. On no account should ergometrin be given, as it will have no effect on bleeding and will only render replacement more difficult.

(3) After treatment of shock, an attempt at replacement of the uterus under general anaesthesia should be made, either manually or using the hydrostatic method of O'Sullivan (1945). Adequate uterine relaxation may be obtained with deep ether or halothane anaesthesia. Henderson and Alles (1948) describe a method of applying ring forceps to the cervical rim to exert counter-traction, while exerting digital pressure on the inverted fundus.

(4) Finally, if tight cervical contraction prevents replacement, operative measures become necessary. Several procedures are described by Howkins (1960): vaginal approaches after Spinelli and Kilstner, and abdominal techniques after the methods of Haultain and Huntingdon.

The maternal mortality rate quoted in the literature remains around 15%. Delay in recognition and treatment appears to be the main impediment to further reduction of mortality from previous inversion.—(Campbell John *et al*, *Med. J. Aust.*, 1972, 2 : 475-476).

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GENTAMICIN (GENTICYN EYE DROPS)

In the treatment of Corneal Ulcer and Conjunctivitis

B. T. MASKATI, M.S., D.O.M.S.,

Hony. Ophthalmologist and Hony. Prof. of Ophthalmology.

AND

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MANY new antibiotics are placed on the market every year, but relatively only a few reach the clinicians. Weinstein¹ in 1963 isolated a new antibiotic — *Gentamicin* — from the fungus *Micromonospora purpurea*. Gentamicin has a potent bactericidal action against an exceptionally wide range of Gram-negative and Gram-positive bacteria.¹ It is very active against common *Staphylococci* and *Streptococci*, *Diplococcus pneumoniae*, *Haemophilus influenza* and *Klebsiella*. Of particular interest is Gentamicin's activity against the problem pathogens, viz., *E. coli*, *Proteus* spp., *Ps. pyocyaneae* and resistant *Staphylococci*.^{2,3 & 4} Against *Proteus*, Gentamicin is about 4 times more powerful than Neomycin⁵ and against *Pseudomonas* it is the most potent antibiotic known.⁶

It was observed by Furgiuele (1967)⁷ that Gentamicin, administered as 0.3% eye-drops or subconjunctival injection, penetrates the aqueous humour of normal or inflamed eyes of rabbits significantly. Halasa (1967)⁸ used Gentamicin locally in various types of bacterial conjunctivitis with favourable results. Breakey (1967)⁹ used 0.3% Gentamicin sulphate ophthalmic solution/ointment successfully in 59 patients suffering from external bacterial eye infections. Brass and Coyle-Gilchrist (1968)¹⁰ reported favourable results with Gentamicin in a majority of cases of conjunctivitis and keratitis. In most cases the infection cleared up in 2 or 3 days and the action of Gentamicin was particularly noticeable in cases of *Pseudomonas*, *Klebsiella* and *Proteus* infections. Magnuson and Suie (1970)¹¹ treated a large series of 111 patients with external eye infections and reported clinical cure in 99% and bacteriologic cure in 70% of patients. Gentamicin has also been reported to be effective against *Morax-Axenfeld* bacillus, *Neisseria gonococci* and *Koch-Weeks* bacillus.¹²

Stimulated by these reports we decided to undertake a clinical study on Indian patients, utilising the bacteriological monitored examinations to evaluate the efficacy, tolerance and safety of Gentamicin (Genticyn) Eye Drops (0.3%). As many effective antibacterial agents are available for simple eye infections, our particular aim in this study was to assess the effect of this new antibiotic in corneal ulcer caused by *Pseudomonas*

* Specially contributed to the 'ANTISEPTIC'.

and resistant *Staphylococci*, which is at present considered a baffling problem.

Material and methods.—Fortyseven patients with external eye infections which clinically appeared to be of bacterial origin were selected for this study. They were subjected to general clinical and ophthalmological examinations as *per pro forma*. All the 47 patients were admitted in the ward especially during the acute stage of the disease.

INVESTIGATIONS:—Smear, culture and antibiotic sensitivity studies:—Soon after admission cultures were taken by cotton swabs from the conjunctiva/cornea of the patients. The swabs were placed into thioglycollate broth without indicator and incubated at 37°C. for 24 hours. If growth occurred, isolations were made on blood or McConkey's medium. All bacterial isolates were identified by standard bacteriological methods. The cultures were then streaked on plates containing the same media. Gentamicin (10 mcg.) and other antibiotic-impregnated paper discs were placed 2 cm. apart on these plates. A clear zone around the disc indicated the sensitivity of the organism to that particular antibiotic. Repeat studies were done on the patients 3 to 5 days and 15 days after starting treatment and finally one month after completion of treatment with a view to detecting any evidence of lapse by the growth of organism or the development of resistance to Gentamicin.

Gentamicin (0.3%) eye-drops were instilled soon after the first swabs were taken, in a dosage of 2 drops 4 hourly to start

TABLE I
Showing the diagnosis of ocular
infections in 47 patients

Disease condition	No. of patients
Simple corneal ulcer ...	14
Corneal ulcer with hypopyon	13
Corneal ulcer with abscess formation ...	9
Acute conjunctivitis ...	7
Chronic conjunctivitis ...	3
Post-operative infection ...	1
Total ...	47

with. The frequency was gradually reduced as the condition of the patient improved. Other adjuvant treatment consisted of:—fomentation, atropinisation of the pupil, padding or shield to the eye and multi-vitamin tablets orally and also a high protein diet whenever necessary. In most cases, 1 to 2 weeks' local therapy was given. A few severe cases received treatment for more

than 2 weeks. In very severe cases, Gentamicin injection was administered subconjunctivally in a dosage of 20 mg. (0.5 ml.) once daily for 2 to 3 days. No other antibacterial agent or corticosteroid was used locally or systemically throughout the period of study. Fortyseven patients in all with external eye

infections were studied; 35 were males and 12 were females; their ages ranged from 16 to 70 years (see Table I, p. 166).

Corneal ulcer was thus the major ailment. The size of the ulcer varied from 2 mm. to more than 5 mm.

All infected eyes were clinically evaluated and observations made regarding erythema, oedema, discharge, infiltration of ulcer, level of hypopyon and subjective manifestations like irritation, lacrimation and photophobia. These were all recorded initially and subsequently during the daily follow-up in the ward.

TABLE II
Organisms isolated and their *in vitro*
Sensitivity to Gentamicin

Organism	Total No. isolated	No. Sensitive to Gentamicin
Coagulase positive <i>Staphylococci</i>	13	13
<i>Streptococcus haemolyticus</i>	8	8
<i>Pseudomonas pyocyanea</i>	14	14
No growth	14	—

The patient was considered, completely cured when signs and symptoms completely abated and there was no indication of their recurrence. He was considered improved when the signs and symptoms had been reduced significantly but not completely. The patient-response was considered a bacteriologic cure when post-treatment culture a month after completion of treatment was sterile.

In 2 patients with corneal ulcer, there was a mixed infection with coagulase positive *Staphylococci* and *Pseudomonas*. 14 out of the 47 patients showed no growth on pre-treatment cultures. All isolates tested proved sensitive to Gentamicin. On the other hand, the organisms in 22 out of the 47 patients proved resistant to various antibiotics like penicillin, streptomycin, chloramphenicol, neomycin, framycetin and polymyxin in pre-treatment *in vitro* studies.

TABLE III
Showing the therapeutic response
to Gentamicin

Response	No. of patients
Clinically cured ...	41
Clinically improved ...	—
Clinically failures ...	6
Total ...	47

Thirteen very serious cases of corneal ulcer were given Gentamicin injections subconjunctivally in addition to local therapy. 41 out of 47 patients (88%) were cured with Gentamicin treatment. The congestion, irritation and lacrimation cleared up completely within a few days.

In cases of corneal ulcer and hypopyon ulcer, the hypopyon levels receded fast and ulcers showed signs of healing within a short period. In all the patients who responded, complete cure was manifest in 2 to 15 days of treatment. Only one patient had a relapse of the infection after a few weeks which was

cured again with Gentamicin. One patient who had developed post-operative infection after cataract surgery was cured with minimal residual damage. Four of the 6 failures had shown no growth on pre-treatment culture, whereas one showed coagulase positive *Staphylococci* and one *Streptococci*. Four of six patients showed fungal growth on special technique whereas in the other two although bacteria were eradicated with Gentamicin, additional fungal growths could not be ruled out. Bacteriologic cultures, 15 days after starting treatment showed negative results in most cases and one month after completion of the treatment all cultures were negative indicating 100% bacteriologic cure. The duration of hospital stay in complicated cases of corneal ulcer was 4 to 10 days on an average, which, in our experience, is certainly much less compared to treatment with other antibacterial agents in such type of cases. Gentamicin eye drops were found to be non-irritating. No side-effects were observed except in one patient who developed increased congestion and smarting which probably was an allergic manifestation. Subconjunctivally, Gentamicin injections were tolerated very well by the patients. No pain or untoward feeling was complained of by any of the patients.

Discussion.—Eye infections always have to fight against time, since the tissues are too delicate and irreversible damage may occur. Among the many eye diseases, corneal ulcer is of paramount interest to the Ophthalmologist. The rapid control of infection with a suitable anti-bacterial agent and the prevention of re-infection are of special importance in the cases of corneal ulcer. The selection of a proper antibacterial agent, however, is rather difficult especially when the treatment has to be started immediately without waiting for culture and antibiotic sensitivity reports. If the infection is not brought under control immediately, the gravity of the situation is enhanced by abuse of antibiotics resulting in a loss of valuable time and the development of resistant strains. All antibiotics are successful so far as the specific sensitivity is concerned, but most of them fall especially in cases of problem-pathogens such as *Pseudomonas pyocyaneae*, *Proteus* and hospital strains of *Staphylococci*. Therefore, it is always desirable to use an antibiotic with the widest spectrum which promises a greater chance of first time success in such cases.

In the present study many difficult cases of infection with *Pseudomonas* and *Staphylococci* were treated with Gentamicin; some of them, in fact, had been treated with other antibiotics in the past without success. They responded very well to Gentamicin therapy. It is significant to note that these difficult-to-eradicate organisms cleared up within a short period of Gentamicin therapy and the post-treatment cultures were negative in

all the patients. The results in our series compare very favourably with those obtained by other investigators.

The high proportion of cases in which no growth was obtained in our series may be explained by the fact that antibiotics or chemotherapeutic agents had probably been used previously and it is not unlikely that with the use of these, the surface organisms had been destroyed although the deeper infection may not have been affected.

Summary.—47 patients with external eye infections (36 of simple or complicated corneal ulcer, 10 of acute and chronic conjunctivitis and one of post-operative infection) were investigated with regard to their clinical and bacteriological pattern and their *in vitro* and *in vivo* response to Genticyn (0.3%) Eye Drops therapy. On culture examination, the chief organisms found were coagulase positive *Staphylococci* and *Pseudomonas pyocyaneae*. On antibiotic sensitivity studies, all the organisms were highly sensitive to Gentamicin whereas 22 out of 47 patients showed organisms resistant to various other antibiotics including the broad-spectrum ones like chloramphenicol, neomycin and framycetin.

Clinically, 41 out of 47 patients (88%) were cured within 2 to 15 days of Genticyn Eye Drops therapy and post-treatment cultures were negative in all the patients indicating 100% bacteriologic cure.

Genticyn Eye Drops are a very useful broad-spectrum topical treatment for external eye infections. It is particularly valuable in cases of corneal ulcer caused by problem pathogens like resistant *Staphylococci* and *Ps. pyocyaneus*, which are generally unresponsive to other antibiotics. Genticyn Eye Drops are well tolerated and safe for use in the eye.

Acknowledgement.—We are grateful to the Dean of Seth G.S. Medical College and K.E.M. Hospital for permitting us to use the clinical material and for publishing our observations. Our thanks are also due to Dr. A. K. Mehta, Medical Adviser of Indian Schering Limited, Bombay, for a liberal supply of Genticyn Eye Drops.

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AMBLYOPIA IN ALCOHOLISM: A REPORT ON THREE CASES

Amblyopia is a recognized occasional complication of alcoholism (Harrington, 1971) but in individual cases the causative agent cannot always be identified with certainty. Tobacco toxicity and vitamin deficiencies may play a part in the development of the condition, and the possibility of exposure to methyl alcohol must always be eliminated.

Between 1964 and 1969, three cases of severe amblyopia were discovered among a large series of patients who were attending a general hospital clinic for the treatment of alcoholism. All three patients were consuming large amounts of bromureides as well as alcohol when they developed their visual symptoms.

Tobacco is probably the toxin which most commonly causes amblyopia in both drinkers and teetotallers. There is considerable difference of opinion, however, as to what part alcohol and other factors such as malnutrition play in increasing susceptibility to the disease. Tobacco amblyopia is commonly associated with alcoholism (Silvette *et al*, 1960) but this could be an indirect association, since alcoholics are commonly very heavy smokers (Rankin *et al*, 1969).

In the case of the three patients reported here, the aetiology of their amblyopia is not clear. None had been exposed to any of the more unusual toxic agents such as iodoform or thallium. All had been heavy drinkers for many years, but all denied drinking methylated spirits or cheap adulterated beverages. Their lesions resembled Harrington's (1971) and Fould's *et al* (1970) descriptions of tobacco amblyopia. Defective appreciation of red was pronounced, and there was no peripheral neuropathy. All were smokers, but not of strong tobacco, although the patient in Case 3 was a pipe-smoker. None had any haematological or neurological evidence of vitamin B12 deficiency, and normal serum levels of total vitamin B12 were found in the first two cases.

All three patients, however, admitted to prolonged bromureide ingestion, and all had had increased serum levels of bromide when they had visual symptoms. They constituted the only cases of severe amblyopia found among all patients who presented to the alcoholism clinic at St. Vincent's Hospital between 1964 and 1969. In all, 87 of the 1,000 alcoholic patients seen during this period were also bromureide-dependent, but no comparable visual disturbances were found in the case of the remaining patients who did not misuse bromureides. It is tempting, therefore, to speculate that bromism, in addition to tobacco and perhaps subclinical malnutrition, contributed to the amblyopia in these cases.—(Wilkinson, P. and Santamaria, J. N., *Med., Jour. Aust.*, 2 : 318-320, 1972).

SURGERY FOR ATRIAL SEPTAL DEFECT IN PATIENTS OVER 60 YEARS OF AGE

Atrial septal defect may be the cause of cardiac symptoms in elderly patients. The results of closure of atrial septal defects have been reviewed in 12 patients over 60 years of age. Once symptoms had begun they progressed rapidly. Many patients had evidence of congestive cardiac failure, with atrial fibrillation and cardiomegaly. The mortality rate of surgical closure in this series was 25% (17% if only cardiac deaths are included). The two who died of cardiac problems were among those with the most severe pulmonary hypertension. Long-term follow-up studies show that, all patients are alive and in improved condition. Age alone should not therefore, contraindicate operative treatment for atrial septal defect. (E. Yalav, St. Thomas' Hosp., London, A.H. Brown and M.V. Braimbridge, *J. Thorac. Cardiovasc. Surg.*, 62 : 788-792, Nov. 1971, via *J.A.M.A.*, 3-4-'72).

CONTROLLED CLINICAL TRIAL WITH DIAZEPAM*

In Anxiety Neurosis and its Frequently Associated Symptom of Depression

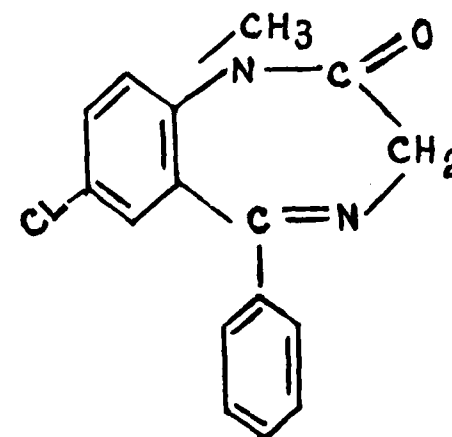
M. SARADA MENON, M.D., D.P.M., M.R.C. PSY.,
Superintendent, Government Mental Hospital, Madras-10

AND

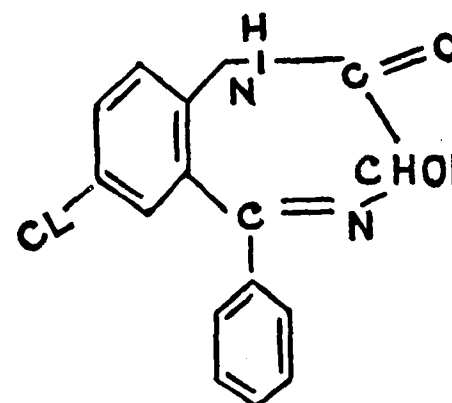
•Md. HANEEF BADSHA, M.A., M.B., B.S., D.P.M.,
Formerly, Asst. Surgeon Govt. Mental Hospital, Madras-10

DIAZEPAM (Calmpose) belongs to a new class of tranquillizers, Benzodiazepines. It is a colourless crystalline compound, insoluble in water and has a molecular weight of 284.74.

DIAZEPAM



OXAZEPAM



Chemically *Diazepam* is 7-Chloro-1, 3 - dihydro-1 - methyl -5-phenyl-2 H-1, 4-Benzodiazepin -2-one, i.e. (see alongside).

Oxazepam (Serepax) also belongs to the same Benzodiazepin agents with the following chemical structure (see below).

These compounds have now established themselves as "New Standard in Tranquillizer therapy," with power to alleviate and dispel anxiety, tension, and accompanying symptom of fear, hyper-irritability, agitation and depression.

Purpose.—The purpose of this study is to evaluate the effect of Calmpose on Anxiety neurosis with specific reference to (a) Somatic symptoms; (b) psychological components and (c) the accompanying depression.

Since it was considered unjustifiable to leave patients with anxiety without any drugs, the controls were placed on *Serepax*.

Material.—The study was conducted at the outpatient services of the Government Mental Hospital, Madras. The subjects of study were the patients suffering from anxiety neurosis in whom depressive features were invariably present. Therefore, all the cases studied related purely to outpatients attending the neurosis clinic once a week. Most of the patients

* (Now) District Family Planning Officer Ramanathapuram.
Specially contributed to the 'ANTISEPTIC'

were not on any known tranquillizer treatment. Those who were on tranquillizers were withdrawn from the same for a few days prior to initiating the research drug. The shortness of drug-free period was due to want of moral justification in such circumstances especially when the individuals were suffering from anxiety.

