MEDICO-SURGICAL SUGGESTIONS

Vol. XVI. APRIL 1947. No. 4.

MEDICO-SURGICAL SUGGESTIONS
(Established 1932.)

VOL. XVI APRIL 1947 NO. 4

RECENT ADVANCES IN THE TREATMENT OF ACUTE MENINGITIS

(Review of 88 Cases).

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The first published accounts of Acute Meningitis were those of Gaspard Vieusseaux (1805) at Geneva, and L. Danielson and E. Mann, (1806) at Massachusettes. Elisha in North America published a large monograph on the subject in 1811. Weichselbaum discovered in 1817 Meningococcus (Diplococcus Meningitidis intracellularis) as the causative organism in a large number of cases of Acute Meningitis, which may also be caused by Pneumococcus, Staphylococcus and Streptococcus. The clinical picture is generally typical. After an incubation period of 4-5 days, the onset is sudden with headache, fever, malaise and vomiting. There may be dilated pupils and even photophobia. Briefly the signs and symptoms can be divided into 3 stages—1st stage is the carrier stage and may be without symptoms or there may be Tonsillitis, Pharyngitis, Sinusitis or Conjunctivitis; 2nd Stage—patient takes to bed and lies curled up on his side, with knees bent, head extended, with stiffness of the neck. The patient is extremely apathetic and his speech is monosyllabic; 3rd stage—there is bursting headache, chilliness, erratic fever, sometimes delirium and coma. Kernig's sign is present and the C. S. F. is turbid and under tension.

For nearly a century (1805-1905) sedatives and symptomatic treatment were used for this ailment, though since 1885, lumber puncture used to be done with benefit to the patient. Corning first performed in 1885 the intraspinal puncture. Frequent drainage of the spinal canal was the sheet anchor of therapy when no specific treatment was available. Even today, frequent drainage of the spinal canal remains the important part of the treatment. Jochmann, and shortly after him Flexner in 1905, introduced the use of the immune serum in the treatment of Meningococcal Meningitis. The immune serum is generally given intrathecally in daily doses of 30 c. c. or more in adults and the dose may be repeated every 8 or 12 hours, if required. The quantity of fluid injected should always

is less than the fluid taken out. The serum is stopped when the C. S. F. is free from organisms but the lumber drainage is continued until the symptoms disappear and the fluid is normal. If internal hydrocephalus developed due to the obstruction of Foramen of Magendine and Luschka by adhesions, it was sound treatment to introduce the serum in the cisterna Magna by occipito atlantal puncture. Sometimes even intraventricular injection of the immune serum was required. In some cases to counteract the bacteriemia, immune serum used to be injected intravenously in doses of about 300 c. c. Kolmar got favourable results by irrigation with warm saline and better still with modified Ringer's solution. Ethylhydrocuprin, Mercurochrome, Gentian Violet, Acriflavine and Rivanol solutions did not produce satisfactory results. Crawford in 1932, stimulated by the preliminary studies of Kolmar, tried intravenous injections of Colloidol Iodine in daily doses of 20 to 30 c.c and reported favourable results. The introduction of the Salfa-group of drugs marked a great advance in the treatment of this disease. The dosage and routes of administration vary according to the severity and tolerance of the case. Roughly, 1 to 2 grammes are given by mouth to start with and afterwards about a gramme every 2 to 4 hours as indicated. The drug is also given intra-thecally, intravenously and intra-muscularly according to the severity of the case or where it is not tolerated by mouth. This drug has markedly reduced the mortality rate and markedly improved the prognosis. The discovery of Penicillin has revolutionized the treatment giving sure and satisfactory results. Penicillin is generally given in doses of 20 to 40 thousand units to start with and subsequently 20 thousand units every 3 hours intramuscularly. In some cases it is also given intrathecally and intravenously in same doses. The Penicillin is stopped when the signs and symptoms abate and the C. S. F. is clear and not under tension. The mortality rate is practically reduced to nil, recoveries being almost cent per cent.

Out of 88 cases under review, Meningococci were detected in 48 cases, Pneumococci were seen in 18 cases, Streptococci in 7 cases and Staphylococci in one case only. No organisms were found in 14 cases. 8 cases were treated with repeated lumbar drainage and anti-meningococcal serum ; only two recovered

4 cases were treated with repeated lumber drainage and anti-meningococcal serum and intravenous injections of Trypaflavine and Mercurochrome, but only one recovered.

14 cases were treated with adequate doses of Sulpha group of drugs orally and out of these 14 cases, 4 received in addition injections of specific sera Lumber drainage was done in all cases. Out of the 4 treated with Sulfa group of drugs and serum 3 recovered ; and out of the remaining 10 cases treated with only Sulfa drugs, 7 recovered.

62 cases were treated with lumber drainage, Penicillin and Sulfa-drugs ; and all recovered. In most cases Penicillin was given intramuscularly in doses of 40,000 units to start with and subsequently 20,000 units every 3 hours till C. S. F. became clear and normal, and recovery was established.

Brief notes of some significant cases were mentioned but the notes of a case of unusual significance are given below.

12-1-45. Patient aged 28 years, male was admitted with fever 101° F. with headache and pain in the neck and back. Patient was conscious. Rigidity of the neck present. Kernig's sign present. Pupils normal. C. S F. under tension and turbid. Smears showed clumps of pus cells and few Grampositive cocci.

Blood—W. B. C. 14,000 per c. m. P-78, L-22. Negative for M. P.

Patient was given injection of Glucose 50 cc. of 25% ; and put on Penicillin 40,000 units to start with and subsequently 20,000 units intramuscularly every 3 hours. Injection of Nikatamide s. o. s.

13-1. Rigidity. Difficulty in swallowing, Temp. between 100 and 101.6. F.

14-1. Temp. came down to 99° F. but rose in the evening to 103° F. Other signs persist. The same line of treatment continued.

15-1. C. S. F. turbid and under tension 30 c. c. taken out.

Blood—W. B. C. 20,000 per c. mm. P. 85% L. 13%. E. 2% Temp. 103° F.

Other signs persist. General condition low. In addition to Penicillin put on Sulphmerazine tablets 8 tabs. to start with and then 4 tabs. every 4 hours; and injections of Dagenan 1 Gm. with Glucose b.d.

16-1. General condition better. Temp. normal, Rigidity and Kernig's sign less marked. Drowsiness continues. Same treatment continued.

18-1. General improvement continues. C. S. F. turbid but not under tension.

19-1. TPR. normal. No drowsiness. Slight rigidity present. General condition better. Penicillin stopped. Inj. Digenan continued and Sulphmerazine tablets given 4 hourly.

20-1. Conditions same. Sulpmerazine tablets 6 hourly.

21-1. General condition markedly improved. No rigidity of neck. Kernig's sign absent. W. B. C.-5000 per c.m.m. P-39, L-61. omit all drugs.

22-1. General condition good. W. B. C.-2200. per c.m.m. P-31, E-7, L-62. Inj. Sod-Pentuncleotide 20 c.c. every day for 3 days.

23-1. Temp. 101° F. In the morning and 104° F. at night. General condition fair- Blood M. P. absent. W.B.C. 4000 per c.m.m. and P-57, L-31, H.-5%.

24-1. Temp. normal in the morning but 102° F. at night. Condition fair. W. B. C. 6,000, per c.m.m. P.-67, L.-26, E-5, H.-2%. No M. P. found.

25-1. Temp. persisting 102° F : had shivering. Inj. Qninine grs. 6 given. In the evening developed headache and rigidity of the neck. W.B.C. 12-000 per c.m.m. P-71, L. 29% Inj. Dagenan grm. 1 given and put on M. & B. 693 4 tablets to start with and then 2 tabs. 4 hourly.

28-1. TPR. normal. Headache and rigidity of neck less. Condition better. W.B.C. 4 200 per c.m.m. P-46, L.-41, E.-9, H.-4% M. & B. 693 tablets 2, t.d.s.

30-1. W. B. C.-4,200 per c.m.m. P.-62, L.-31, E. 7%. Condition fair. TPR. normal. Slight headache and rigidity persist. M. & B. omitted.

31-1. TPR. normal. Slight headache and rigidity of neck present. C.S.F. hazy but not under tension. Blood W.B.C.-3,800 per c.m.m. P.-51, L.-41, E.-8%. Put on Penicillin 20,000 units I. M. 3 hourly. The specimen of blood showed Microfilaria Loa. Penicillin, 29,000 unit intravenously twice a day.

2-2. TPR. normal. No headache. No rigidity. General condition good.

3-2. Improvement continues. W.B.C. 6,500 per c.m.m. P. 57, L.-40, E. 3% Omit Penicillin and put on Mist. Tonic 1 oz., t.d.s.

4-2. Complaints of headache, pain in the neck and back. Rigidity neck. Kernig's sign present. W. B. C,-7200 per c.mm. P-71, L.-26, E. 3. %. C. S. F. Turbid and under tension. Pus cells †† Stained smears show gram-positive capsulated diplococci (pneumococci). Put on Inj. Penicillin 20,000 units I. M. 3 hourly and Inj. Dagenan 1 grm. I. V. bd. and Sulphmerazine tablets 8 to start with and afterwards 4, 4 hourly.

Temp. 99° F. in the morning and 101o F. in the evening Pt. drowsy.