The study comprised 20 patients on *Calmpose* and 17 (three were 3 drop outs) on *Serepax*. The sampling procedure adopted was 'Block Design' with the assignment of treatment randomised as shown *alongside* :—

A1	A11	A21	A31
B2	B12	B22	B32
B3	B13	B23	B33
A4	A14	A24	A34
A5	A15	A25	A35
B6	B16	B26	B36
A7	A17	A27	A37
B8	B18	B28	B38
B9	B19	B29	B39
A10	A20	A30	A40

Note :—A = Calmpose group
B = Serepax group

The randomisation of the treatment was resorted to in order to match the two groups. The selected patients were given a thorough physical examination and underwent routine laboratory investigations, including Hb%, total W.B.C., differential leucocyte count, E.S.R. and urine examinations both at the beginning and at the end of the trial. These patients after having been assigned to the two groups, were started on *Calmpose* 1 tablet (5 mg.) *t.i.d.* and *Serepax* 1 tablet (15 mg.) *t.i.d.* Patients were not given any other treatment during the whole trial period of 6 weeks. Double blind conditions were maintained throughout. The drugs were issued by the Social Worker according to the random chart prepared by the Clinical Psychologist.

TABLE I

Showing the age and sex incidence

Drug Groups	No. of patients	Sex		Age	
		M	F	Range	Average
1 Calmpose	20	15	5	18-40	28.7
2 Serepax	17	11	6	17-42	25.4

Assessment.—The severity of the patients' illness and the degree of change, brought about by treatment were assessed at the beginning and at fortnightly intervals. Each patient was rated on a specially designed anxiety symptoms-rating scale for depression, both of them being modifications of Hamilton's rating scales. The somatic symptoms of anxiety and its psychological components were separately rated before the total symptom rating quotient (T.S.R.Q.) was worked out.

Along with these, a more objective assessment of anxiety was also made with the help of Taylor's manifest anxiety scale. The test was administered in English, and its Tamil translation, agreed upon by a group of Hospital Psychiatrists, was also used. The test was given twice, once before the treatment and again at the close of the treatment.

Results.—The reduction in the mean scores of the two groups is as under :

TABLE II

Showing various ratings of anxiety etc.

Ratings	Drug Groups	Mean Scores			
		Before trial	1st fortnight	2nd fortnight	3rd fortnight
Somatic symptoms	Calmpose	30.91	20.63	14.17	9.61
	Serepax	35.67	24.26	15.83	10.07
Psychological symptoms	Calmpose	41.25	21.41	14.24	10.17
	Serepax	48.76	35.82	25.49	16.88
T.S.R.Q. for Anxiety	Calmpose	39.13	20.10	13.40	8.96
	Serepax	41.45	29.30	19.95	12.96
T.S.R.Q. for Depression	Calmpose	48.84	26.44	19.13	12.30
	Serepax	49.39	35.30	24.79	15.91

NOTE :—It will be seen that the drugs have been effective throughout the total period of 6 weeks.

The data were further analysed to know during which interval of the trial, the drug was most effective against the symptoms of anxiety and depression.

TABLE III

Calmpose group on T.S.R.Q. for anxiety, with comparison of mean scores obtained at various intervals

Interval	Mean	Variance	Mean difference	Std. error	t observed	t expected at 5% level	Significance
Pre-trial assessment and 1st assessment	39.13	113.60	19.02	3.66	5.20	1.96	Significant
1st assessment and 2nd assessment	20.11	153.74	6.70	3.66	1.83	1.96	Not significant
2nd assessment and 3rd assessment	13.41	114.39	4.44	9.56	0.46	1.96	Not significant

TABLE IV

Serepax group on T.S.R.Q. for (anxiety) with comparisons of the mean scores obtained at various intervals

Intervals	Mean	Variance	Mean difference	Std. error	t observed	t expected at 5% level	Significance
Pre-trial assessment and 1st assessment	41.45	158.26	12.14	4.08	2.96	1.96	Significant
1st assessment and 2nd assessment	29.30	124.88	9.36	3.98	2.35	1.96	Significant
2nd assessment and 3rd assessment	19.95	143.91	6.99	4.13	1.69	1.96	Not Significant

Table III, on p. 173 and Table IV *supra* show that *Calmpose* brings about significant improvement in the symptoms of anxiety in the first fortnight itself. Thereafter, the improvement is maintained throughout the period of 6 weeks. The mean score of the *Calmpose* group is almost halved even in the first fortnight.

The same picture is also seen in the analysis of the scores for somatic aspects and psychological components of anxiety made separately.

As regards depression on the T.S.R.Q. rating, the drug is seen to be active throughout the trial period. Significant improvement from depression is achieved by *Calmpose* in the first fortnight itself (see Tables V, below and VI, overleaf).

TABLE V

Calmpose on T.S.R.Q. for Depression—Giving the comparison of the mean score obtained at various intervals

Intervals	Mean	Variance	Mean difference	Std. error	t observed	t expected	Significance
Pre-trial assessment and First assessment	28.85	349.29	22.40	5.87	3.81	1.96	Significant
First assessment and 2nd assessment	26.44	340.89	7.31	5.36	1.36	1.96	Not significant
2nd assessment and 3rd assessment	19.13	233.55	6.83	4.43	1.54	1.96	Not significant

TABLE VI

Serepax group on T.S.R.Q. for depression—Giving mean scores obtained at various intervals

Intervals	Mean	Variance	Mean difference	Std. error	t observed	t expected	Significance
Pre-trial assessment and First assessment	49.39	335.62	14.09	5.75	2.45	1.96	Significant
First assessment and Second assessment	35.30	226.23	10.51	5.29	1.99	1.96	Significant
Second assessment and Third assessment	24.79	249.81	8.88	5.66	1.57	1.96	Not significant

Before further analysis of the data it may be pointed out that the groups of patients on *Calmpose* and *Serepax* were similar in their anxiety and depressive features. The pre-trial assessments made for each group for anxiety and depression are compared in Table VII and the similarity of the two groups is once again confirmed by statistical evidence.

TABLE VII

Showing the comparison of pre-trial assessments of the two groups

Symptoms	Drug groups	Mean	Variance	Mean difference	Std. error	t observed	t expected	Significance
Anxiety T.S.R.Q.	<i>Calmpose</i>	39.13	113.60	-2.32	3.88	-0.60	1.96	Not significant
	<i>Serepax</i>	41.45	158.26					
	<i>Calmpose</i>	48.85	349.30					
Depression T.S.R.Q.	<i>Serepax</i>	49.39	335.72	-0.54	6.00	-0.09	1.96	Not significant

It will be seen from the data given in the above statements that *Calmpose* effect a significantly greater reduction of symptoms of (1) anxiety rated under T.S.R.Q. for anxiety; (2) somatic symptoms of anxiety; (3) psychological features and (4) T.S.R.Q. for depression during the first fortnight. Thereafter the improvement achieved was maintained for the next four weeks.

Tables VIII and IX (*below*) which compare the two drugs on T.S.R.Q. scales for depression and anxiety separately, bring out the difference with statistical evidence.

TABLE VIII
Calmpose (vs.) Serepax on T.S.R.Q. for depression

Intervals	Drug Groups	Mean	Variance	Mean difference	Std. error	t observed	t expected at 5% level	Significance
1st fortnight	Calmpose	22.41	180.66	8.31	3.76	2.2091	1.96	Significant
	Serepax	14.10	87.37					
2nd fortnight	Calmpose	7.01	81.40	-3.20	2.66	-1.20	1.96	Not significant
	Serepax	10.51	51.17					
3rd fortnight	Calmpose	6.83	72.82	-2.06	3.13	-0.66	1.96	Not significant
	Serepax	8.88	104.67					

TABLE IX
Calmpose (vs.) Serepax on T.S.R.Q. for anxiety

Intervals	Drug Groups	Mean	Variance	Mean difference	Std. error	t observed	t expected at 5% level	Significance
1st fortnight	Calmpose	19.02	85.50	6.88	2.67	2.58	1.96	Significant
	Serepax	12.14	48.28					
2nd fortnight	Calmpose	6.70	63.79	-2.65	2.24	-1.18	1.96	Not significant
	Serepax	9.36	81.79					
3rd fortnight	Calmpose	4.44	28.66	-2.55	1.75	1.45	1.96	Not significant
	Serepax	6.99	27.72					

The reduction in the mean score brought about in the 1st fortnight by Calmpose was 19.02. (*see* Table IX). This is almost equal to the reduction in the score brought about by Serepax in two fortnights (1st fortnight 12.14 + 2nd fortnight = 9.35 = 21.49). This clearly shows that Calmpose dispels anxiety twice as fast as Serepax.

TABLE X
Showing the results of the two groups on Taylor's Manifest anxiety scale

Drug Groups		Average	Scores	No. of patients with severe anxiety	No. of patients still show in anxiety	No. of patients free from anxiety	Percentage
		Before trial	After trial				
Calmpose	...	18.05	10.95	15	6	9	60%
Serepax	...	18.94	12.94	12	6	6	50%

On Taylor's Manifest Anxiety scale also, the very good effects of Calmpose are seen. At the beginning of this study 15 out of 20 patients on Calmpose showed severe anxiety. The average score is 18.05, the standard being 13 only. At the end of the study, 9 of them exhibited anxiety with scores of 13 and over. However, the average of the group came down to 10.95. Sixty per cent of the patients in the Calmpose group and 50% in the Serepax group were free from anxiety. In the case of Serepax the average score of the group i.e., 18.94 came down to 12.94.

Side-effects :—No patient showed any dermatological or hæmatological disturbances or any deviations in the urine analysis. Even though the daily dose of Calmpose was 15 mg., drowsiness was not met with as a disturbing experience.

Discussion.—The development in recent years of drugs that aim at reducing anxiety, tension, agitation and depression which are all on the increase, has given the psychiatrist a wide choice of agents for controlling emotional distress, in psychoneurotic patients who need psychological help. In most cases, psychotherapy had to be started as quickly as possible. Psychotherapy itself is a slow process and can be instituted only after a certain amount of calm composure, confidence and co-operation of the patient is established. A patient in acute anxiety is not suitable for and cannot be co-operative in psychotherapy until his anxiety has been relieved to a certain extent. This should be achieved in the minimum possible time, and a tranquillizer that will achieve this end, is necessarily to be considered a great boon to the psychiatrist. In such circumstances Calmpose furnishes the answer. It is very effective in the alleviation of anxiety and depression.¹ It renders the patient more accessible in a very short time and his interest in the environment improves. As a result, his participation in adjunctive therapy also improves. The same good results from Calmpose in earlier clinical trials, have also been reported in the literature. Krakowski^{2,3} reported excellent to good results in 86.5% of psychoneurotic patients, treated with Diazepam whereas he could get good results in only 44.67% with Oxazepam.

Smith, M.E. *et al*⁴ compared the effects of Diazepam, Chlorpromazine and Trifluoperazine in a group of 60 patients with psychoneurotic disorders in a double blind study. They reported that the therapeutic effect of Diazepam was superior to that of Chlorpromazine at a level of P=0.05 and to Trifluoperazine at a highly significant level of P=0.001.

Baldev Kishore⁵ and associates compared Diazepam with Chlordiazepoxide and stated that it was 3 times more effective. They also noted its effectiveness on depression accompanying anxiety neurosis.

According to our observations, Calmpose proves to be equally effective both as an anti-depressant and as an anxiolytic.

Conclusion.—1. Calmpose was found to be significantly effective in alleviating the symptoms of anxiety neurosis and its depressive features through a trial period of six weeks. This conclusion was reached with reference to the symptoms of anxiety neurosis, considered as a whole or separately, the somatic symptoms, the psychological symptoms, and the depression.

2. Calmpose brings about a significantly higher degree of reduction in the symptoms of anxiety neurosis considered separately or as a whole during the first fortnight.

Summary.—Two perfectly matched groups of 20 out-patients with anxiety neurosis were tried on Diazepam and Oxazepam under double blind conditions. The results showed that Calmpose is significantly superior as regards the quick control of the distressing symptoms of anxiety, tension, irritability, agitation and the accompanying depression; rapid effect is exceedingly useful to gain the confidence of the patient and rendering him more suitable for psychotherapy and social readjustment.

In view of the impressive clinical response in the first two weeks of treatment with Calmpose tablets, the duration of psychotherapy could be successfully reduced and the patients co-operated willingly.

Acknowledgement.—We are thankful to Dr. K.G.S. Nanda of M/s. Ranbaxy Laboratories (Private) Limited, New Delhi for affording the necessary assistance in this study. We also wish to thank Mr. R. Srinivasan, the Statistician, Government Mental Hospital, Madras for his painstaking validation of the data. Our thanks are due to the Social workers and members of the nursing staff of the Hospital for their kind co-operation. We should not forget to offer our thanks to the patients who have borne with us very well throughout the trial study.

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5. Baldev Kishore (Feb. 1962)—*The Antiseptic*, 69 : 101.

RENAL FUNCTIONAL RESPONSE TO FUROSEMIDE IN CHILDREN WITH ACUTE GLOMERULONEPHRITIS

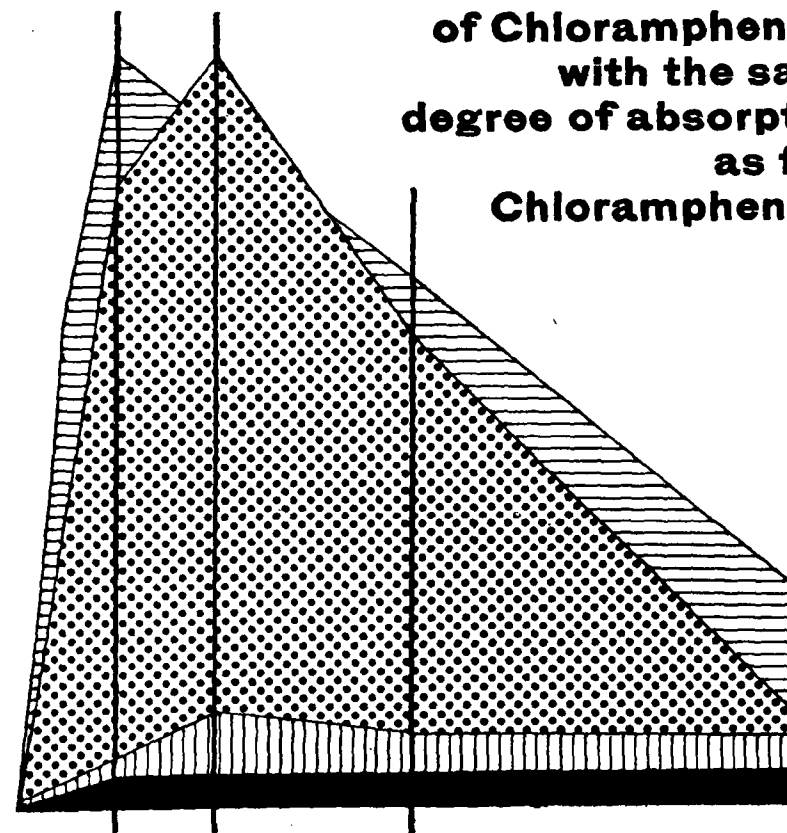
Furosemide was administered to five children with acute glomerulonephritis and marked fluid retention. All patients responded with a brisk diuresis and improved symptomatically despite the fact that their glomerular filtration rates were reduced. No significant changes in renal hemodynamics or glomerular filtration rates were noted acutely. Creatinine clearance was not an accurate estimator of inulin clearance in acute glomerulonephritis after injection of furosemide. About 25% of oedema was removed within four to six hours.—(H. A. Repetto *et al*, *J. Paediatr.*, 80 : April 1972, via *J.A.M.A.*, 17-7-1972).

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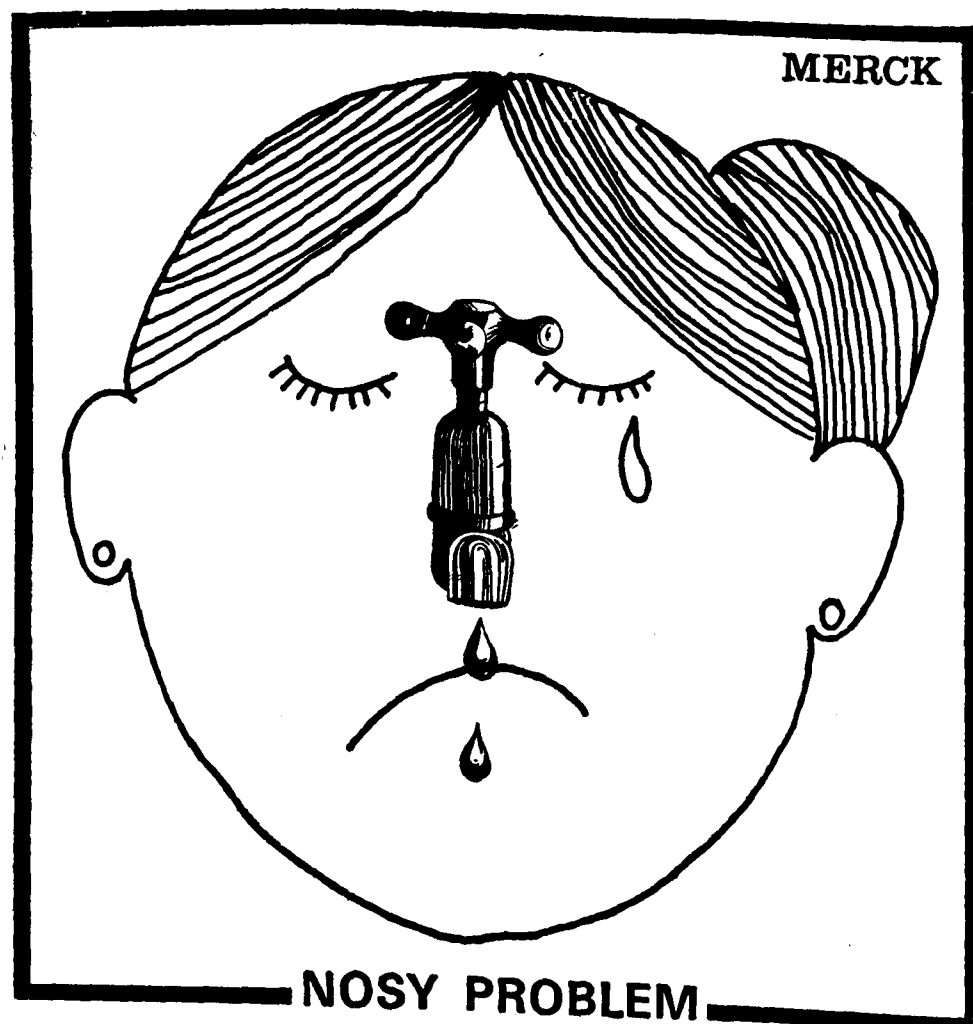
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PRINCIPLES IN THE MANAGEMENT OF CONGESTIVE HEART FAILURE*

With Reference to Recent Advances and Concepts

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HARRISON AND RESNICK⁸ have stated in their book on "*Principles of Medicine*", that 'heart failure should include all disorders in which congestive phenomena occur as the result of the inability of the heart to receive and propel the blood which is offered to it.'