5-2. Temp. normal. Kernig's sign and rigidity present. Less drowsy. Has nausea and vomitting. W. B. C.-19,000 per c.m.m. P-90, L-8, E-1 & H-1% ENT specialists report. No septic focus. Same treatment continued.

7-2. 99° F. throughout the day. Vomiting less. Other signs persist W. B. C. 16,000 per c.m.m. P.-93, L.-7% same treatment.

8-2. C. S. F. slightly turbid, tension normal. Pus cells+. Very few organisms seen in stained smear. Inj. Penicillin 20,000 units I. T. given once only in addition to the I. M. injections.

9-2. Temp. normal. General condition better. W. B. C.-4,400 per c.m.m. P.-55, L.-43, E.-2% Omit Sulphmerazine. Continue Penicillin.

10-2. C. S. F. slightly turbid, normal tension. Few Pus cells and very few organism seen. W. B. C.—2,800 P-31, L-61, E. 6, H. 2%. General condition improving. Penicillin continued.

12-2. TPR.-normal. No drowsiness. No Kernig's sign no rigidity. C. S. F.-clear and not under tension. Cell count normal. No organisms. Blood-Count :—R. B. C.-4,050,000 per c.m.m. ; Hg. 80% ;

C. 1-1. W. B. C.-3,000 per c.mm. P.-43, L.-48, E-7, H-2%. Microfilaria seen. Inj. Sodium Pennucleotide 10 c.c. every day. Penicillin continued.

13-2. TPR.-normal-General improvement satisfactory. Omit Penicillin.

14-2. W. B. C.-6000. P.-43, L.-41, E-8, H.-2%. Patient put on Tonics and hereafter made an uneventful recovery ; and after a fortnight was discharged completely cured.

Summary :—At present, treatment of Acute Meningitis by lumbar drainage. Sulpha drugs and Penicillin gives best results and in 62 cases treated with this line of treatment all recovered.

It may be mentioned in passing that Inj. Penicillin given I.M., I.V., I.T., and Sulpha drugs given parentarilly and orally have no effect on the micro-filaria.

Subsequent to the lecture a few cases were treated by Inj. of Penicillin-in-oil-and-wax with the same satisfactory results, the procedure adopted being, besides lumbar drainage and Sulpha drugs, to start with Inj. Penicillin 100,000 units in aqueous solution and Inj. Penicillin-in-oil-and-wax-300,000 units was given I. M. afterwards only Inj. Penicillin in Oil and Wax was repeated every 24 hours.

(Abstract of lecture delivered before the Grand College Medical Society on the 20th June 1945).

CAN CLIMATE CURE TUBERCULOSIS?

DR. P. K. SEN, M B., (Cal.), M.D., (Berlin), Ph. D. (Wales).

A few years back there was a strong opinion among the public that a change to a good climate cured tuberculosis. That impression is still there but it is not so strong now, and that is rightly so. Climate alone cannot cure tuberculosis. If that were so, then people living in renowned good climates would never have got the disease. Yet, there is no land to-day, whatever its climate may be, where tuberculosis does not take its toll. At one time the climate of the Alps in the Swiss mountains, Riviera on the sea, Palmary islands in the sea etc., were regarded as ideal climates where one got cured of the disease. Once one was diagnosed as tuberculous and if one could afford the expenses one would run to these places to get the cure. Such search for cure by climatic effect is getting less and less, as people are realising that climate alone cannot cure tuberculosis.

The foregoing remarks do not mean that climate has no effect on the cure of tuberculosis. There are advantages of a good climate. The temperature of such a place is probably more comfortable. There are more hours of sun-shine, less dust, less humidity, less

bustle and noise and better out-look areas. Cool climate increases the metabolism, that is the digestive capacity of the person. Freely moving air also does it. These help a patient to eat and drink well and improve his general health. Comfortable atmosphere generates a feeling of well-being, and good sceneries please the mind. Both have psychological effect and are likely to be factors in the improvement of the general health. Dust will irritate the air passages and produce cough. Dustless atmosphere will not have this effect and therefore by lessening cough will give more rest to lung, a good thing for tuberculosis. All these effects combined will certainly have some beneficial influence on the healing of tuberculosis.

Though these are good effects, there are potentialities in a climate to do harm also. High altitude is stimulant to the body, and an acute case of the disease must not be submitted to this. If a patient suffering from an acute attack of the disease, that is running high temperature and showing in the lung acute exudative lesion, is transferred to a high altitude climate, then he is likely to do worse than in the plains. An old and debilitated man, and a person with bronchitis or bronchiolitis should not go up to a high altitude for the treatment of tuberculosis. A patient with some complications like diabetes or laryngeal tuberculosis should be careful in choosing a high altitude for his treatment of tuberculosis. A patient having acute disease should also not go the sea climate or to the desert climate. In choosing a climate for a patient there are many considerations and these can only be done by the medical man versed in the subject. If such consultations are not made, harm may befall the patient.

Whatever may be the good or bad effect of the climate it is the opinion of most of the authorities on the subject that climate plays very little part on the cure of tuberculosis. Proper medical care is the most important thing in its cure. A place where this is lacking should never be chosen. There are many factors which help in the cure of tuberculosis, *e.g.*, good food, better and proper housing, mental and bodily rest etc. Medical care is more important than anything else and climate is probably the least important amongst them all. The glorious reputation of the Swiss sanatoria is definitely dwindling away as better medical measures are available now. They had their time when collapse therapy was unknown and the so-called sanatorium regime was not perfected to the extent as it is to-day. At that time cure of tuberculosis was judged by the increase in weight and the feeling of well-being of the patient. Good climate does both ideally. But modern knowledge, specially after the discovery of XRay, has abundantly shown that these criteria of the cure of tuberculosis are not good enough. In many cases they really do harm by lulling the patient to a false sense of security. The disease may be as active as before but a patient may get rid of

the fever due to rest and may increase in weight by abundant good food as is generaliy supplied in a Swiss sanatorium and may feel quite well because of the stimulating effect of the climate. What happens to these kinds of patients is that when they come down to the normal life or into the normal surrounding of his home a relapse becomes inevitable. In fact a very great percentage of such cases did relapse on coming back home, and a relapse is generally worse than the initial disease.

To-day we have better methods to assess the cure. It requires thorough and repeated examination of the sputum and blood, and of the chest by X'Ray. By such assessment, it has been abundantly shown that the disease can be arrested and ultimately cured in any climate. The cure is at the door step of everybody, provided he is judiciously treated for the disease and he need not go to expensive climatic changes. As the treatment of tuberculosis is fairly long in an average case, as he has to live a restricted life for a long time, it is probably more useful to go for a change of climate when the disease has been arrested and the limitations of his life have been slackened to a certain extent. It is then only that he can enjoy the sceneries better and "pick up" quicker. This change need not be too long.

What has been said before does not imply that tuberculosis can not be cured in a good climate. If there is good medical treatment available in a good climate, then it is all right and tuberculosis can be cured there. This is the reason why the sanatoria are not banking on climate alone but have introduced in it all the modern methods of treatment. The sanatorium superintendents also know that the main curative factor in the cure of tuberculosis is not the climate, but the efficiency of the medical treatment available at his place. I am putting so much emphasis on this because it is true and not generally recognised by the public. In my short experience I have seen many cases who went for a change as soon as the disease was diagnosed, lived a life as an ordinary changer does or even had lived a restricted life, felt well for the time being and suddenly was in the grip of worse disease while in the place of the change or soon after coming back. In some cases gross indiscretions had been done, as for example climbing a hill etc., which was the cause of the flaring up of the disease. It must be realised that the temptations for doing such a thing is much more in such a place, unless the patient is under the strict control of the doctor or a guardian. The feeling of well-being dupes them at first and they become less attentive to the rest regime; even some have thought that they have been cured because they had nothing to complain of. The stimulating effect of the climate naturally misled them and made them put their feet on the false track. That is not all. I have studied such cases from the history and from the X'Ray

pictures taken before going to the change. In most such cases the time was opportune to institute a kind of treatment which would have made his case very favourable for complete recovery. That treatment was not accepted but a change of climate was preferred. When they came back the stage for simpler treatment was long passed and more complicated and dangerous treatment had to be instituted to have any hope of recovery. This is not only more time and money-consuming but even when good results are obtained such treatment leaves the patient in greater disability than what would have been if the simpler modes of treatment were accepted first. Naturally, of course the ultimate chance of recovery also becomes less.

What I intend to convey here is not that a change to a good climate is bad, but to destroy the misconception that climate alone will cure tuberculosis. This mis-conception or this fad had, to my mind, done more harm to the patient than anything else in the treatment of tuberculosis. This must be abolished from the public mind. Disastrous results caused by such fad is becoming evident daily even to non-medical but intelligent persons and I wish fervently that a day will come soon when it will be evident to everybody.