The concept that heart failure occurs when cardiac output is inadequate in relation to filling load is also of importance in understanding the significance of the high output-disorders which may be curable.

Myocardial failure may be due to pressure overload (as in hypertension or aortic stenosis), a volume overload (as in mitral or aortic regurgitation), or a myocardial injury (as with myocardial infarction or cardiomyopathy). When overload is the problem the cause may be treated directly, as with antihypertensive drugs or by surgical treatment of valve disease. In the management of myocardial failure, the treatment is in fact directed also to other systems and organs, and to the heart itself⁷.

The main aim in attempting the efficient management of C.H.F. is to improve the contractile power of the heart muscle. This may be achieved by:—(1) Reduction in the workload of the heart. (2) Use of positive inotropic agents. (3) Oxygen therapy. (4) Anticoagulants. (5) Relief of venous congestion by diuretic agents and other measures. (6) Prevention and control of precipitating factors and (7) Dealing with the underlying aetiological factors.

I. Reduction of work-load of the heart.—For this purpose, both (a) *Physical and mental rest* are of prime importance as they reduce the metabolic demands of the tissues and thereby the cardiac work-load. Heart failure denotes the inability to maintain an output adequate for the needs of the body. Those needs can be minimized by eliminating physical exertion. The renal blood-flow will then increase, the G.F.R. will rise, and diuresis may ensue. A semiprone position may allow renal blood-flow to increase more than a sitting or standing position.⁹ The application of rest as a therapeutic measure requires judgement and individualization.

The amount and type of rest (i.e., partial or complete) must be tailored to each patient depending on the severity of failure,

*Specially contributed to the 'ANTISEPTIC'

response to treatment and the presence of associated diseases which might precipitate failure or by complications of heart failure. Thus patients with acute coronary occlusion and failure may have to be kept in bed for 4 to 6 weeks and sometimes for several months. The patients with active rheumatic carditis should remain in bed as long as there are symptoms and signs of rheumatic activity. Thus the clinical course of the patient and *not* any arbitrary time limit will be the determining factor.⁵

Sometimes rest in bed fails to bring about satisfactory symptomatic improvement unless it is rigidly enforced and activity is absolutely banned. Bathroom privileges, trips to the telephone, getting out for meals, and occasional excursions out of the bedroom may completely nullify the therapeutic effects of bed rest. When heart failure is associated with coronary thrombosis, active rheumatic fever or other febrile diseases or when it fails to respond to partial limitation of activity, complete bed-rest should be enforced. Complete bed-rest does not imply that the patient must lie flat in bed. Patients with severe heart failure usually have a remarkable capacity for finding the position best suited for their circulatory status and the attending physician should assist them to maintain that position with comfort; he should not arbitrarily modify it.

The enforced use of the bed-pan is often a distortion of the purpose of bed-rest, a bedside-commode is definitely preferable.

Deep breathing and leg exercises, changes in position and the use of anticoagulants are measures designed to overcome the dangers of phlebothrombosis, pulmonary infections and pulmonary embolism.

There has been interest in chair-rest as a means of treating patients not only with G.H.F, but also those with myocardial infarction. It is important to recognise that chair-rest does not mean ambulation. It implies rest in a chair in a comfortable position with proper padding of pressure areas and proper measures to ensure venous return from the extremities.

This degree of severe restriction of activity is seldom needed in patients with moderately severe heart failure. Most of them do quite well with room ambulation.

Complete bed-rest is ineffective unless there is mental composure along with the physical rest.⁵ The sick room should be quiet with a pleasant atmosphere. Visiting hours should be completely forbidden at first and limited later. Psychotherapy, including optimism, encouragement and reassurance, will all add to the advantages of rest. Parenteral morphine is necessary for the first few days in certain forms of heart failure but later, milder sedatives will suffice, Tranquillisers such as Meprobamate (400 mg.) or Chlordiazepoxide (10 mg.) may be

administered once or twice daily to allay restlessness and anxiety. Soporifics like Cap. Nembutal or Tab. Mandrax or Vesparax may be necessary to induce sleep.

(a) *Diet: Sodium fluid restriction*—Dietary sodium restriction remains an important adjunct in the treatment of most patients with C.H.F.⁶ The extent of sodium restriction will depend on the severity of the cardiac failure. The sodium intake should not be more than 200 to 500 mg. daily (the equivalent of about 0.5 to 1.0 gm. of common salt). In milder cases diets containing 1.0 to 2.0 gm. sodium (2.5 to 5.0 as common salt) may be permitted.⁸ Readily available salt-poor foods and salt substitutes *e.g.*, Co-salt or Uni-salt powder have made preparations of such diets easier and more acceptable to the patients.

Bland, low residue diet is better tolerated than one with considerable roughage. Fruit juices, bananas, sodium-free powdered milk or the more palatable Walker-Gordon low sodium milk are preferable to the traditional Karell diet (800 ml. milk per day, containing about 400 mg. sodium), for the first 2 or 3 days and then allow a balanced light diet containing rice, barley, sago may be given.

The palatability of the diet may be increased by seasoning it with onions, vinegar, pepper, lemon, bay leaves, chilli powder, garlic, mustard or by flavouring it with cocoa, coffee, honey, jams, cloves, orange, cinnamon, nutmeg, ginger or almond extract. Tonics and mixtures may often be the cause for the sodium intake which must always be remembered.

Caloric restriction has been observed to cause a decrease in B. M. R. with less myocardial demand. A low calorie diet (1500 to 1800 cal.) with small frequent feedings may curtail postprandial increase in gastro-intestinal demands for cardiac output and assist the patient to avoid postprandial angina and dyspnoea.⁹

The intake of water should usually be regulated by the desire of the patient; strong tea or coffee must *not* be allowed. Small quantities of sherry, whiskey or brandy are permitted to those who are addicted to it. Parenteral multivitamins help in improving the appetite in those with anorexia.

In some patients with C.H.F, an increase in free water clearance and sodium diuresis may be achieved by sodium restriction and forced fluid intake. Scheme has popularised this approach to treatment and emphasised the need for an acid-ash diet, acidifying salts and careful observation of the patient. Patients with more severe forms of heart failure or those with associated kidney disease may not be able to excrete large water loads. In addition, many patients with advanced CHF, develop severe dilutional hyponatraemia which can be

corrected only by rigid fluid restriction to 750 or even 500 ml. per day. It is seldom feasible to restrict fluids beyond this limit.⁹

II. Use of positive inotropic agents.—1. *Digitalis and its allies*:—Since, 1785, when William Withering noted the usefulness of foxglove; digitalis has been the mainstay in the treatment of patients with CHF, for improving the function of the failing myocardium as a positive inotropic agent which increases the speed of myocardial contraction and shortens its total duration. In the normal heart muscle, the contractility is increased but the output remains unaffected, whereas in the failing heart, the cardiac output increases. This effect appears to be brought about by the influence of digitalis on the rate of calcium uptake by the myocardial cell which is diminished in the failing myocardium and is restored to normal by digitalis. This effect of digitalis on the failing myocardium as distinct from its effect on the rhythm and conduction, is beneficial to almost all patients with CHF, and it sometimes proves valuable in cases with cardiogenic shock,⁷ with high central venous pressure.

The general use of the drug and the dosage schedule of the various digitalis preparations are not germane to this discussion. However, it may be pointed out that the dose requirements depend primarily upon the renal function³ and other factors which increase the patient's sensitivity to digitalis, which include a low level of potassium and magnesium, high serum calcium, hypoxia, hypothyroidism, autonomic activity, the underlying myocardial disease¹⁴ and gross renal and hepatic impairment.¹⁷ Again patients with cor pulmonale are particularly sensitive to digitalis.¹⁶ Some diseases of the heart seem to have an inherent capacity to tolerate the average dosage of digitalis, e.g., some forms of viral myocarditis, endomyocardial elastosis and experimentally in the obstructive forms of cardiomyopathy.¹⁷

Adequate digitalisation is one of the most potent remedies we have for dealing with the patient with CHF since it is one of the few agents that will directly improve cardiac function. Plasma digoxin concentrations can now be measured simply and rapidly by radio-immuno-assay but there is no clear-cut relationship between plasma concentrations and therapeutic effects. Toxicity is usually associated with plasma-digoxin concentrations above 2 to 3 nanograms per ml. (radio immuno.assay) but classical digoxin intoxication has been recorded with concentrations so low as 0.4 nanograms per ml. and in a recent study involving 104 patients it was impossible to discriminate between patients with or without toxicity on the basis of the plasma digoxin concentration. Therefore, a confident diagnosis of digitalis intoxication cannot often be made solely on the basis of the plasma concentration.¹⁴

Digitalis intoxication can manifest itself by precipitating intractable heart failure.^{5, 9} This fact must be stressed.

Digitalis toxicity may also manifest itself in several unusual ways. In the elderly persons for instance, confusion and disorientation may be the first and only evidence of digitalis toxicity.¹⁷ Unexplained cerebral symptoms, toxic psychosis, paraesthesias around the lips in addition to cardiovascular, visual disturbances and familiar gastro-intestinal manifestations, may be other important clues to toxicity. The various manifestations of digitalis toxicity have been graded clinically in a recent review¹.

Degrees of Digitalis Toxicity

Grades		Manifestations
1. Slight	...	Anorexia, ventricular ectopic beats and bradycardia.
2. Moderate	...	Nausea, vomiting, headache, malaise and ventricular premature beats.
3. Severe	...	Diarrhoea, blurring of vision, confusion, disorientation, ventricular tachycardia, Sino-atrial or A—V block.
4. Extreme	...	Abdominal pain, high degree conduction blocks and atrial or ventricular fibrillation.

The prevalence of hypokalaemia has been reported in patients with digitalis intoxication,^{18, 23} although no significant difference in serum potassium level was found by other workers in patients with or without digitalis intoxication.^{20, 21} Recently, the measurement of potassium and calcium concentrations in whole-saliva has been found to be a reliable, rapid, and simple method of identifying patients with digitalis toxicity²⁶.

Atrial and ventricular arrhythmias have occurred within 24 to 48 hours in digitalised patients after the administration of diuretics²⁴ and supplements of potassium in an effort to correct this, only further aggravate it¹⁰. So, it is advisable in most cases to withhold the drug and for established arrhythmias lignocaine and phenytoin are often found effective³. Beta-adrenergic blocking drugs are also potent for this purpose but they carry the risk of precipitating heart failure in the presence of seriously impaired myocardial function.^{3, 5, 7} The routine oral supplementation with potassium solutions in digitalised patients should be discouraged. Only when there is established hypokalaemia, oral potassium salt solutions (Kay Ciel elixir or Martin's KCL sol.) in recommended doses, well diluted in a glassful of water may be administered after meals

for short periods. Its palatability may be increased by mixing it with tomato juice.²⁵

On the basis that digitalis glycosides undergo significant biliary excretion and intestinal reabsorption^{11,13}, bile acid binding polymers would be important adjuncts in the treatment of digitalis intoxication. Digoxin appears to have a lesser enterohepatic circulation than digitoxin. Due to the structural similarity of digitalis and bile acids, these resins bind digitalis preparations in the intestinal lumen, thus interrupting their enterohepatic circulation and shortening their physiologic half-life. These types of exchange resins include Cholestyramine (Quemid, Questran), Colestipol—a new anion exchange resin and Epichlorohydrin. The results of experience with Colestipol, in digitalis intoxication have been recently reported.¹

2. *Glucagon*⁷:—Interest has now been centred on another positive inotropic agent, Glucagon, a hormone secreted by the *alpha* cells of the pancreatic islets. It appears to act in a way similar to *beta* adrenergic stimulating drugs. It is effective in patients with heart disease, increasing the blood-pressure and the cardiac output without increasing vascular resistance. The place of Glucagon in these patients is still uncertain, but it may prove to be of real value.

The insulin-K-glucose regimen has been found to improve myocardial function in the failing heart in animals. In general, this form of therapy has proved disappointing.^{5,7}

III. *Oxygen therapy*.—Oxygen must be resorted to either by B.L.B. mask or through intranasal catheter at the rate of 5 or 6 L/mt. This is of special value in CHF with infarction or complicated by acute pulmonary oedema, anoxic cor pulmonale, and intractable CHF. Hyperbaric oxygenation may offer hope in refractory failure.⁹

IV. *Anticoagulants*.—Death from thromboembolism is common in elderly patients in severe heart failure and so prolonged bed-rest and intensive therapy are essential. Hypercoagulability occurs generally in patients who have had diuresis and hæmoconcentration. Hampton and Castleman reported an incidence of 90% pulmonary infarction in cardiac patients with pulmonary emboli, as compared to 60% for non-cardiac patients. Hines and Hunt found an incidence of pulmonary infarction in 35% of the 235 patients with heart disease.

The short term use of an anticoagulant, especially in the elderly patient is recommended in the treatment of CHF. Again in chronic cor pulmonale, due to recurrent pulmonary emboli, anticoagulant therapy gives good results and if necessary ligation of inferior vena cava may be considered. Initiation with heparin along with oral anticoagulants is to be preferred; for an interesting quality of heparin, of value to

patients in severe heart failure, is its ability to block the secretion of aldosterone.⁹

V. *Reduction of venous congestion*.—1. *Diuretic agents*:—Our knowledge of diuretics has greatly advanced in recent years and we now have a better understanding of their mode of action and also their ill-effects.¹⁷ Long term administration of the diuretics in common usage, increases the urinary excretion of potassium, lowers the serum potassium and depletes the exchangeable or whole body stores.⁴ Oral potassium supplements are useful in preventing and correcting the potassium loss associated with long term diuretic therapy but they have their own disadvantages which include heart-burn, a metallic taste in the mouth, loose motions and abdominal discomfort, whereby patients associate with oral preparations of potassium chloride.^{19,22} Enteric-coated preparations provide no answer to the problem because the large concentration of potassium released from them in the small intestines was found to cause local ulceration and in some cases also producing stenosis and obstruction¹⁹; it may also be irregularly absorbed.¹² The use of additional foods that are high in potassium and low in sodium, like orange juice, raw carrots and bananas, are all of some help but not adequate for the patient who has a strong stimulus to loss of potassium¹².

Among the diuretics, the time honoured organomercurials are still potent but are now less used after the advent of the more potent oral diuretic-like Furosemide and Ethacrynic acid. Thiazides are potent and being cheap, are also used, but not extensively. The site of action of thiazides is probably in the cortical diluting segment of the distal nephron and has no effect on free water-reabsorption.⁹ Besides photosensitive skin eruptions, other major side-effects are hypokalaemia, hyperglycaemia, hyperuricaemia, agranulocytosis and thrombocytopaenia. Furosemide (*Lasix*) and Ethacrynic acid (*Endocrin*) are very popular and potent diuretics and offer new benefits to many patients with intractable heart failure. The site of their action is in the medullary diluting segment of the ascending limb of the loop of Henle. Both Ethacrynic acid and Frusemide act, inspite of the presence of hypoalbuminaemia, hyponatraemia, hypochloroemia, hypokalaemia, alkalosis; and occasionally even in the face of a marked decrease in glomerular filtration rate.⁹ Mercurials and thiazides do not act at any G.F.R. below 5 ml. a minute, although Furosemide may be a potential diuretic for patients with G.F.R. so low as 1 ml. a minute.² Its speed of action makes it most useful in the treatment of acute heart failure and pulmonary oedema.¹⁵ Furosemide causes a lesser degree of hyperglycaemia than thiazides but a greater increase in

blood sugar than Ethacrynic acid. Skin rashes, hypokalaemia and blood dyscrasias have been reported following the use of Furosemide and Ethacrinic acid.

Potassium - conserving diuretics.—Gifford⁶ says "Experience has shown that 60 to 100 *mEq* of potassium is required daily to correct diuretic-induced hypokalaemia. Based on these figures, a patient would have to consume 4 to 6 (or more) bananas a day or drink 5 to 9 (or more) glasses of orange juice a day to adequately counter the potassium loss. As this is not feasible, there are now three substances available which make it possible to avoid the potassium loss associated with oral diuretic therapy and in many cases render potassium supplements unnecessary. These are:—Spironolactone, Triamterene and Amiloride. In addition to preventing potassium depletion, all these three drugs are useful in augmenting the response to oral diuretics already in common use.¹⁹ Therefore, K-conserving diuretics are acceptable alternatives to potassium supplements for preventing K-depletion caused by the conventional oral diuretics. It is hazardous to use K-supplements simultaneously with any of these K-retaining diuretics, since hyperkalaemia has been found to occur with this therapy.⁹

The continued use of vigorous diuretic therapy should include frequent estimations of serum levels of sodium, potassium, chlorides and the carbon-dioxide-combining power, as electrolyte imbalance; also acid-base disturbances may be a factor in the refractoriness of a case of cardiac failure.

Spironolactone (Aldactone-A):—As aldosterone enhances renal sodium for potassium exchange, it may aggravate sodium retention particularly in patients with heart failure who have been treated by salt-restriction and diuretics. Spironolactone is an aldosterone antagonist, acts as a competitive inhibitor with aldosterone and mineralocorticoid activity in the exchange area. By itself, its diuretic action is feeble but it potentiates the action of other diuretics. In addition to hyperkalaemia, skin rashes, painful gynecomastia in males or menstrual irregularities in women have been reported after its prolonged use¹⁰.

Triamterene (Dytac):—It has been shown to be active in blocking a distal sodium-for-potassium exchange-mechanism. It probably acts directly on the distal tubular cell⁹. It increases sodium and chloride excretion and conserves potassium irrespective of aldosterone levels. Triamterene itself has only a weak diuretic action and is therefore, usually given with thiazides (*e.g.*, Dytide). Continued use in large doses may lead to hyperuricaemia, nausea, diarrhoea, hyperkalaemia and increase in blood-urea nitrogen.

Amiloride (Colectril, Midamor):—This is a recently introduced drug having properties similar to Triamterene but with a greater diuretic effect. Amiloride given concurrently will prevent the K-loss caused by vigorous oral diuretics such as Ethacrynic acid and Frusemide. The daily dose used in this way varies between from 5 to 10 mg., the maximum being 20 mg.

Use of diuretics in combination:—A combination therapy of diuretics may be evolved once the mechanism and site of action of each diuretic is understood. The importance of this will be realised in combination of two diuretics with different sites of action as it would be unwise to combine two thiazides in combination or to use Ethacrynic acid and Frusemide together since there will be no additive effects. A useful plan has been suggested by Kirkendall *et al* (1968)⁹ and is recommended for further reference.

Glucocorticoids (*e.g.* Prednisolone 5 mg. *t.d.s.*) along with the combined regimen of diuretics has also been found useful especially in refractory cases,⁵ because there may be depletion of adrenocortical hormones due to long continued strain.¹⁷

2. Role of dialysis:—This is advised for patients in refractory heart failure. Peritoneal dialysis is commonly used for the purpose as it is more effective in removing the fluid. The use of hypertonic dextrose solutions in the peritoneal dialysate will result in the mobilisation of large quantities of oedema-fluid. Mailloux *et al* have published their experience with 15 patients and several other investigators have also obtained similar good results in selected patients.

VI. Removal or control of precipitating factors in C.H.F.—The common factors are:—abnormal rhythms (paroxysmal atrial or nodal tachycardia, atrial fibrillation or flutter, rarely ventricular tachycardia), sub-acute bacterial endocarditis, digitalis-intoxication itself, myocarditis, severe anaemia, broncho-pulmonary-infections, covert or overt hyper or hypothyroidism, nutritional and vitamin deficiencies like beri beri, emotional stress, electrolyte imbalance and acid-base upsets, pulmonary embolism and infarction, pyrexia due to any cause and the continued use of drugs causing cardiac depression (*e.g.*, Reserpine, Guanethidine and Propranolol). These factors are to be treated on their own merits concurrently with the cardiac failure as the persistence of the above factors may result in intractable heart failure.

VII. Management of the underlying causative factors.—The common causes that are noticed in our country are:—rheumatic, hypertensive and ischaemic heart disease and cor pulmonale, congenital heart disease, thyroid disorders and cardiomyopathy which play a minor role. Syphilitic heart disease is

now-a-days rare. The management of heart failure cannot be effective unless adequate steps are taken to correct or control the aetiological factors.

There are a few cases which are really true ones of refractive failure. The important causes are:—(a) Advanced degree of myocardial weakness or dysfunction; (b) cardiomyopathies; (c) secondaries in the myocardium and (d) certain types of congenital heart disease which are not amenable to treatment. Nothing much can be done to help patients in this category of true refractive failure¹⁷.

Problem of refractory heart failure:—When confronted with a case of apparently refractory heart failure, a constant review of the case particularly for the adequacy of treatment, effectiveness of salt restriction and the possible existence of associated diseases as mentioned earlier, should be made before pronouncing it as 'real refractive heart failure'.

Recent advances in the management of cardiac failure with the use of fasting with free access to water, peritoneal dialysis, artificial kidney and other mechanical devices, like cardiopulmonary bypass with either pump oxygenators or mechanical pumps and methods to provide diastolic augmentation of the circulation with aortic balloon inflation and counterpulsation for short periods, thoracic duct cannulation and removing excess of extravascular fluid, cardiac transplantation and artificial hearts are all restricted to a few very well-equipped cardiothoracic centres. A better understanding of electrolyte disturbances, the use of the more powerful recent diuretics and their combinations, an increasing awareness of digitalis toxicity, eliminating the errors in diagnosis and treatment will all go a long way in the better management of cases in refractory heart failure¹⁷.

Rehabilitation:—Once the symptoms and signs of CHF have been relieved the patient should be allowed physical activity within the limits of tolerance, as it not only does not damage the heart but actually also improves its working capacity.

Finally, after all the effective steps have been taken in the management of CHF, the patient should be encouraged to return to his previous routine work or should be advised to take up a job suited to his working capacity and at the same time, if possible, suited to his task and needs.

Summary.—The conventional therapeutic regimen (i.e., physical and mental repose, salt restriction, fluids, diuretics, digitalis and oxygen therapy) and the more recent concepts in their clinical implication have all been discussed at length while a passing reference has been made to other specialised regimens.

Recent concepts are mainly in the judicious use of digitalis, early recognition, prevention and correction of (i) digitalis toxicity; (ii) precipitating and (iii) aetiological factors, with improved therapeutic applications.

With the advent of potassium conserving diuretics and their combination with conventional diuretic agents the routine policy of K-supplementation is to be deprecated, as their value and utility are controversial.

The use of peritoneal dialysis, artificial kidney, fasting with free access to water, assisted circulation using a pump system with or without oxygenator, thoracic duct cannulation and paired electric stimulation to improve the myocardial contractility, have all to be considered for patients in intractable heart failure. Cardiac transplantation and artificial hearts are recent additions, restricted to well equipped cardiothoracic institutions with expert trained staff.

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PREDICTING CORONARY ARTERY DISEASE

It is becoming clear that there is no single cause of the high incidence of coronary artery disease in developed countries. The Framingham study in the U.S.A. showed that hypertension greatly increases the risk of its developing, and there is also considerable evidence that smoking cigarettes and a positive family history of arterial disease do so. In the last few years interest has risen in the elaborate analysis of plasma lipids other than cholesterol, and in younger patients especially there is some evidence that hyperlipidaemias predispose to the development of coronary artery disease.

Diastolic blood pressure proved the best discriminator, and in decreasing order of importance were the presence of corneal arcus, degree of baldness (increased baldness being associated with coronary artery disease), presence of xanthelasmata, family history of hypertension, number of cigarettes smoked, plasma cholesterol, plasma triglycerides, and low-density lipoproteins.

At best a doctor asked by a patient to assess his chances of developing coronary thrombosis can make only a rough guess. If the person concerned is muscular, obese, carries much responsibility and works long hours, smokes heavily, takes little exercise, bald, has xanthelasmata, an arcus, a raised blood pressure, and his parents had arterial disease, he would obviously be at high risk. If his physical build, personal habits, blood pressure, and other attributes were the opposite, he would have a low risk.

If a patient with many known adverse factors were to ask for advice on preventing coronary disease, what should his doctor say? The evidence of prospective and retrospective studies indicates that the patient should keep his weight somewhat below average, eat as little as possible of known cholesterol-raising foods such as eggs, shell-fish, and animal fats, stop smoking cigarettes, and take plenty of light exercise. Frank hyperlipidaemias should be treated, where appropriate, with drugs (e.g., clofibrate). But it must be admitted that much of this advice is based on guesswork and that one could probably find world authorities to take exception to virtually every one of the recommendations. It is unfortunate that recipes for health seem to be so negative, but the results from the Cambridge study certainly underline the extent of our ignorance about the causes of occlusive arterial disease.—(Editorial: *Brit. Med. Jour.*, 7-10-1972).

ORAL CONTRACEPTIVES CONTAINING ONLY PROGESTOGENS

Oral contraceptives containing only a progestogen have had a chequered career. In 1965 trials in Latin America showed that very small amounts of a progestogen, chloramadinone acetate, when given without any added oestrogen had a strong antifertility effect. Not all progestogens are suitable, most commonly used in the late 1960s the amount of oestrogen was critical at low dosage.

The preliminary trials in Britain of oral contraceptives containing only progestogen were encouraging, and when it became evident that the thromboembolic deaths associated with oral contraceptives could be attributed to the oestrogenic component it seemed that the progestogen-only pill might in many cases be an acceptable alternative. These hopes were dashed when Eleanor Mears and colleagues did a clinical trial of four progestogens in Yugoslavia. They found an appreciable failure rate with meggestrol acetate, chlormadinone, norgestrel, and norethisterone, and concluded that continuous administration of small doses of progestogen were unlikely to offer a serious challenge to the existing oestrogen progestogen mixtures. Professor P. Eckstein and his colleagues have returned to the charge with a clinical trial of norgestrel (published in this issue of the *B.M.J.*).

It is true that in the earlier study norgestrel was associated with a pregnancy rate of 4 per 100 women-years while the worst interpretation of Professor Eckstein and colleagues' data gives a pregnancy rate of 2 per 100 woman-years, but in the earlier study a lower dose of norgestrel (50 ug) was used than in the present one (75 ug). One conclusion is inescapable: there is a small but indubitable failure rate with norgestrel, but when the mixed oestrogen-progestogen pills are taken correctly the pregnancy rate is virtually nil.—(Leading article: *Brit. Med. Jour.*, 22-7-1972).

ADDICTIVE DRUGS IN SOCIETY*

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"A dungeon horrible, on all sides round
As one great furnace flam'd, yet from those flames
No light, but rather darkness visible
Served only to discover sights of woe
Regions of sorrow, doleful shades, where peace
And rest can never dwell, hope never comes
That comes at all."—(Milton's *Paradise Lost*).

THE word 'Drug,' causes a feeling of revulsion and apprehension in the older generation, but a sense of fun and frolic in many of the younger generation. 'Drug' does not mean medicines, but the chemical substances which have a psychic effect, causing mood-changes, alteration in consciousness and perception, hallucination etc. The individual who takes them for fun, wants them again and again; also demands more and more. Addiction or dependence begins, then comes a state of tolerance i.e., the addict needs larger and larger doses to obtain the same effect. These drugs can be pharmacologically classified as under:—

A. Depressants:—1. Narcotics:—(a) Opiates: Opium, Morphine, Heroin, Codeine, Meperidine; (b) Barbiturates: Nembutal, Amytal, Seconal, Luminal, Phenobarbital, Tuinal etc, 2. Alcohol.

B. Stimulants:—1. Cocaine and 2. Amphetamines like Benzadrine, Dexedrine, Methedrine and Ritalin.

C. Hallucinogens:—1. Psychodelic: L S. D. (Lysergic acid diethylamide), Mescaline, Demethyltyptamine (D.M.T.).

I. Depressants.—1. **Opiates:—**Well-known for centuries; described by Homer in his 'Iliad' as 'Including the sense of evils'. Therapeutically described by Thomas Sydenham (1680) as 'Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so efficacious as opium'. They are effective as analgesics, antitussives etc. Tolerance to Heroin is achieved quickly resulting in increased consumption, leading on to addiction. In this group the emotional dependence is severe and physical dependence develops quickly. Tolerance is marked, and cross-tolerance develops to the related drugs. During the withdrawal stage, the patient experiences restlessness, loss of sleep, anxiety, apprehension, general bodyaches, pains, hot flushes, perspiration, muscular cramps, nausea, vomiting and loss of appetite etc. Nalorphine induces abstinence syndrome. The opiates are also taken with barbiturates for better kicks. There is a wrong popular notion that opium is a good sex tonic. It has

*Specially contributed to the 'ANTISEPTIC.'

been definitely proved that opium possesses no aphrodisiac properties.

2. *Barbiturates*:—Basically derived from barbituric acid (Melanyl urea), they are long, medium or short acting. Therapeutically used as hypnotics they control convulsions. The emotional dependence is severe. The physical dependence develops slowly and is very severe too. They have also cumulative effect on the body, leading to the increased need for larger doses to achieve identical effects. There is cross tolerance with alcohol, chloral, paraldehyde, meprobamate, chlordiazepoxide etc. A state of mental confusion and an emotional instability develop, resulting into barbiturate-intoxication. The intoxicated patient shows generalised sluggishness, lack of memory and thinking, irritability, depression and develops suicidal tendencies. Barbiturates are responsible for a large number of deaths. Amongst the drug users they are known as golfballs, downs, yellow-jackets (Phenobarbitones) Red doll or devil (Sod. Seconal). As tolerance increases the margin of safety decreases. Despite the tolerance the minimum lethal dose remains the same, leading to accidental poisoning.

3. *Alcohol*: The history of alcohol forms part of the history of civilization. It is an intoxication which is socially acceptable. Alcoholism is a more significant problem than all the other forms of drug abuses put together. In Delhi alone the figures for illegal alcohol bottles seized by the police are: in 1970: 61309; 1971: 60998; 1972, upto March: 94 48. In the present day society this is the most common social evil leading to broken homes, human misery and loss of socio-economic standards. The question whether it is at all a stimulant has long been debated. Pharmacologically it has been proved that it is primarily a depressant. Hyperactivity, when it occurs, is the removal of inhibitory effects. Alcohol in lower doses act chiefly on arousal mechanisms of the brain reticular formation. Direct cortical depression probably only occurs with large doses, resulting in disorganization of thought processes and dislocation of motor processes. With increasing doses the subject passes through all the stages of anaesthesia and may even die due to respiratory depression. As regards the psychic effects, Sathana (1957) described 'The first functions to be lost are the finer grades of judgement, reflection, observation and attention; the faculties largely acquired through education, which constitute the elements of restraint and prudence that man usually imposes on his action. Both mental and physical efficiency are reduced. There is one exception that the subject with anxiety, or nervous tension may improve his performance with a proper dose, i.e., due to the depression of inhibitory control mechanism. It reduces visual acuity, impairs taste, smell and hearing, causes

unstable coordination and unsteadiness and it prolongs reaction time. As regards sexual function—it is not an aphrodisiac. Shakespeare rightly mentioned that alcohol 'Provokes the desire, but it takes away the performance.' Tolerance to alcohol occurs. For clinical purposes there are three stages:—(a) *Acute alcohol poisoning*:—Acute intoxication with behaviour changes. Generalized incoordination, mental confusion and even coma. (b) *Dipsomania*:—Periodic urges for heavy drinking. (c) *Chronic intoxication*:—Alcoholism. Causes many psychotic changes, nutritional deficiencies, and vitamin deficiency, especially of Vit. B₁. It causes chronic gastritis, hepatic cirrhosis, chronic myocardial failure and peripheral neuropathy. The end stage is dementia with loss of memory, slowed speech, deterioration in gait and social habits. The subject may have delusions, hallucinations and delirium tremens. Sudden withdrawal of alcohol may precipitate an acute psychotic attack. Withdrawal becomes less unpleasant if the patient is sedated with Chlorpromazine, chlordiazepoxide or paraldehyde. Psychosocial therapy is more important than drugs which are only of limited use. If the patient is cooperative, an attempt may be made to discourage him by using antabuses or emetics.

II. *Stimulants*.—A. *Amphetamines*. They are sympathomimetic drugs causing—a reduction in appetite, an increase in metabolic processes, stimulation of cardiac action, an excitatory action on the smooth muscles, such as those of the skin and on the blood vessels and stimulation of C.N.S., also an inhibitory action on the smooth muscles of the intestinal wall and bronchial tubes. Therapeutically amphetamine has a variety of uses against mental and physical fatigue, in enuretics to lighten sleep, in obesity, depressed appetite, as a respiratory stimulant, in hypnotic poisoning against narcolepsy, to correct the behavioural disorders in children etc. The therapeutic dose is 10 to 30 mg. per day in divided doses. It produces a sense of well-being and increased alertness, increases self-confidence and stimulates energy. The subjects use it as a 'Superman' drug. The common names are Bennies (Benzedrine), Dexy (Dexedrine), Meths (Methedrine) etc. The subject gets used to it in four ways:—(1) Teen age students who want an anti-sleep agent to prepare for examinations. (2) Persons who want temporary breaks to their endurance e.g., long distance truck-drivers, heavy manual workers in factories, who want to work efficiently without sleep at nights and athletes who want to give better performances. (3) Overtired executives, businessman and exhausted housewives for overcoming mental and physical fatigue. (4) As it decreases inhibitions—the user can adapt to different sets of behaviour and morals.

Emotional dependence is severe, physical dependence is *nil* and tolerance develops.

It is used orally, intramuscularly and intravenously. The injections are called as 'speed'. The user gets marked euphoria, increased physical strength and mental capacity, experiences loss of appetite and sleep. It is claimed that after its use, sex is more pleasurable by delayed orgasms in both male and female. Afterwards there is deterioration in accuracy, increase in anxiety and a sort of nervousness. The user gets tremors and confusion, then feels dizzy. Cardiac stimulation causes palpitation to the point of causing discomfort. In acute poisoning—excitement, convulsions and a state of hyperactive paranoid schizophrenia with hallucination—leading to hyperpyrexia, hypertension, cardiac arrhythmias, and ultimately vascular collapse and death. The treatment in such cases is *alpha* and *beta* adrenergic blocking agents and barbiturates. There is no characteristic abstinence syndrome.

B. Cocaine is used as a surface anaesthetic in medical practice. Orally it is used for checking vomiting and nausea in gastric carcinoma (10 to 15 mg. cocaine hydrochloride). It is claimed to afford relief from fatigue and hunger and to induce a pleasant introverted mental state, and courage, sometimes, even for the commission of crimes. Its continuous use causes physical exhaustion. It is used orally, intravenously or as a snuff 'snow' which however may cause nasal ulceration. Emotional dependence is marked, physical dependence *nil*. Tolerance is absent.

III. Hallucinogens.—1. *Psychodelics*:—They stimulate sensory perception having no basis in physical activity. All the senses are affected. The common drug in use is L.S.D.—Synthesized by Hoffmann (1938).

Normal subjects experience:—Blurred vision and visual hallucinations. These do not occur in the blind and is less when the subject is blind-folded. Objects appear distorted.

Auditory acuity increases but hallucinations are uncommon. Subjects not only hear music but also feel it. Foods may feel coarse and gritty in the mouth. The body may be held in uncomfortable positions. Regarding passage of *time* the usual feelings are:—it may seem to stop, or to pass slowly and sometimes to run faster as if a thousand years had elapsed. Physically he feels relaxed and emotionally happy or depressed or apprehensive; becomes mentally imaginative and problem-solving becomes difficult. He becomes introverted. Sometimes he may have a feeling of union with cosmos or mankind. These experiences last but for a few hours. Intervals of normality occur and may become progressively longer. An overdose

can cause parasympathomimetic effects, it can also stimulate the sympathetic system. Physiologically these drugs are not over toxic and do not cause any permanent physical damage. Deaths have been reported. According to some workers, chromosome damage in human beings has been reported. Tolerance develops but there is no physical dependence. Psychic dependence however, may develop.