It may rightly be asked that good medical care in a good climate will have some advantage over such treatment conducted in an ordinary climate. Why should not one take that advantage if it is available? In some cases such an advantage may be appreciable and such cases should take advantage of it. In many cases this advantage is not of importance and they may have treatment in any climate with almost the same effect. There are, of course, cases for whom a stimulating climate is not only good but may cause harm. Such cases should better refrain from going for a climatic change. Some authorities have a very strong opinion that the patient should have his treatment conducted in or near about the place where he lives and works. Their reason for saying so is that if an arrest of the disease is made to occur in another climate, then the patient runs a greater chance of relapse of the disease on coming back to his own climate. The physiological effort to acclimatise him again to the ordinary climate causes enough strain on the lung to increase the chance of the flare-up of the disease that has been arrested. There is force in this argument and there is some evidence that it is true to a certain extent. To me the strength of this argument depends mainly on the nature of the case. All cases may not have this strain to a sufficient extent to cause this flare-up.

In my opinion *what matters most to a tuberculous patient is good medical treatment.* Wherever it is available he may go there. If equally good treatment is available in the place where the patient lives and works he should ordinarily have himself treated there. It

has many advantages. When the disease is arrested by adequate treatment and the regime of his life has been regulated nicely he may go out for a change to break the staleness of long treatment in one place and refresh both his mind and body. He must also remember that he should obey the same regime in the place as at home, unless otherwise instructed by his physician. He must know that it would be a great folly to wrench as much out of a holiday as he used to do when he was well.

(Journal of the Bengal Tuberculosis Assn., Nov. 1946.)

Extract.

PENICILLIN IN ESTABLISHED SURGICAL INFECTIONS.

Melency reviews the results obtained with pencillin in surgical infections under the direction of the Committee on Chemotherapy of the National Research Council. There were 744 cases with sufficiently complete data. Penicillin controls the disease either alone or as aid to surgery in about two thirds of surgical infections. It is most effective in cases of furuncle, cellulitis, mastoiditis, carbuncle, suppurative arthrities, lung abscess, superficial abscess, brain abscess, and esteomyelitis. It is moderately successful in cases of deep abscess, thrombophlebitis, sinusitie infected soft part wounds, infected operative wounds, otitis media, infected compound fractures and ulcer of the skin. It is not so successful in cases of empyema, infected burns, gas gangrene, actinomycosis, gangrene of the skin, miscellaneous surgical infections, post-operative pneumonia, peritoneal abscess and diffiuse peritonitis. It is more successful in the treatment acute than of chronic infections and if given early rather than late. It is often effective when the sulfonamides have failed. Many localized surgical infections can be successfully treated with local injection of pencillin solution or local application of penicillin in ointment form. "Adequate dosage" may vary from a few thousand to several million units. Penicillin is not as successful in mixed infections as in those caused by a pure culture of susceptible organism. Clostridium welchi is so often found in a mixed culture with other intestinal organisms that clinical cases of gas gangrene often fail to respond to penicillin. An analysis of the cases in which pencillin had no appreciable effect revealed that in a large proportion of these cases the cultures showed organisms capable of producing penicillinase. Other imporatnt causes of failure were resistant strains of staphy loococci or streptococci, too little or too late administration of penicillin, associated tuberculosis or diabetes with arteriosclerosis and too conservative surgery. In the septi-

cæmia cases the results were better in those due to the hemolytic streptococcus than in those due to the staphylococcus probably because in the latter type the infection more quickly produces deep metastatic abscesses and vegetation on the heart valves. Four points warrant special emphasis: 1. Penicillin is a valuable adjunct to surgery in surgical infections, and in many instances it can obviate surgery, but it is not a panacea. 2. Local application of pencilin is effective in localized surgical infections if the organisms are susceptible. 3. "Adequate dosage" is the amount which will bring the infection under control and it cannot be determined before the beginning of treatment. 4. A careful and complete bacteriologic analysis is essential to obtain the best results.—*J.A.M.A.*

Medical Notes & News.

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S.F. 259A-6—1,00,000—30-1-84.

Regd. No. M. 2853.

Edited and Published by Dr. P.R. Venkappaya, at 2/337, Mint Street, Madras.
Printed by Mr. S. Sundaresan, L.P.T, for the C.C.P. Works, Ltd., 1/17, Mount Rd., Madras.

MEDICO-SURGICAL SUGGESTIONS

Vol. XVI. MAY 1947. No. 5.

MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVI MAY 1947 NO. 5

CHRYSOTHERAPY IN PULMONARY TUBERCULOSIS

BY RAJINDAR SINGH, L.S.M.F., (Pb.)

M.O., Dalmia Cement Ltd., Karachi.

Introduction.—Gold has been employed as a therapeutic agent since ancient times. It still constitutes an important ingredient of many tonics in the *Ayurvedic* and *Unani* systems of Medicine. Though the records show that it was used in the treatment of pulmonary tuberculosis as early as 1526 A.D., by PARACELSUS and later by several other workers, yet the writings of these early workers do not advance our knowledge of chrysotherapy to any appreciable extent.