2. *Marijuana group*:—In India, it is believed to be in extensive use. The common forms are bhang, ganja, Charas, Indian hemp, Hashish, Cannabis etc. These drugs are eaten and/or smoked. It is recognized by many as being relatively innocent, causing fewer side-effects and complications than many of the 'hard' drugs. The effect is similar to that of alcohol intoxication, slow but prolonged, without subsequent hangover. The subject gets a pleasurable sensation causing a heightened reaction to external stimuli and an appreciable acuteness of all senses. It induces mental excitation with a feeling of well-being. There are hallucinations and disorientation in time and space. It enhances appreciation and response to auditory rhythm, that is why it is popular amongst musicians singing bhajans and religious songs. It has got no aphrodisiac properties. The users, do not become violent, under its influence but tend to be passive. Emotional dependence is marked, physical dependence absent and tolerance is trivial. There is no characteristic abstinence syndrome. Its occasional use is less harmful than the occasional use of alcohol. Its larger use may create depression and psychotic states which are infrequent when taken orally with foods or drinks the effect is slow and prolonged, the appetite increases—especially for sweets, the mouth and throat become dry. There is dizziness and nausea, the pulse-rate increases when it is used as a smoke, the effects are quick and the duration is short. The most common reaction experienced by the user is:—a dreamy state of alerted consciousness, with unconnected, uncontrollable and freely flowing ideas. Memory becomes distorted, things long forgotten come to memory while well-remembered things could not be recalled. Alterations in mood are common—sometimes uncontrollable laughter or cries and weeping to minimal stimuli. The psychotomimetic properties are caused by T.H.C. (Tetra-hydro-cannabinols). This drug is the cheapest and most easily available; and so is largely used.

IV. Tobacco.—Derived from the dry leaves of *Nicotina tabacum* used for smoking, chewing or snuffing. Nicotine is the main content, which varies from 0.5 per cent to 1.5 per cent. The average cigarette gives an average yield of 6 to 8 mg. of nicotine, while the nicotine content of an average cigar ranges from 15 to 40 mg. The common and worst hazard is lung

cancer in smokers and mouth cancer in chewers; bladder cancer is also reported. Smoking causes chronic pharyngitis, laryngitis and bronchitis leading to emphysema of the lungs. Tobacco smoking can also cause coronary heart disease. Heavy smoking causes loss of appetite and nausea. Tolerance develops to nicotine, emotional dependence is intense, while physical dependence is *nil*.

Mortality from peptic ulcer is high amongst smokers. Thromboangiitis obliterans occurs only in smokers. Smoking during pregnancy is responsible for the high incidence of abortion and these women deliver babies of lower than average weight. Sometimes tobacco amblyopia develops. Tobacco is very dangerous and hazardous to the individual's health, but it is very commonly accepted in society. The heavy smoker sits really on a volcano, which may erupt at any time.

Drugs.—One can very well visualize the extent of the use of drugs in Indian from a police report about Delhi. Within 2-25 years, the Delhi Police have seized the following illegal drugs:—

Drug	1970	1971	Up to March 1972
Alcohol (illegal) ...	61309 bottles	60998 bottles	24248 bottles
Charas ...	220.412 kg.	834.88 kg.	249.955 kg.
Bhang ...	2123 kg.	3088.50 kg.	431.101 kg.
Ganja ...	1240.227 kg.	869.02 kg.	39.782 kg.
Opium ...	264.234 kg.	449.395 kg.	58.301 kg.

Conclusion.—The increasing and open use of drugs by the younger generation has resulted in family, society and community disruption. School and hostel authorities and law enforcement officers are faced with a variety of difficult problems. It is high time that our people learn a lesson from the failures and experiences of western countries in the matter of drug taking. Adequate measures for prohibition and prevention should be instituted to save our younger generation from disruption.

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DIAGNOSIS AND TREATMENT OF GIARDIASIS

Giardiasis was diagnosed in three of five children by means of small intestinal biopsy and smears of biopsy mucus when stool examinations failed to demonstrate the parasite. In a fourth patient the biopsies and smears were positive for the trophozoites, but one of three stools examined contained cysts. Biopsies were not taken from a fifth patient who had cysts in the stool. Treatment with metronidazole for ten days reversed the symptoms and malabsorption completely in all but one patient who had granulomatous colitis.—(M. E. Ament, *J. Paediatr.*, 80: April 1972, via *J.A.M.A.*, 17-7-1972).

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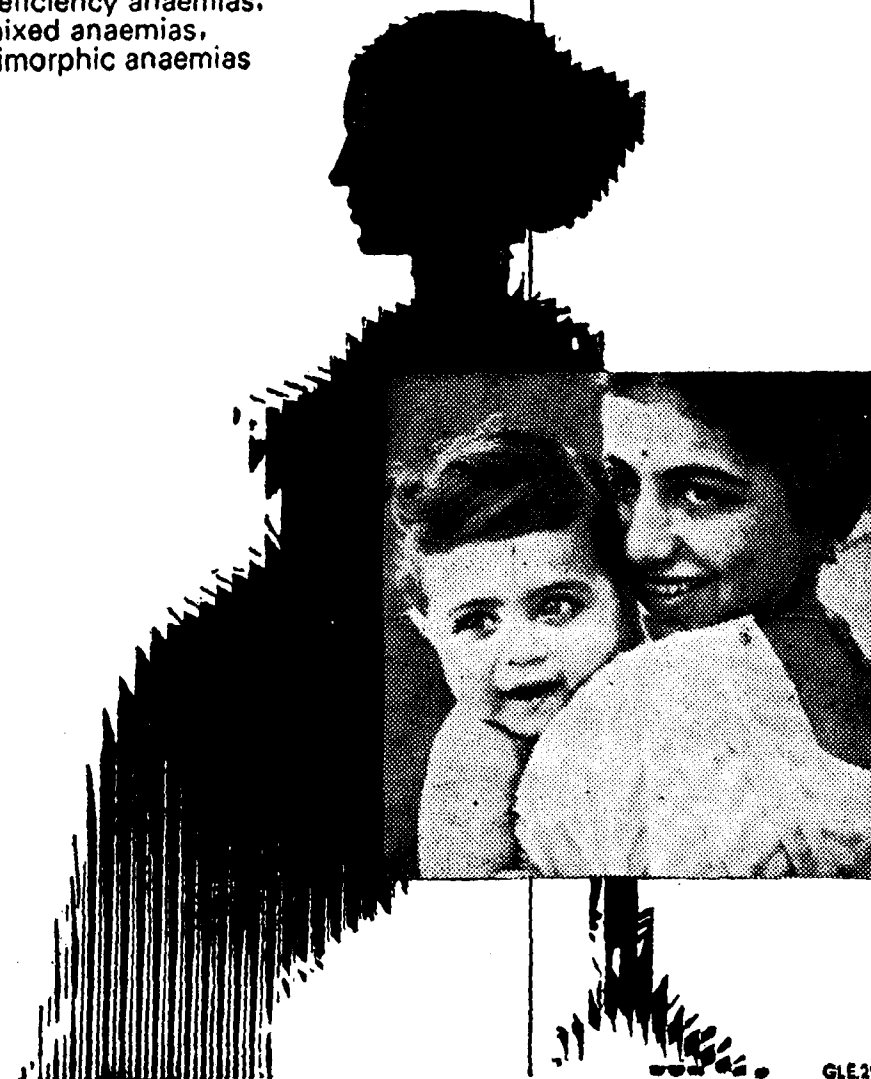
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Cases and Comments

TUBERCULIN SENSITIVITY IN TUBERCULOUS MENINGITIS

(A Study of 3 Cases)

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INTRODUCTION:—Tuberculosis of the serous membranes has been known for many centuries and the meningeal reaction to this infection was probably first graphically described by Whytt R.¹ in 1768. In spite of the tremendous advances in medicine, the disease continues to be severely prostrating, and carries a high morbidity and mortality. Tuberculin reaction (T.R.) considered to be diagnostic in tuberculosis has been difficult to interpret in meningitis. This reaction, dependent on hypersensitivity, has been inconsistent and has led to conflicting opinions on the role of hypersensitivity in the causation and manifestation of tuberculosis of the lymph sacs.

Of late, there has been a number of reports on negative T.R. in established cases of tuberculosis.^{2,3} These unexpected negative responses have given rise to many unsatisfactory explanations and they have also complicated the technique and interpretation of this reaction as evidenced by the recent trends in Western literature³.

Originally it was thought, that all diseases of tuberculous aetiology gave a positive Mantoux reaction; but experience has shown that a decrease in tuberculin sensitivity is possible in certain stages of disease and health:—namely: (1) the pre-allergic phase of tuberculous infection; (2) certain cases of serosal tuberculosis; (3) miliary tuberculosis; (4) in association with viral infections; (5) debilitated and toxic patients; (6) disease of the lymphatic system; (7) uræmia; (8) extremes of age; (9) pregnancy and (10) during the administration of corticosteroids, cytotoxic drugs, radiation and large doses of Vit. C. The interest in the above enlarging list of conditions where cutaneous hyposensitivity was marked, stemmed from the realisation that none of these were absolute preconditions for a negative response and that in many, without the above prerequisites, the tuberculin sensitivity, remained negative. Obviously this cutaneous reaction is not yet properly understood.

The inconsistent behaviour of tuberculin reaction has been under study in the Government General Hospital, Madras, since 1965 and a definite set pattern of its behaviour has been observed

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consistently in "Serosal tuberculosis." The present report is on three cases of Tuberculous Meningitis showing varying tuberculin sensitivity at different stages but the reactions were the same in all the three at any one stage of the disease.

Tuberculin tests were made with 1 T.U.=P.P.D. of the B.C.G. Vaccine Laboratory, at Guindy, Madras and the results read 48 hours later.

CASE I:—An 18 year-old girl was brought to the hospital on 8-3-'72 with symptoms of vague ill health of 10 days' duration, fever for 5 days, headache, vomiting and clouded consciousness of 3 days' duration, with repeated convulsions in the last 2 days. There was no previous history pointing to tuberculous infection.

On examination, she was moderately nourished, semiconscious and there was no sign of dehydration. Her oral temperature was 103°F. Central nervous system showed marked neck rigidity and bilaterally constricted pupils. The tone of the limbs on her left side was diminished with an extensor plantar reflex. Optic fundi were normal. Lumbar puncture yielded a clear fluid dropping out at 60 drops per minute. The cell count of the fluid was 640 per c.mm. with a predominance of lymphocytes. The biochemical analysis of the fluid showed:—total protein : 116 mg %; chloride : 550 mg %; sugar : 45 mg.% with the presence of globulin. Blood analysis showed:—Total leucocyte count of 6900 per cubic mm. with a differential count of:—P 60, L 35, E 5. The ESR was 65 m.m. in the first hour.

The patient was treated with Streptomycin one gm. (*i.m.*) INH 600 mg. and PAS 12 g. orally every day, with intramuscular injections of Decadron 1 cc. *b.i.d.* In addition the patient was symptomatically managed with *i.v.*, fluids and cerebral decongestants. The day after admission the patient exhibited denser hemiparesis on the left side with dilated but reacting pupils and Jacksonian fits. Conservative management helped the patient to recover. On the 11th March the patient's general condition was better, and the level of consciousness had improved. There was response to commands. On the 15th, the neck rigidity had disappeared and plantar reflex was bilaterally flexor, the temperature had come down to normal and so corticosteroids were withdrawn. On 17th March the higher cerebral functions returned to normal. On 24th March tuberculin test was negative. (There was no induration at all). On 10th April the patient's general condition was good and she was discharged with advice to continue antituberculous therapy in the same dose in the out-patient department. On 10th June a tuberculin test was repeated when it showed 5 m.m. induration. Streptomycin was reduced to 1 gram on alternate days from the 10th June and was stopped after the completion of 130 grams. Since discharge she was on 400 mg. of INH and 12.0 g. of P.A.S.

which she was advised to continue for 2 years. On 13th September, the Tuberculin test was repeated which resulted in 8 x 10 m.m. of induration and on the 18th October 12 x 14 m.m. of induration. On 12th January 1973, when the patient was in very good general health and had none of the known conditions which could reduce the tuberculin sensitivity the tuberculin test resulted in 2 m.m. induration.

CASE II:—A 21 year-old girl, was brought to hospital on 30-8-'72 with a history of continuous fever and headache for 7 days and vomiting of 3 days' duration. There was no history of contact with tuberculous individuals.

On examination, she was moderately nourished but toxic. There was minimal dehydration and disorientation. Temperature was 100°F. Central nervous system examination revealed incoherent speech, marked neck rigidity, normal pupils with sluggish light reflex and bilateral extensor plantar response. Bladder was distended. Fundi were normal. There was no lateralising sign. Rest of the systemic examination was normal.

Cerebrospinal fluid was clear and under tension, 80 drops per minute; cytology showed 740 cells/cm. with lymphocytosis. Biochemistry showed total protein was 190 mg.%; chlorides were 460 mg.% and sugar 54 mg.%. Globulin was present. Haemogram showed a total leucocyte count of 8700/c.mm. with a differential count of:—P. 60%; L. 38%; E. 2%. E.S.R. was 60 m.m. per hour; she was treated with Streptomycin, I.N.H. and Decadron same as was administered to Case No. 1 (*supra*) and symptomatically managed from the day of admission. On 8-9-'72 the patient's general condition had improved, temperature touched normal and Decadron was withdrawn. On the 16th September there was no neck rigidity and on the 18th, the tuberculin test was negative with no induration at all. Tuberculin test was repeated on 18-10-1972 when the patient was on continued antituberculous treatment with oral prednisone 5 mg. *b.i.d.* and resulted in 10 x 14 m.m. induration. The patient was discharged on 30-10-1972 when there was no symptom or neurological deficit and the biochemistry of the CSF was normal, she was advised to continue the antituberculous treatment in the out-patient department.

On 4-1-1973 when the tuberculin test was repeated there was 18 x 30 m.m. induration which persisted for 4 days before showing signs of regression.

CASE III:—An 18 year-old girl, was admitted on 6th September 1972, with a history of irregular fever for 1 month, headache of 20 days' vomiting of 10 days' and disorientation of 4 days' duration. There was no past history of tuberculosis in this patient though many episodes of vague illness had occurred.

On examination, the patient was found to be poorly nourished, and was semiconscious. Temperature was 100.2°F. Examination of Central Nervous System showed that she was responsive only to strong painful stimuli; neck rigidity was present and pupils were bilaterally constricted. There was no lateralising sign. Deep reflexes were diminished and Plantar response was bilateral extensor. Fundi were normal. Rest of the systemic examination was not contributory. Routine investigations revealed a differential leucocyte count of:—P. 57%; L. 40%; E. 3% and the ESR was 28 m.m. per hour. Lumbar puncture yielded clear fluid under tension with a cell count of 560/c.mm., predominantly lymphocytes. Biochemical analysis showed the total proteins to be 58 mg.%; chlorides 520 mg.% and sugar 36 mg.% with a trace of globulin. The patient was given the same treatment as for the first two cases. The temperature touched normal and the general condition began to improve from the 18th September; when Decadron was withdrawn. Four days after the tuberculin was tested and was negative with no induration. On the 20th, patient developed weakness of the left lateral rectus and by the 15th October the headache and lateral rectus weakness cleared and on 20th October the tuberculin test was repeated which showed 12x16 mm. induration. Lumbar puncture was made and the C.S.F. was found to be normal. Patient was discharged without any neurological deficit.

Discussion.—All the three cases reported were undoubtedly of tuberculous meningitis, though no attempt was made to have bacteriological confirmation, owing to difficulties in isolating the offending organism.⁴

Since exudative serosal tuberculosis is a manifestation of hypersensitivity to tuberculoprotein, it was presumed that tuberculin-tests would have been positive if it had been done before the onset of meningitis in these three patients. At the time of exudative inflammation—when the patients were brought to hospital and for 20 days thereafter—all the three showed a negative reaction. When the inflammation subsided with treatment for about a month, the tuberculin reaction became positive. Thus there appears to be "Three phases" to tuberculin sensitivity in tuberculous meningitis:—an early or 'premeningitis' positivity, which is usually missed because the patients do not present at that stage; a mid-phase negativity which is most often seen and a late phase enhanced positivity which is often neglected and not tested. These three distinct phases of tuberculin sensitivity have been observed in patients with tuberculosis of all the major lymph sacs and what is interesting and thought-provoking is the absolute loss of tuberculin sensitivity at the height of the disease process and a conversion to positivity at a time of healing, especially when the patients

were on antituberculous drugs and corticosteroids:—a paradox which cannot be easily explained by the immunological concepts of today.

A suggestion has been made that it might be due to a loss of circulating antibodies during the active exudative phase of the disease that caused cutaneous hyposensitivity and the subsidence of inflammation permitted a reaccumulation of the antibodies to effect a "conversion."

Our observations recorded here are, however liable to criticism. The poor general condition of the patients at the time of admission is a long accepted factor known to cause a negative response. However, here the patients were revived to a considerable extent and the tuberculin tests were purposely delayed till a stage of reasonable recovery was reached. The administration of steroids, which is known to suppress tuberculin sensitivity had been stopped for 10, 11 and 4 days respectively in the three cases before the first tuberculin tests were done. The development of allergy to the previously inoculated P.P.D. is another controversial possibility that may be raised, to explain the tuberculin positivity at the second inoculation. A strongly positive reaction particularly in the second case which persisted for four days before subsidence, should settle this argument.

To have a counter-check on these observations, the hospital case records of Tuberculous meningitis from the year 1968 to 1971 were reviewed. There were 28 patients with proved Tuberculous meningitis in whom Mantoux tests had been done and read 48 hours later. The quality and strength of the material used for the Mantoux tests had not been specified in these records, but is believed to be 1 in 1000—O. T., produced by the B.C.G. Vaccine Laboratory at Guindy in Madras.

It will be observed that of the 22 patients who gave a negative Mantoux reaction, 20 had the test done within 40 days of the onset of meningitis. Of the six Mantoux-positive cases four had the tests done beyond 40 days (actually after 90 days). These findings are statistically significant as supporting our observations.

Summary.—Three patients with Tuberculous meningitis have been followed-up for a period of 4 months and over, with repeated Tuberculin tests. Tuberculin sensitivity appears to be nil during the active exudative phase of meningitis and becomes hyper-positive on the subsidence of the exudative inflammation.

TABLE I

Showing the details of the Mantoux reaction				
Mantoux reaction	When done within 40 days	Beyond 40 days	Total	
Positive	2	4	6	
Negative	20	2	22	
Total	22	6	28	

Acknowledgement.—We are thankful to the Superintendent, Government General Hospital, Madras for according permission to publish this paper.

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TRANSIENT UNILATERAL DILATION OF PUPIL ASSOCIATED WITH HEADACHE

Question:—A 38-year-old woman had sudden onset of a moderately severe one-sided headache associated with ipsilateral dilation of the pupil and some retrobulbar burning sensation. Within 24 hours, the symptoms disappeared and the pupil returned to normal size. Results of physical examination, including neurologic examination, were normal. What was the most likely cause of this woman's ailment? What additional studies would you suggest?—(M.D. New Jersey).