In 1890 KOCH, working with gold-potassium-cyanide, demonstrated the bacteriostatic action of this salt in solution, on cultures of tubercle bacilli, following which a few cases of lupus were successfully treated with it. The interest aroused by these early researches led to the introduction of a number of gold preparations, organic, and inorganic, by various scientists. Thus Krysolgan, a complex organic compound of gold, was introduced by FELDT in 1916. In 1924, a Danish scientist, MOLLGAARD, published the results of his researches on gold-sodium-thiosulphate in chemotherapy of tuberculosis, and afterwards it was used clinically by some other eminent doctors, whose work aroused a world-wide interest. Since then gold has been more extensively used in the treatment of tuberculosis and other diseases and has found a large number of advocates in Europe, though some eminent American authorities like GOLDBERG and FISHBERG are against its use. The frequent toxic effects of gold treatment in early trials were, to a great extent, due to the employment of too large doses by over-enthusiastic workers, and these are uncommon nowadays.

Pharmacology.—When a soluble gold salt is administered orally, only minute traces are absorbed. Following parenteral administration of a suitable compound, absorption is almost complete. Excretion is slow and the metal exerts a cumulative action. Excretion takes place mainly through kidneys, and to a smaller extent through the intestines (and possibly through bronchial mucous membrane also) and in so doing may cause nephritis or ulceration of the bowels.

The amount excreted increases as larger doses are given but not in direct proportion. The excretion is greatest on the day of injection, and steadily decreases on the succeeding days, but continues for a long period. The absorbed metal is readily taken up by the R.E.S., particularly in the liver and spleen. It is also found in kidneys, heart, lungs, pancreas, skin, even C.S.F. and brain.

After intravenous administration, there occurs a fall in blood-pressure, probably as a result of dilatation of mesenteric blood vessels.

The effact of a dilute solution of some of the gold salts on cultures of tubercle bacilli is bacteriostatic, rather than bactericidal, and this bacteriostatic action is impaired by the addition of body fluids.

Mode of action in pulmonary tuberculosis.—The manner in which gold acts in tuberculosis is yet a mystery. The following hypotheses, however, are put forth to explain the mode of action :—

(1) *Direct or specific action theory* :—According to this theory, it is claimed that gold penetrates the fatty capsule of the tubercle bacillus and destroys its protoplasm by a process of lysis. That gold may reach the tubercles when injected, does not seem to be impossible, because the older conception of the tubercle being avascular is no longer held to be correct. Dr. JAFFE in his chapter on "The Pathology of Pulmonary Tuberculosis" in "Goldberg's Clinical Tuberculosis", states that fine capillaries extend between the epitheloid cells of the tubercle Further it has been shown that potassium iodide and dye-stuffs like trypan red and methylene blue (De Witt) are capable of penetrating the tuberculous foci, when injected into an animal. The next question is that gold having reached in the vicinity of tubercle bacillus, how it overcomes the next barrier, *viz*, the resistant covering of the baccillus. In 1942, Doctors KIME and KRAJIAN studied the morphological changes in the bacillus in patients responding favourably to gold treatment. They observed that the bacillus showed lytic changes in those cases and finally disappeared, similar to "Pfeiffer Phenomenon." "The unanimity of their occurance (lytic changes)," they write, "however, on every slide and on every day, is conclusive that these changes are due to gold." They further write, "Apparently, gold first attacks and damages the waxy substance covering and entering into the substance of the bacillus, in a manner similar to that whereby a polished steel blade left wet and exposed to the air, eats away with rust. When thus injured the bacillus is attacked by the leucocytes, is phagocytosed and otherwise lysed until it is completely destroyed."

Experiments on the cultures of the tubercle bacilli, however, furnish no evidence to show that gold can kill the bacilli in vitro or in vivo. Certain gold compounds do inhibit the growth of the bacilli in vitro, but this in vitro activity is minimised in the presence of body fluids and tissues. Further, it has been demonstrated that the growth of the tubercle bacilli in the plasma of patients, drawn after injecting Sanocrysin is just the same as in the plasma drawn before the dose. So whether or not the metal acts at the focus of infection, the action seems to be an indirect one.

(2) *R. E. S. stimulation theory* :—It is an established fact that following the administration of gold, it is picked up by the cells of the reticulo-endothelial system, from where it is slowly released. It has been suggested that gold exerts its curative action by virtue of stimulating the cells of the R. E. S., which are endowed with a great phagocytic power. In support of this theory, FELDT has shown in animal experiments, that the action of Solganol is minimised by splenectomy and injection of substances which tend to block the R. E. S. In therapeutic doses gold salts tend to produce lymphocytosis. This theory seems to be a more probable one.

(3) *Catalytic acceleration theory* :—It has been observed that in cases benefitting under chrysotherapy, the lesions heal in a slow spontaneous manner, and it has been suggested that gold causes catalytic acceleration of the process of natural repair.

There are some doctors who believe that any improvement under chrysotherapy is purely psychological in origin, or that the case under treatment might have been one of "benign exudative tuberculosis", in which spontaneous cure takes place even in the absence of special treatment.

Value of gold in pulmonary tuberculosis.—Although there has been considerable conflict of opinion in the past regarding the therapeutic efficacy of gold, now "there appears to be an almost general agreement that gold therapy is valuable if used conservatively and is employed only in those types of cases, in which by wide experience, it has been shown to evidence response. . . . . gold salts are valuable adjuvants to collapse therapy, particularly in preventing spread to the contralateral lung."

Improvement manifests itself in three ways, *viz.*,

(1) *Clinically* the general condition of the patient improves (in some very promptly), with increase in weight and appetite, reduction of temperature, cough and sputum, and diminution or disappearance of ascultatory signs.

(2) *Radiologically* tuberculous infiltration slowly disappears. Gold increases tendency to fibrosis and may effect contraction of cavities in exceptional cases. Radiological changes may not appear till some time has elapsed after a course of chrysotherapy has brought the desired clinical improvement.

(3) *Favourable laboratary signs* :—The sputum becomes negative and the blood sedimentation rate may come down to normal and continue to be normal.

Indications.—Generally the more acute types of cases respond best to chrysotherapy. Gold is of little use in chronic proliferative cases or cases with fairly large cavities. The following types of early or moderately advanced exudative tuberculosis in which marked cachexia or anæmia have not developed, are suitable for chrysotherapy provided no contra-indication co-exists :—

(1) Cases of unilateral disease in which general measures alone having been thought to be or found to be inadequate (*e.g.*, in acute spread of the disease), collapse therapy is instituted, but the same has not been successfully achieved due to the presence of adhesions.

(2) Unilateral cases in which the disease is spreading steadily or desired improvement is not effected, in spite of maintaining proper collapse of the diseased lung in addition to conservative treatment.

(3) Cases of early bilateral tuberculosis, in which the disease continues to progress in spite of sanatorium treatment, A. P. being used for the worse lung, along with chrysotherapy. (If the worse lung cannot be properly collapsed due to adhesions, gold may still be helpful.)

(4) Cases in which the disease spreads to the opposite lung (a) as a late event and to a slight extent, and (b) during the course of A. P. (double A. P. is generally a failure in the end).

(5) Cases which respond to general treatment, but in which the sputum continues to be positive.

To these may be added "those cases of chronic fibroid tuberculosis which begin to show an acute exacerbation."

Contra-indications:—1. *Absolute*: Gross hepatic, renal or cardiac disease; severe diabetes; marked leucopenia or thrombocytopenia; cases with high temperature and, or marked cachexia and anæmia; co-existing pronounced intestinal tuberculosis; hæmorrhagic diathesis; severe diabetes; previous history of exfoliative dermatitis. Simultaneous arseno-therapy is contra-indicated. Some of the toxic reactions (described later) that may appear during chrysotherapy call for discontinuation of gold, while others necessitate modification of the course.

2. *Relative*:—Exercise caution in cases with chronic alcoholism marked hypertension, history of dermatoses (except psoriasis), pregnancy, slight liver deficiency and slight kidney dysfunction.

Healthy liver has a great detoxicating power, and toxic reactions due to gold are more prone to occur if hepatic damage exists. Excretion of gold takes place mainly through kidneys, and any pre-existing renal damage however slight (*e.g.*, lowered function manifested by traces of albumin, polyuria, low specific gravity with normal intake of fluids) is likely to increase.

In pregnancy gold treatment of tuberculosis may be helpful in preventing postpartum exacerbation, but smaller doses should be employed, as pregnancy taxes the detoxicating and excretory functions of the body. Administration of gold should be avoided during and immediately preceding menses.

Administration:—*Channels of administration*: Oral administration has no Allopathic advocates, but this is the only route by which the metal is given by the *Unani* and *Ayurvedic* physicians. They administer it in the form of *Kushtas* and *Bhasmas* which, they believe, are easily absorbed from the alimentary tract. I have often used an Ayurvedic gold preparation named *Vasant Malti* (Zandu) in tuberculosis patients with gratifying results. I administer it as a single daily dose of ¼ to ½ rati with butter in the morning. Whether the improvement brought about by supplementing the usual treatment with this preparation, is due to its gold content or to other constituents, I can't say.

Allopathically gold is administered by injection only, either intramuscular or intravenous, depending upon the preparation used.