Answer:—A transient unilaterally dilated pupil, associated with localized headache, may be due to sympathetic irritation (*Arch. Neural*, 3: 223-229, 1960) caused by disease of the carotid sheath. In the absence of other signs of localized or generalized sympathetic discharge, this clinical picture may be part of the syndrome of ophthalmoplegic migraine. This so-called migraine equivalent may present as it did in the patient you describe (*Arch. Ophthalmol.*, 84: 130-136, 1970).

Perhaps, a more common cause of isolated unilateral pupillary dilation is the parasympatholytic effect produced by reflux of sympathomimetic drugs, via the nasolacrimal duct, from the nose, or accidental introduction of a dilating agent directly into the conjunctival sac. The latter may result from gardening in an area where jimsonweed, containing stramonium, and atropine-like alkaloid, grows wild. The accidental spread of dust from this plant into the eye would cause pupillary dilation, without headache (*Ohio State Med. J.*, 62: 921, 1966). These cases can be identified through bilateral instillation of one drop of 0.5% or 1% pilocarpine, which will constrict the normal pupil but will not affect the pharmacologically dilated pupil (*Arch. Ophthalmol.*, 86: 21-27, 1971).

In the absence of visual loss and ocular pain, acute narrow angle glaucoma may be excluded from the differential diagnosis. Aide's syndrome (tonic pupil) can also be ruled out because of the short duration of the mydriasis.—Thomas J. Stafford, M.D., Northwestern University Medical School, Chicago.—(*J.A.M.A.*, 4-9-1972).

THERAPEUTIC ABORTION BY INTRA-AMNIOTIC INJECTION OF PROSTAGLANDINS

Intra-amniotic injection of either prostaglandin F_{2x} or prostaglandin E₂ was used in an attempt to induce therapeutic abortion in mid-pregnancy in 27 patients. Termination of pregnancy was successful in 11 out of 13 cases when prostaglandin E₂ alone was used, but in only 6 out of 14 cases when prostaglandin F_{2x} was used. A further eight patients aborted after additional intravenous oxytocin stimulation, but the combined procedures failed altogether in two patients who were initially given prostaglandin F_{2x}. The technique was simple, free from serious side effects, and reasonably effective when prostaglandin E₂ was used.—(Roberts, G. *et al*, *Brit. Med. Jour.*, 1972, 4: 12-14).

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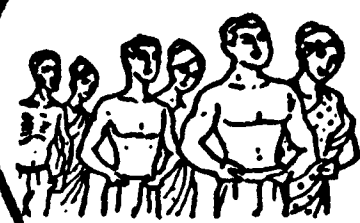
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CYSTIC LYMPHANGIOMA

(A Case Report With a Review of the Literature on Lymphangiomas)

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This report presents the case of a patient with Cystic Lymphangioma which is a rare condition.

CASE REPORT:—Patient, M.A., a male child, aged 3 months, was admitted to our Surgical Unit in March '72. The parents complained that the child had a swelling on the left side of the chest and abdomen since birth. It was about 25 cm. x 20 cm. in size, with a patch of hæmangioma about 6 cm. x 5 cm. in the centre of the swelling. As the swelling was not troublesome and also as the child's general condition was low, he was discharged with supportive treatment, and advised to come for an operation after three months.

Again on the 11th September '72, the parents brought the child with the complaint of difficulty in breathing and an increase in the swelling. During the previous 6 months, the child had lost considerably in weight and had also cough and a low grade fever.

Personal, past, and family histories were non-contributory.

Physical examination revealed malnourishment and anæmia. There were no congenital anomalies.

On local examination, a huge swelling about 35 cm. x 25 cm. in size, involving the whole of the left side of the chest and abdomen extending from the midline anteriorly and crossing the midline posteriorly towards the opposite



FIG. I. A cystic lymphangioma on left side of chest

scapular region, vertically from the left clavicular to the left iliac crest. (Fig. I, see above). It had an ill defined edge and margin. There was one patch of capillary hæmangioma about

9 cm. x 6 cm. in the centre of the swelling. No impulse on coughing and no visible vessels or pulsations were seen. It had a variable consistency from soft to firm, and had a smooth surface. The skin was not free from the swelling. At some places there was fluctuation.

There were no enlarged lymph glands in the cervical, axillary or inguinal regions.

A provisional diagnosis of hæmangio-lymphoma, Lymphangiectasis or Neuro-haemangioma was made.

INVESTIGATIONS :—(i) *Urine* showed a trace of albumin, no sugar, and no abnormality on microscopic examination.

(ii) *Blood* showed Hb. 8.5 g.% ; W.B.C. : T.C. 10,000 per cu.mm. and D.C. : P. 61% ; L. 33% ; E. 2% ; M. 3% ; B. 1%.

(iii) Aspirated fluid from the cyst examined microscopically showed 80% lymphocytes.

(iv) A plain X-ray picture of the abdomen and chest showed a huge soft tissue shadow extending from the left clavicular region to the left iliac crest. Evidence of pressure erosion at the right and left 5th, 6th, 7th ribs. No evidence of bone destruction was seen. Radiologically it appeared to be a fibroma.

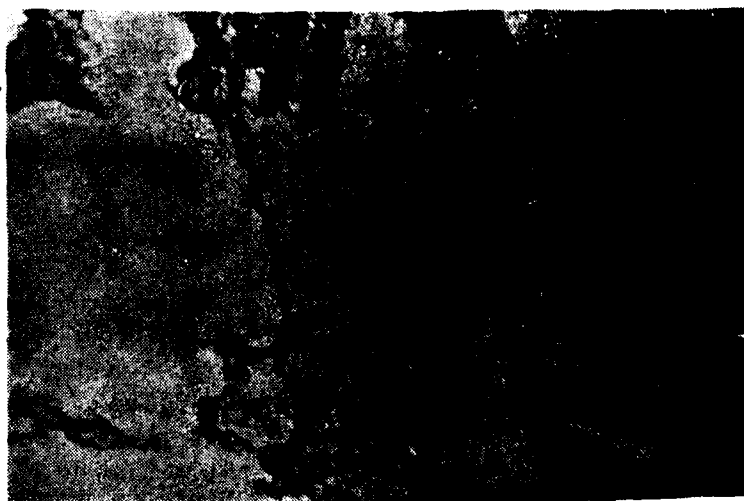


FIG. II. Photomicrograph of cystic lymphangioma. (Low power)

As the child experienced great difficulty in respiration on 16.9.72, an operation was performed under general anaesthesia. As his general condition was not good, blood transfusion was started before the operation. With an elliptical incision—around the patch of the hæmangioma, the mass was opened. It was found fixed to the subcutaneous tissue, on cutting which numerous thin walled small and large cysts with cystic spaces

were seen. Some were filled with clear fluid, some with straw-coloured fluid. Some of the cysts were communicating with one another. In short, it had a honeycomb appearance. The cystic mass was excised completely. After cutting away the redundant skin, the opening was closed in two layers, with a drainage tube in the space.

During operation, the patient's general condition was not good. So vasopressors, cortisone, and blood transfusion were resorted to. In spite of the above treatment the child got into irreversible shock and expired on the same day.

Histopathology :—The microphotograph of cystic mass shows dilated cystic spaces lined by endothelial cells, which contained homogeneous pink staining lymph. The intervening area between the cysts contained blood vessels, fibrous tissue, lymphocytic aggregation, and adipose tissue—a *cystic lymphangioma*. (see Fig. II, page 204).

Discussion.—Lymphangiomas are uncommon and are frequently congenital. They are benign tumours of the lymphatic channels that originate in the displaced foetal cells of the lymphatic system.

These tumours are also believed to arise as congenital rest, or hemartomas. They are usually associated with other congenital anomalies. The tumours are mostly noted at birth or in the first year of life. They may occur anywhere in the body but are frequently seen in the extremities. The head, face, neck, shoulders, and chest are however, unusual sites. They may also occur internally in any viscus. Only a few cases occur in the mediastinum and retroperitoneally. Both sexes may be equally affected.

According to sites they are termed as :—Naevus lymphaticus when in the skin; Macrochelia when in the lips; Macroglossia when in the tongue; Macrocheiria when in the dorsum of hand; and Cystic hygroma when in the neck and axilla.

Pathologically the growth may be divided into three varieties :—(i) Capillary or simple lymphangioma ; and (ii) Cavernous lymphangioma and (iii) Cystic lymphangioma.

(i) *Capillary or simple lymphangiomas* may occur in the skin as colourless moles, often also on the lips, cheeks, tongue or on the skin and in the subcutaneous tissues, less often in the muscles and internal organs. This type consists of anastomosing small and medium sized vessels, separated by thin trabeculae of connective tissues. They show little or no propensity for growth.

(ii) *Cavernous lymphangioma* :—Generally affects the skin and subcutaneous tissues. Occasionally it is found between muscles, in the mesentery and also retroperitoneally.

They almost invariably occur in the neck or axilla, and are composed of cavernous lymphatic spaces and are therefore analogous to the cavernous hæmangiomas. Spaces are lined by flattened endothelium.

(iii) *Cystic lymphangiomas*:—These are more common in children than in adults; and a little more common in females than in males, and on the right side rather than on the left. This type (90%) occurs chiefly in the neck, axilla and inguinal regions occasionally, rarely in the greater omentum. This is caused by germ-rests. In some cases, trauma or chronic inflammation may be a contributory factor. They consist of small and large cysts which are incompressible. They are lined by flattened endothelium, and filled with lymph. Chemically, the cystic fluid is composed of a small amount of protein and a large quantity of cholesterol. Microscopically they show desquamated endothelium, lymphocytes, a few R.B.Cs, and W.B.Cs.

The complications noted include extension of the tumour with compression of vital structures and infection.

The treatment of choice is surgical excision.

Summary.—A somewhat rare case of cystic lymphangioma on the chest and abdomen of a 3 month, old child is reported. The literature on the subject is reviewed.

Acknowledgement.—My grateful thanks are due to Dr. B. D. Miera, M.S., Superintendent of the Civil Hospital, Ahmedabad for accoring permission to report this case. I am also thankful to the staff of the Pathology and Radiology Departments for their useful help.

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HEPARIN ADMINISTRATION IN ACUTE CORONARY INSUFFICIENCY (Its Value in the Initial Stages of Treatment)

Thirty-one episodes of acute coronary insufficiency were treated orally with anticoagulant drugs alone. On 29 occasions, heparin sodium was administered intravenously additionally during the first two to four days. During the first ten days of treatment, one patient receiving anticoagulant drugs orally alone developed a myocardial infarction and three suffered a further episode of acute coronary insufficiency. One patient receiving heparin died suddenly, one developed a myocardial infarct, three suffered a further episode of acute coronary insufficiency, one had a pulmonary infarct. The differences do not warrant a conclusion that initial administration of heparin is actually harmful. However, it may be concluded that the drug is without any demonstrable positive value in patients suffering an attack of acute coronary insufficiency. In such individuals, anticoagulant therapy can be instituted with orally administered drugs alone.—(Michaels Leon, J.A.M.A., 11-9-1972).

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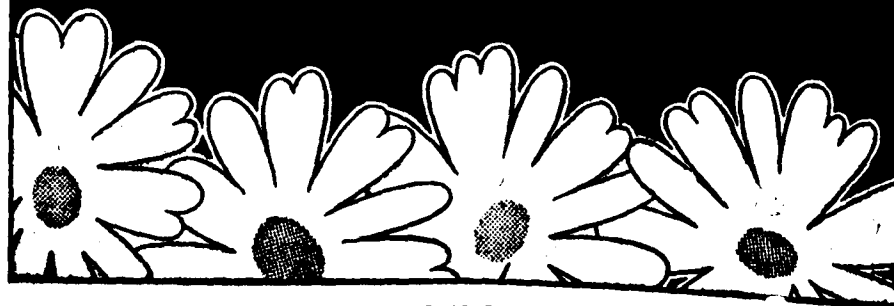
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Recent Advances in Medical Technology * * *

SELECTION OF INTENSIVE CARE EQUIPMENT

WITH the growing awareness in the country about the utility of Intensive Care Units, most of the hospitals have started thinking in terms of providing such facilities to their patients.

In Intensive Care, critically ill-patients are grouped together in a separate ward, consisting of four to eight beds, and specially trained nurses keep a continuous vigil on their condition. They can detect any significant changes occurring in the physiological parameters and take timely action to avoid critical malfunctions which might be fatal.

The actual monitoring of the parameters is done conveniently by means of electronics. Although this means strapping the patient with half a dozen wires and transducers, including possibly some transvenous catheters, it offers a very reliable and accurate means of keeping a watch over the values and trends of these parameters. Modern electronic apparatus can also trigger visual and audible alarms when certain specific malfunctions which the electronic apparatus can learn, occur. Moreover, data from all the patients can be brought to a central station where automatic emergency recorders, memory systems etc., can be provided and one nurse-specialist can keep an eye on all the beds, thereby maximising the utilisation of her time.

The first step in selecting such equipment is obviously to determine the parameters to be monitored. Customarily, one or more of the following parameters are monitored with certain values derived from them :

<i>Monitored Parameters</i>	<i>Derived Parameters</i>
1. E.C.G. Wave	Heart rate
2. Peripheral Plethysmogram	" "
3. Blood Pressure Wave—Sanguinous or Catheter method	Arterial/Systolic/Diastolic/ Mean B.P. Mean Venous pr. (C.V.P.)
4. Respiration Thermistor or Impedance Pneumography	Respiration rate
5. Temperature	
6. Systolic/Diastolic B.P. by the 'cuff method'	

Most of the equipment available comprises various nodules or boxes, each nodule capable of handling one or more of the above parameters.

These can be assembled together as per requirement to give the desired monitoring system. It is also not mandatory to select the same parameters to be monitored at all beds. One can hence make a rough schematic of the system with the lists of the desired parameters at each bed displayed and those to be monitored at the central station, and also of the other facilities required like automatic recorders, remote alarms, telemetry systems etc.

The next step is to translate this in terms of equipment and fit the whole system in the budget available. It is advisable to contact the suppliers' representative and discuss the system with him. He should be in a position to work out the most economic combination and also advise of any special requirements of his equipment.

It is also essential to discuss with him the safety precautions taken by the manufacturer, which is an important criterion in the selection. Wherever the equipment makes an electrical contact with the external parts of the body, the equipment should be guaranteed to have leakage currents into the electrodes not exceeding 100 micro amperes or one-tenthousandths of an ampere. If any intra-corporal contact is made the leakage should be less than 10 micro amperes even in case of single fault conditions. The input amplifiers should be isolated from the mains and should preferably be floating with respect to earth.

Another criterion of selection is the ease of operation. It should be borne in mind that the equipment is to be operated by people who are primarily qualified in Medicine and not Electronics. The number of controls on the front panel of the instruments should hence be minimum. The labelling of these controls should be such as to be easily comprehended by the nurses and physicians. There must be adequate safeguards against faulty operation.

Finally, the long term serviceability of these instruments should be taken into account. This is especially true in case of custom-designed equipment which is produced in small quantities where spare part availability can pose serious problems at a later date.

To cut a long story short, we could take a single hypothetical example of a two bed unit, one for coronary care and one for intensive care. The medical specifications for the two bedside units and the control station might appear as stated *overleaf*.

Coronary Care Bed		Intensive Care Bed
ECG/Peripheral Pulse	To be presented on a two-channel	ECG/Peripheral pulse
B. P. Wave Catheter Method		B. P. Cuff type Systolic Diastolic
Heart rate with alarms		Respiration rate
Systolic/Diastolic/		Temperature
Mean arterial pressure		
Mean Venous pressure/C.V.P.		
Central Station		
DCG's of both patients		
Heart rates of both patients		
Alarm Systems		
Auto/Manual Strip recorder		
Remote alarms		

The above system was on display in the Philips Pavilion at the Asia '72 Trade Fair at New Delhi. Some of the salient features are:—

1. An unique six-in-one display where the values of all six parameters monitored on the face on one 11" television screen along with a Dynamic E.C.G. channel.
2. The amplifiers of the Coronary Care System are suitable for intra-corporal applications, whereas those for the I.C.U. are designed for extra corporal operations.
3. The alarms sounded at the central station can be switched off only from the bedside.
4. All controls which are to be operated by Physicians only are hidden behind hinged flaps.
5. The system is backed by an international know-how and a nation-wide service net-work.

LEVODOPA THERAPY OF PATIENTS WITH PARKINSONISM AND HEART DISEASE

Forty patients with Parkinsonism and heart disease were studied before and during the administration of levodopa. Patients with increasing angina, myocardial infarction within the previous year, pre-existing severe postural hypotension, or transient cerebral ischaemia were excluded. Thirty-eight patients showed no adverse effects; angina improved in one patient but later worsened; one patient died of myocardial infarction after a severe gastrointestinal haemorrhage. Therapy with levodopa appears to pose little increased hazard to patients with most forms of heart disease. Inpatient monitoring is recommended at the beginning of therapy, and antiarrhythmic agents should be used when required.—(Ramon B. Jenkins *et al* in *B.M.J.* of 26-8-72, pp. 512-514).

LONG-TERM TRIAL OF DISODIUM CROMOGLYCATe AND ISOPRENALINE IN CHILDREN WITH ASTHMA

A year-long double-blind trial was carried out in 53 asthmatic children with severe perennial symptoms who were not receiving corticosteroids or corticotrophin. The treatment group were given disodium cromoglycate with isoprenaline (Intal Co.) while the placebo group were given lactose with isoprenaline four times daily. The groups were closely matched for clinical, physiological, and immunological features. Evaluation was based on the use of a diary and clinical and physiological investigations, including exercise tests.

After one year 71% of the treatment group was still well controlled while 76% of the placebo group had dropped out because of inadequate control of symptoms. There was no rise in the rate of failure towards the end of the trial period and there were no seasonal variations in the failure rate. No important toxic effects were noted. It was impossible to predict the outcome of the trial in any given patient from his clinical, physiological, or immunological status at the beginning. However, the prevention of exercise-induced asthma by premedication with disodium cromoglycate in a laboratory exercise test did correlate well with the satisfactory clinical response to the drug.

This trial has shown that D.S.C.G. is highly effective in the long-term management of childhood asthma. Altogether 71% of asthmatic children were well controlled on the drug compared with only 24% in the placebo group. This means that 24% of asthmatic children whose illness could be called severe responded adequately to regular inhalation of 0.1 mg. of isoprenaline four times daily, or that some of them may have tended to grow out of their disease in the course of 12 months. Allowing for this response in the placebo group about 50% of the severe asthmatic required and benefited from regular treatment with D.S.C.G. This is close to the estimate arrived at by Jones and Blackhall (1970) in an open trial of the drug based on patient's statements, severity of illness, number of attacks, and physical signs — (Silverman, M. *et al* in *B.M.J.*, 3: 378-381, 1972).

GUILLAIN-BARRE' SYNDROME IN HERPES ZOSTER

Herpes zoster, an ancient disease of man recognized since the time of "Celsus" is well known as a benign viral infection affecting the dorsal nerve roots and dorsal root ganglia.

Wohlwill reported occurrences of Guillain Barre' syndrome in association with herpes zoster. Since then there have been a few reports of ascending polyneuritis developing following herpes zoster. To the best of our knowledge only 13 such cases have been reported in the literature

The present case included herpes zoster of the left dorsal fourth and fifth spinal segments, and ascending paralysis which developed within eight days of appearances of herpetic rash. The rarity of this complication and good response to steroid therapy has prompted us to report this case.

This unusual case of ascending paralysis (Guillain-Barre' syndrome) appeared eight days following herpes zoster. A good response to steroid therapy, contrary to some reports in the literature is stressed — (Singh Sarjit, M.D., Malhotra Vinod, M.D. and Malhotra, R.P. M.B.C.P. of Amritsar, India, *New York St. Jour. Med.*, 15-8-1972).

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Editorial

EQUALITY IN MEDICAL SERVICES AND INCENTIVES FOR RURAL HOSPITALS

IT is indeed refreshing to know that, while delivering the Eleventh Convocation Address of the All India Institute of Medical Sciences at New Delhi on the 17th February 1973, the Union Education Minister Mr. S. NURUL HASSAN, strongly emphasised the necessity for ensuring equality in the medical services provided to urban and rural people. "The country must strive" he said "for equality in the Medical Services provided to urban and rural people alike. I cannot accept the view that urban areas need good doctors while those who are ill-equipped could be licensed for rural areas."

Mr. HASSAN said the country was faced with the problem of how to provide medical facilities to the rural population within a reasonable time and at a cost which would be within their reach.

The Institute, he said, should face this difficult challenge. On the one hand, it should develop research and expertise and, on the other, evolve programmes to deliver good medical services at the door step of every village family at a reasonable cost.

It was more advantageous and cheaper to emphasize the prevention of disease through education and improvement of socio-economic conditions, he said, and added that a big programme of preventive measures should be developed in rural areas.

He suggested that a large properly trained and organized para-medical service should be developed and linked with medical colleges.

In his presidential address, Mr. R. K. KHADILKAR, the Union Health Minister stressed the urgency for examining the present system of medical and para-medical educations in great depth in the light of the tremendous advances made in the medical service during recent years. We think that Mr. NURUL HASSAN's address is singularly free from any professional or political bias in the matter of medical education and frankly sets forth what the country really needs now.

We have however, had in recent months differing views expressed by leaders of different schools of thought, all VIPs, suggesting that rural medical relief being an urgent problem half baked, "desi" doctors or basic doctors (as some call them), may be given a short course of training in allopathy and sent to villages to afford relief to suffering humanity.

Thus, President V. V. GIRI, speaking at the inauguration of a Seminar sponsored by the Central Council of Research in Indian Medicine and Homœopathy at Delhi on 10th February 1973, stated that "Society must have doctors that it needs. Our people should have the choice to undergo treatment in whatever system they like. What is needed is that we must have qualified persons to treat people."

Mr. GIRI was happy that different aspects of research had been undertaken in the field of homœopathy and yoga in the country. "The entire work appears to have been taken up with a spirit of zeal and enthusiasm which is vital for scientific pursuit."

"In this endeavour, prejudice, fanaticism, pre-conceived and fixed ideas have no place. Research is nothing but rational investigation, out of which information of great value and importance will emerge," Mr. GIRI added. He was of the firm opinion that the Indian systems of medicine which had stood the test of time, could not have survived without some intrinsic merits of their own. The systems had a temporary set-back and now it was up to the researchers to develop them further with the aid of modern technology.

The Union Minister for Health and Family Planning, Mr. R. K. KHADILKAR, who is also the President of the Council, called upon the researchers in Indian Medicines and Homœopathy to uncover and reactivate through research, the vital principles that lay embedded in these systems. He said the Council should establish a link between our different systems and reactivate through modern technology.

The Tamil Nadu State Governor Mr. K.K. SHAH, while distributing prizes to the successful students of the Stanley Medical College, Madras, on the 14th February 1973, stressed the need for allopaths to study the Indian Systems of Medicine, so that they could prescribe simple but effective medicines for the general ailments of the poor, who could ill-afford the costly medicines of the allopathic systems of medicine, which are becoming increasingly costly from day to day.

A great responsibility is cast on medical men to look after the country's medical needs, especially of the rural population who form over 75% of the total; so unless Indian Medicine was pressed into service and the concept of a *basic doctor* who should be able to treat common diseases developed, the country cannot provide medical facilities for all its citizens.

The Union Planning Minister Mr. D. P. DHAR, while delivering the Convocation Address at the Indian Academy of Medical Sciences that the benefits of modern medical sciences must be extended to the rural areas on a large scale. He detailed the difficulties in the way of achieving this goal, even by the end of the Fifth Plan. There were millions of people in India who were too poor to pay for the sometimes expensive medical help. "We have to reach those people in an effort not only to cure their diseases but also to make them less vulnerable to disease. This is a task of gigantic magnitude. We have to think of new methods, new procedures and new organisations by which we can meet the expectations of our people. Research should take into account the widely practised indigenous remedies also. A proper integration of health, family planning and nutrition programmes has to be achieved. The Central Government is now considering a proposal to provide an incentive to voluntary institutions for establishing hospitals and dispensaries in rural areas.

We have thus been treated to a variety of well and ill-informed opinions and suggestions, all of course well meant no doubt.

"In the midst of counsel there is wisdom"—is an old adage. We sincerely wish and hope that from the multitudinous suggestions from responsible authoritative sources, a proper, rationalised, workable and profitable plan will be evolved.

TREATMENT OF HYDROCEPHALUS

Choroid plexectomy is an operation for treating hydrocephalus by decreasing the amount of cerebrospinal fluid production. Clinical results from this procedure have been reported and reviewed. Extracranial shunting techniques have emerged as the primary method for treating most forms of congenital hydrocephalus.

The results of treating congenital hydrocephalus by extracranial shunting alone and by extracranial shunting with choroid plexectomy were analysed and compared four years after the initial operation. Results were considered *good* if the patient showed an intelligence quotient of at least 70 or appeared completely normal in behaviour and intelligence, only *fair* if he had an intelligence quotient between 50 and 69 or was receiving special assistance for the educable retarded, and *poor* if he had an intelligence quotient below 50 or was completely helpless and uneducable. Survival occurred in 27.8 per cent of the "shunt with choroid plexectomy" group and in 27.3 per cent of the "shunt without choroid plexectomy" group. Possible reasons for these similar results are discussed.—(Brisman Ronald *et al* in *New York St. Jour. Med.* of 15-8-1972).

GLEANINGS

PÆDIATRICS

Urinary tract infection in newborns.—(Brit. Med. Jour., 2-9-1972).

Infection of the urinary tract in infancy and childhood is a dangerous condition. In about half the cases radiological investigation shows an abnormality such as pyelonephritic scarring or vesicoureteric reflux. It may be associated with progressive renal damage unless the infection is controlled.

The peak incidence is during the first 4 weeks of life, and at this age mortality is high during the acute stage of the illness. But despite the possibility of reliable diagnosis from examination of the urine and effective treatment with antibiotics cases probably still remain undetected. The problem is that at this age the symptoms are varied and most of them are nonspecific.

In a recent review of 66 infants with urinary tract infection in the first month of life J.M. Littlewood found that the commonest features were low weight, pyrexia, lethargy, and gastrointestinal symptoms such as anorexia, vomiting, and loose stools. Though the kidneys were palpable in more than half the patients, in only some were they thought to be enlarged. In no case did a macroscopic abnormality of the urine or an observed disorder of micturition draw attention to the diagnosis. The more serious symptoms such as dehydration, irritability, and convulsions were found in only a minority of patients, probably as a result of early diagnosis in this series. Jaundice, which occurred in 11% of the cases, has been reported before as a result of renal tract infection, but could be a trap for the unwary. Boys were more often affected than girls, and predisposing factors were an abnormal mode of delivery, perinatal anoxia, and low or high birth weight.

It is not easy to obtain uncontaminated urine from infants, and quantitative culture is especially useful in this

age group. However, obvious bacteriuria on simple microscopy of fresh uncentrifuged urine correlates well with a count of more than 100,000 organisms per ml. on culture. The problem of contamination can be overcome by obtaining urine by suprapubic puncture, and provided conditions are suitable this is a safe technique in infants. Littlewood also confirmed the well-known facts that neither the absence of proteinuria nor the absence of pyuria excludes the diagnosis of infection.

The severity of the illness in newborn babies in contrast to adult patients was emphasized by the finding of positive blood culture in 30% and a blood urea higher than 50 mg./100 ml. in over half of the patients. Two of the deaths occurred in infants with major congenital abnormalities of the urinary tract incompatible with survival, while the other five were in patients treated some years ago by means (alkalis and sulphonamides) which would be considered inadequate now. No deaths occurred in the latter part of the series, when ampicillin was the drug of choice and streptomycin or chloramphenicol were used for the more severely ill infants. Pyelonephritis in infancy can cause acute renal failure, which may be completely reversible and peritoneal dialysis has been used successfully in this situation.

The clinical features of neonatal urinary infection may be classed in four groups: *firstly*, a severe systemic illness, often with septicæmia, and with clinical evidence of pyelonephritis; *secondly*, infection secondary to a major congenital abnormality of the urinary tract; *thirdly*, mild nonspecific symptoms with no signs to incriminate the renal tract; and *fourthly*, asymptomatic infants in whom infection of the urine is an incidental finding. The clinical spectrum is so wide that urinary tract infection should be suspected in any newborn baby whose progress is in any way abnormal, and examination of the urine should be carried out as a routine.

MEDICINE AND THERAPEUTICS

Tetracyclines for malaria.—(Leading Article: Brit. Med. Jour., 26-8-1972).

Recent reports on the treatment of malaria by tetracycline indicate that some therapeutic conclusions reached 20 years ago may be revised in new circumstances. A field trial carried out in Thailand where chloroquine-resistant *falciparum* malaria is fairly common, indicates that combination of quinine and tetracycline produced a radical cure in 97% of the patients, while a 'standards' three days' treatment with quinine and chloroquine was successful in only 42% of cases.

Attempts to assess the value of antibiotics for treatment of malaria go back to the 1950s, when, after animal experiments showed that chlortetracycline had some antimalarial effect, a trial of this compound in 10 volunteers infected with *Plasmodium vivax* gave evidence of a slow but definite therapeutic action. This was not unexpected since many antibiotics inhibit the synthesis of protein or nucleic acid. While such observations extended still further the wide spectrum of activity of tetracyclines, the general opinion was that "to rely on antibiotics for the treatment of *P. falciparum* infections might reasonably be held to be serious malpractice and to endanger the life of the patient. But during the past five years the problem of resistance of *P. falciparum* to 4-aminoquinolines, among which chloroquine is the most useful and reliable compound, has led to the re-examination of the value of many drugs previously rejected because of their less satisfactory performance. An excellent example of this therapeutic "court of appeal" is provided by the sulphones and sulphonamides given together with

antifolates (pyrimethamine or trimethoprim). Their utility in cases of chloroquine-resistant *falciparum* infection is now fully recognized.

When it comes to tetracyclines, the American authors, who are concerned with a large number of cases of *falciparum* malaria in the U.S. forces in South-East Asia, are satisfied with the early results of combined treatment with quinine and tetracycline. They recognize that the duration of this treatment (10 days) and its slow action represent shortcomings. It could be argued that the quinine-chloroquine regimen might have been given a fairer chance if its duration had been extended to at least one week.

Nevertheless, the confirmation of antimalarial action of tetracycline is of considerable interest, though the side-effects of this group of antibiotics can be troublesome in children, in late pregnancy and whenever the renal function is impaired. Further trials with the older tetracyclines (oxytetracycline, chlortetracycline, demethylchlortetracycline) as well as with some newer congeners of this group (pyrrolidinomethyl tetracycline, tetracycline-L-methylenelysine, 6, methylene oxytetracycline, and others) may provide fuller data for the assessment of their place among antimalarial drugs. Meanwhile it may be useful to remember that resistance of *P. falciparum* to 4-aminoquinolines is still limited to a relatively small part of the tropical world and that even in these areas many cases of malaria respond to chloroquine or to sulphones and sulphonamides combined with antifolate compounds. Further research on the chemotherapy of malaria is imperative, as the gaps in our armoury of antiparasitic drugs are now becoming increasingly evident.

REVIEWS OF BOOKS

Human Heredity and Birth Defects
—By Mr. E. PETER VOLPE, Pp. 166.
Published by: M/s. Willey Eastern Private Ltd., J.41, South Extension 1, New Delhi-49.

[Price : Rs. 10-50]

A deformed child is delivered every 30 seconds into the World. How and why it happens, and how it can be prevented and avoided forms the theme of this book. The author explains how scientists today are creating methods

that will spare future generations such agonies like the much dreaded Rh disease, which till recently was a baffling infant killer. He also tells how they are seeking and finding means to control sex prenatally—i.e., to predetermine the sex of the unborn child. The effect of drugs on the human embryo is also discussed—in the context of the Thalidomide tragedy of recent times.

This book is an eminently readable, accurate overview of one of the most exciting areas of biology.

T.N.S. BAGHAVACHARI.

ABO Haemolytic Disease of the New-born—By Dr. E. R. GOLD, M.D., and Dr. N. R. BUTLER, M.D., F.R.C.P., D.O.B. Pages 212. Published by: M/s. John Wright and Sons Ltd., 42-44, Triangle West, Bristol, England BS8, 1EX.

[Price: £ 4.00]

This is a well written book on a small but complicated and important subject, Haemolytic disease of the new-born (HDN) with special reference to ABO incompatibility. The authors have dealt with diagnostic tests and their interpretations in an elaborate manner which will be definitely useful to the serologists. Historical aspects and haemolytic disease in animals will be of much interest to the readers and it is surprising to note that this disease has been discussed even so early as the 18th century.

In our country ABO incompatibility is supposed to be more common because of comparatively less incidence of Rh incompatibility. So we require much research work on ABO HDN in our country and this book will be an asset to our teaching institution libraries, where such research projects should be undertaken. One would have been very happy if more details had been given in the technique of exchange transfusion which is essential from the practical point of view and one feels that it would have made the chapter on treatment complete. Use of phenobarbitone and phototherapy in the treatment of kernicterus has been very well dealt with. The subjects of

infertility, abortion and foetal wastages in the chapter on interaction between the mother and foetus will be of much use to obstetricians and paediatricians.

As the authors have rightly mentioned, the physiology and biochemistry of jaundice is essential in a book like this and they have been clearly discussed with simple illustrations.

Each chapter has an addendum which gives briefly the recent work done in that particular field and it keeps the reader abreast with latest developments. A large number of references at the end runs to about 30 pages and these references themselves speak of the enormous amount of research work done by the authors in the field of HDN.

This book will be useful to serologists, obstetricians and paediatricians and essential for all medical college libraries.

U. RAMA RAO, M.B., B.S., D.O.B.

Computers in Medicine—(Proceedings of Second Symposium held at Blackburn College of Technology and Design)—By J. ROSE, M.Sc., Ph.D., F.R.I.C., F.I.L., M.B.I.M., M. Inst. C.Sc., Director General, World Organization of General Systems and Cybernetics, Pp 166; Published by: M/s. John Wright & Sons Ltd., 42-44, Triangle West, Bristol, England BS8, 1EX.

This book is a record of the proceedings, lectures and discussions on the Second International Symposium on 'Computers in Medicine' held in March 1971 at the Blackburn College of Technology and Design presided over by the Lord Rosenheim, President of the Royal College of Physicians. Besides the opening and closing addresses, this book is divided into four parts. The first part deals with a general survey of computer-based information systems in general practice and in hospitals, while the three papers in the second part draw heavily on practical applications of computers to hospital case and clinical records. In the third part, the topics considered are applications in electrocardiography patient monitoring, X-ray diagnosis and clinical biochemistry. The fourth

part deals with the use of computers in hospital administration and in making medical examinations. Of particular value are the discussions at the end of the lectures and the panel discussions at the end of the day's work. The emphasis is on critical appraisal of the realities of computer usage in medicine without the spurious and extravagant claims made by some in regard to the so-called 'omnipotence' of the machine.

In most medical applications the computer plays the part of a tool like the microscope. Once the appropriate techniques have been developed the computer may well have as fundamental an effect on medicine as the microscope has in pathology. The first symposium held in 1968 was concerned with methodology and the problems of areas where computers could be used, the present event dealt with the practical uses and the general theme was how to use these machines for better medical services and more effective utilization of resources. Above all, the emphasis is on a critical appraisal of the art.

The chapters on the use of computers in hospital administration and in the assessment of medical students contain very useful and most up-to-date techniques in computing and should prove immensely useful to professors of medicine.

T. N. S. BAGHAVACHARI.

Selected Topics in Experimental Pharmacology—By U. K. SHETH, N. K. DADKAR and USHA G. KAMAT, Pp. 227, Published by: The Kothari Book Dept., Parel, Bombay (India).

[Price: Rs. 40/-]

The authors who are experienced members of the staff of the department of Pharmacology in the Seth G.S. Medical College, Bombay, have utilised the material which they used in training

post-graduate students over the last 15 years in preparing this text book for the use and reference of Post-graduate students. They have described selected topics in experimental pharmacology, which would meet with the curricular requirements of the post-graduates. Techniques in biochemical pharmacology, use of radioactive isotopes, use of highly sophisticated techniques involving polygraphs, transducers and oscilloscopic recording are not however, included because only a few colleges possess the necessary equipment for carrying out such elaborate techniques. So, they have limited their field techniques which could be carried out by the Post-graduates in the pharmacological department of most of the medical colleges in India for whom this book is primarily intended.

Each chapter covers a very brief theoretical background and gives details of experimental techniques. This is followed by practical exercises which the students can carry out and compare their results with those illustrated. This will help in establishing techniques with known drugs so that one can then handle problems using these techniques more confidently. For further detailed work references to original techniques have been indicated. The appendices at the end of the book cover the subjects of anaesthesia in animals, elementary statistics, and certain important details about perfusing solutions.

The illustrations and line drawings must be very helpful in understanding the complicated processes involved in the testing of drugs used in pharmacology relating to the various human systems, e.g., cardiovascular, respiratory, etc. The principles of drug action and bio-assay are clearly described so as to be easily understood by the medical students.

T.N.S. BAGHAVACHARI.

BOOKS RECEIVED

Essentials of Medicine—Section VII on Diseases of the Nervous System, Pp. 120, Dr. O. K. Parikh, Medical Publications, 6, Owners Court, Near Strand Cinema, Colaba, Bombay-6. Price: Rs. 6/-

Age Changes in the Neuromuscular System—By Mr. E. Gutmann and Mr. V. Hanzlikova Pp. 195, M/s. John Wright and Sons Ltd., 42-44, Triangle West, Bristol, England, BS8 1EX. [Price: £ 6.50]

NEWS AND NOTES

**Shah's Plea to Combat Blindness
Among Children**

The Governor, Mr. K. K. Shah, Feb. 14 at Vellore, underlined the need for evolving a national programme of health inspection in educational institutions to combat blindness among children. Blindness among children, was due to malnutrition he added.

Mr. Shah inaugurated the 300th eye camp organised in connection with the silver jubilee of the Schell Mobile Eye Hospital attached to the Christian Medical College Hospital at Vellore.

The Governor said a plan should be evolved to medically examine every child below five for the purpose of making up the nutritional deficiency.

Dr. M. A. Thangaraj, Chairman of the governing council of the CMC Hospital, who presided, pleaded for liberal contribution from the public for expanding the buildings of the Schell Eye Hospital. Dr. Anna Thomas, head of the mobile hospital, in his report on the work of the mobile unit stressed the need for a

comprehensive programme to help starving children in the country and thus stop or limit the cases of preventable blindness.—(*Hindu*).

Vaccine For Flu

A French medical research team has claimed that it has discovered a vaccine against influenza which will be effective against all strains of the disease.

Production of the revolutionary vaccine has already started and it will be available in France shortly, said the researchers at the Pasteur Institute in Paris.

If claims made for the vaccine prove true, it could mean a cure for one of the world's most common ailments which strikes hundreds of millions of people every year.

Professor Claude Hannoun, who heads the Pasteur research team, told reporters that the new vaccine differs from all others in that it anticipates future strains of influenza.

"It is effective not only against current strains but against those that will break out over the next few years", he explained.—(*Hindu*, 13-2-1973).

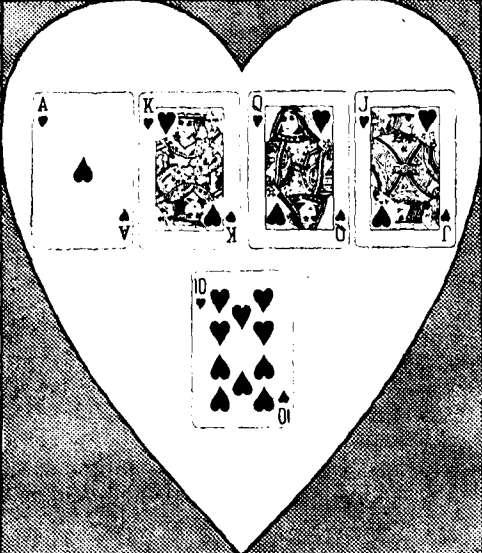
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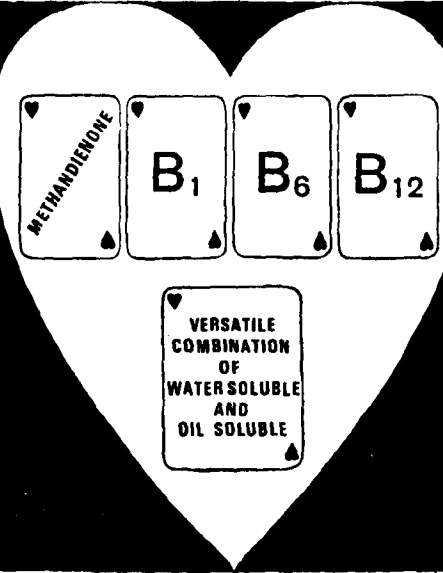
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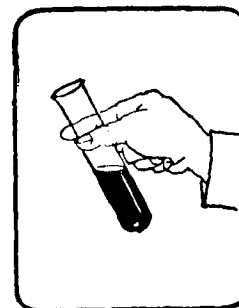
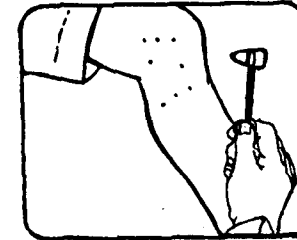
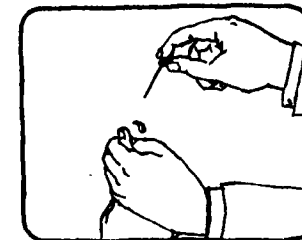
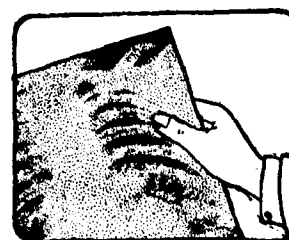
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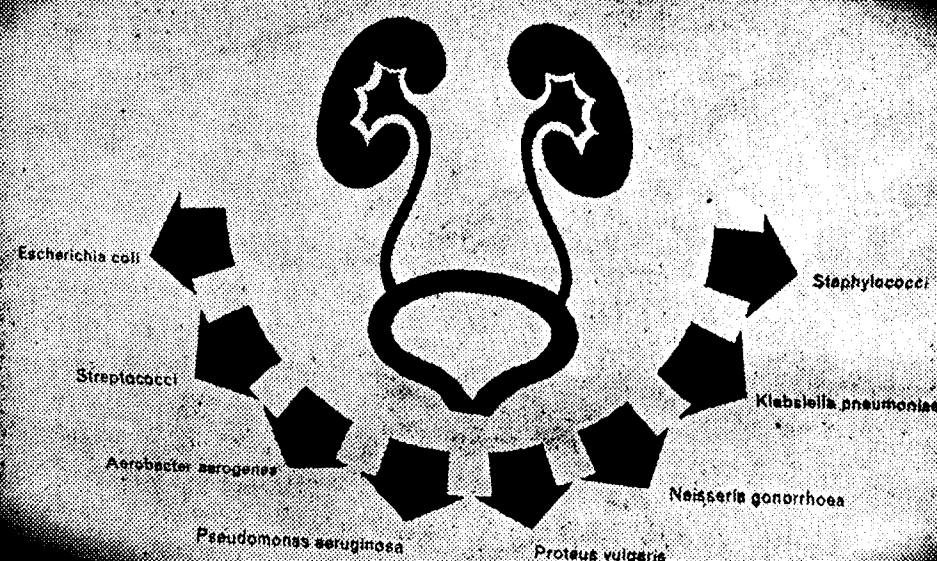
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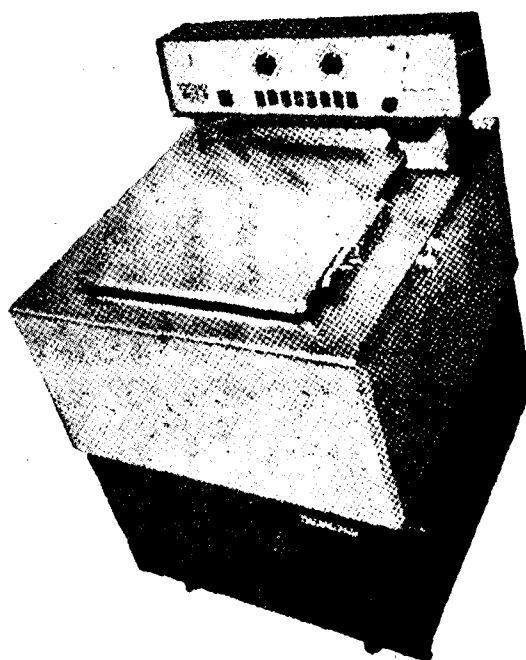
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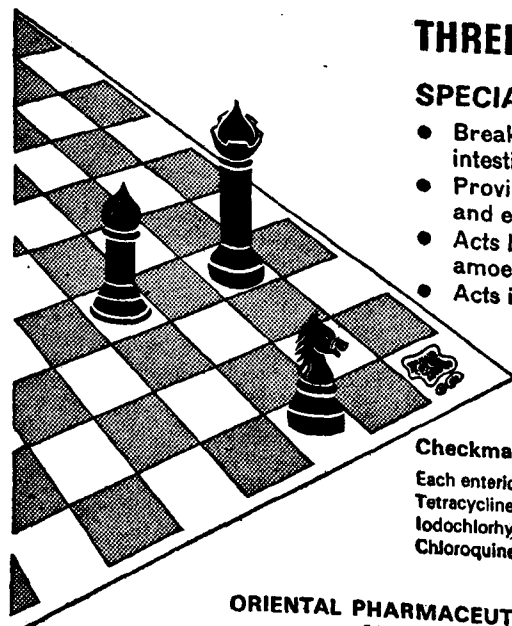
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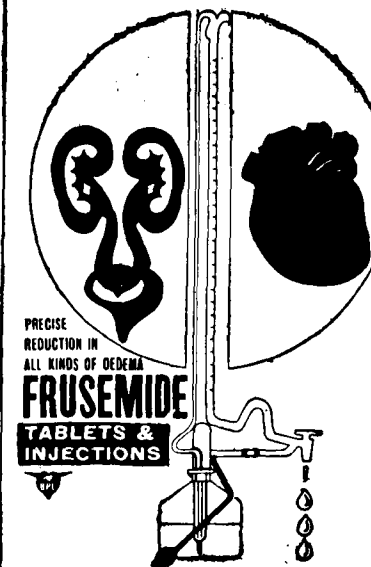
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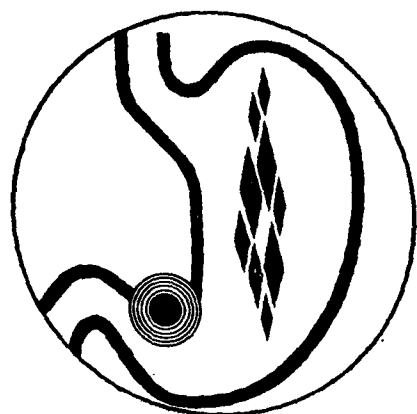
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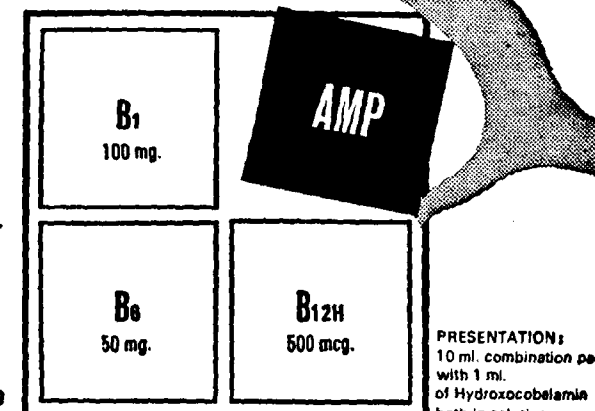
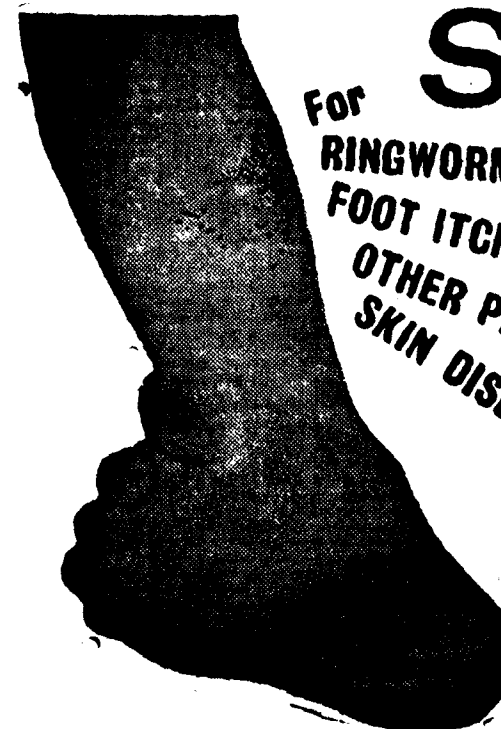
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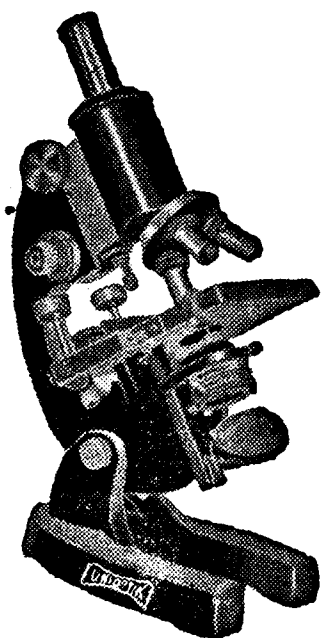
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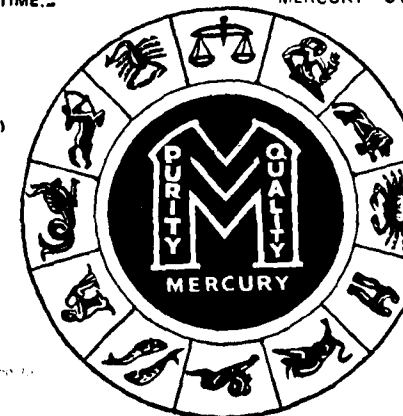
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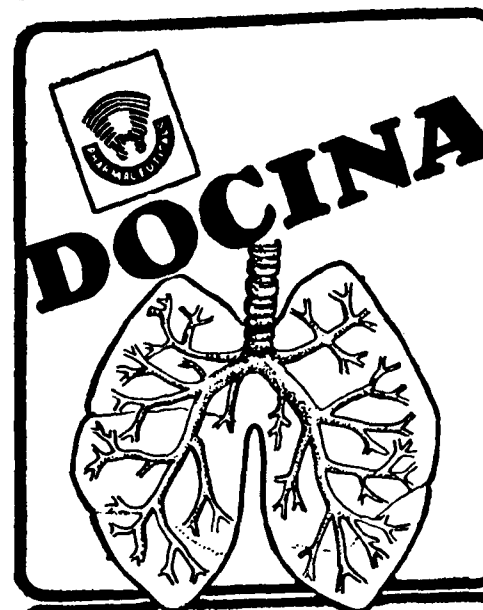
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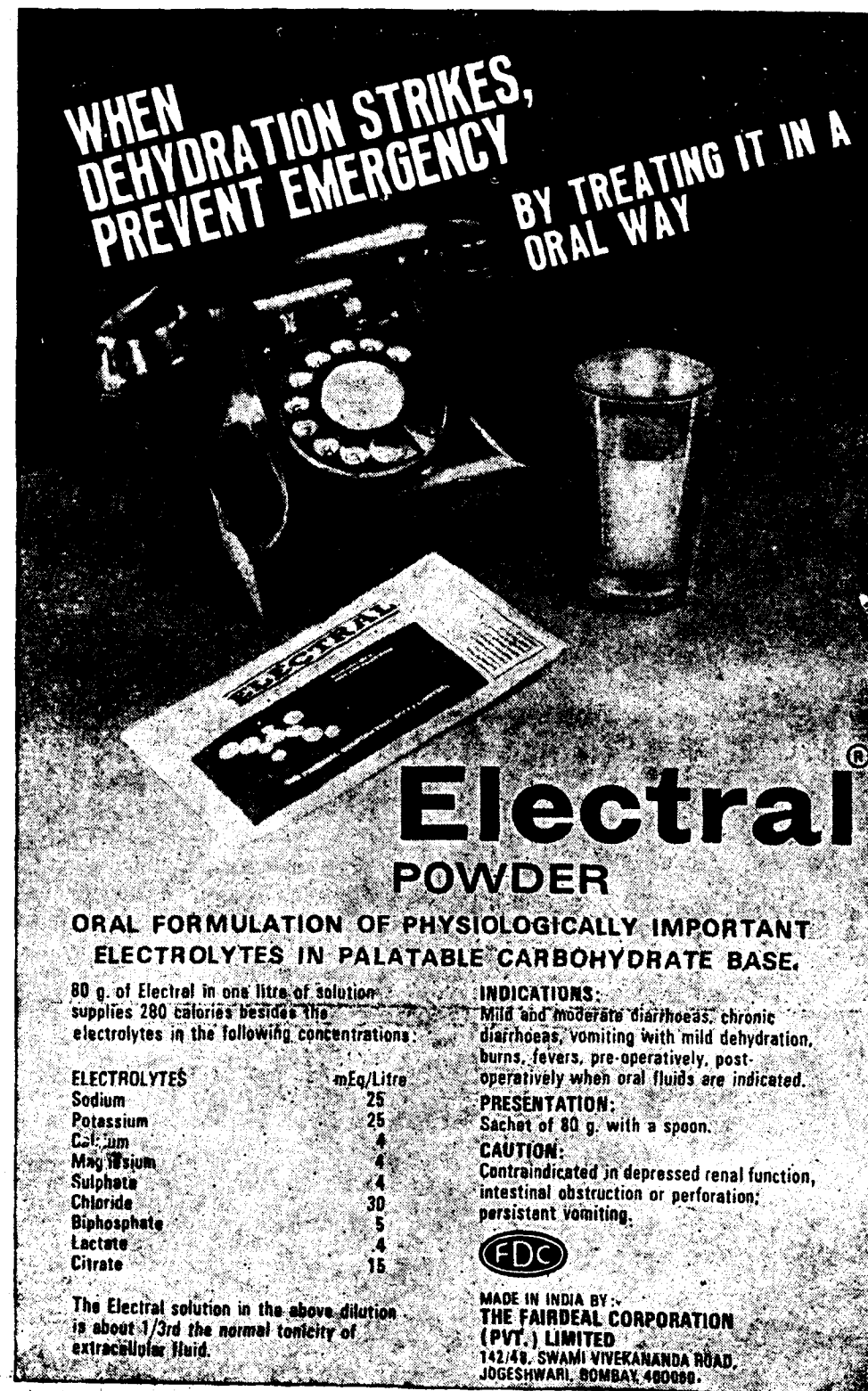
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