(*a*) *Intramuscular route*:—All oily suspensions, colloidal preparations and some of the aqueous preparations (*e.g.*, Myocrisin aqueous) are administered by this route. The injection is made deep into the upper and outer quadrant of the buttock. Intramuscular administration has some obvious advantages. The technique is simple and can be easily employed in children and in those adults in whom a suitable vein cannot be found. Immediate reactions such as shock, nausea and vomiting that sometimes follow intravenous administration, are practically unknown. Inflammatory reaction of perivascular tissues due to accidental leakage of the drug during intravenous injection, is out of question here.

(*b*) *Intravenous route* is employed in the case of Sanocrysin and Crisalbine. The solution should be freshly prepared and isotonic, and injected slowly. Myocrisin aqueous is also sometimes given intravenously. Never inject immediately after meal. Ambulatory patients should be in bed for 3 or 4 hours after the injection. It has been generally supposed that in pulmonary tuberculosis intravenous administration gives better results than intramuscular administration, but such a belief is erroneous.

Preparation used and dosage:—Three types of preparations are generally used:—

(*a*) *Aqueous—e.g.*, Crisalbine, Sanocrysin, Myocrisin aqueous. These are generally preferred to other types of preparations nowadays. These are administered intravenously but intramuscular route is preferred in case of Myocrisin.

(*b*) *Colloidal—e.g.*, Colloidal gold sulphide, Collosal Aurocalcium, Auroprotasin. Their absorption is uncertain.

(c) *Oily suspensions*—These are Myocrisin in oil, Solgœnol B Oleosum, Parmanil. These should be warmed up and injected intramuscularly through a heated syringe fitted with a wide bored needle. These were introduced with a view to avoid local reaction which sometimes follows the injection of aqueous preparations and to minimise general toxic reactions by prolonging the period of absorption and excretion of the metal when injected in this form. But in actual practice, the chances of cumulative poisoning are more with oily than with aqueous preparations, because toxic effects may not be observed until several foci have formed, from which absorption is still going on and cannot be stopped.

No fixed scheme of dosage can be laid down. "Gold should never be given by rule-of-thumb methods, but must be administered with due regard to the reactions which may occur."—DUNLOP. The dose should be increased gradually and any reaction from the previous dose should be allowed to subside.

Commercial products :—Of these there are not many available these days.

Myocrisin is Sodium Aurothiomalate with a gold content of about 45 per cent and occurring as pale yellowish needles, freely soluble in water. It is available in two forms, *viz.*, aqueous and oily, in ampoules of 0·01, 0·02, 0·05, 0·10, 0·20, 0·30 and 0.50 gramme. It is most suitable for intramuscular administration, though the aqueous form can be given intravenously if well diluted.

It is usual to start treatment with doses of 0·01, 0·02 and 0·5 gm. at weekly intervals. If these are well tolerated, 0·10 gm. may be given every week for about 12 weeks. The course may be repeated after two or three months. Smaller doses and longer courses may be employed with a total of 1 to 2 gm. of the drug per course. As already stated it is better to avoid oily suspensions. Myocrisin is M. & B. products.

Crisalbine (M. & B.). *Auroform* (C.D.C.) and *Sanocrysin* are brands of gold sodium thiosulphate, with a gold content of 37 per cent and occurring as white shining needle-shaped crystals, freely soluble in water, giving a neutral solution. 45 per cent solution is isotonic with blood serum. The solution should be freshly prepared using 2 c.c. of a solvent for every 0.10 gm., and administered by slow intravenous injection. The solvents employed are double distilled water, calcium gluconate 10 per cent, or thiosulphate of calcium or sodium 10 per cent. The last named three are preferred in febrile cases and are said to lessen the risk of skin reactions. Crisalbine is available in ampoules of 0·15, 0·10, 0·15 0·20, 0·25 and 0·50 gm. of the powder.

Treatment is usually started with 0·5, 0·10, 0·15, 0·20, 0·25, 0·30, 0·35, and 0·40 gm, doses at weekly intervals, after which 0·50 gm. is

administered every week till 4 to 5 gms. have been given. The course is repeated, if necessary, after three or four months. Improvement is verified by X-rays from time to time. In pregnancy a dose of 0·25 gm. should not be exceeded.

Other preparations are:—

Solganol (Scherring). Gold content 36·5 per cent.

Solganol B Oleosum (Scherring).

Krysolgan (Scherring), Gold content 60 per cent.

Lopion (Bayer) used intravenously.

Parmanil (Bayer) is an oily preparation.

Collosal Aurocalcium (Crookes) is calcium aurothiomalate in colloidal form. Used intramuscularly.

Auroprotasin (Dinklage) is also a colloidal preparation.

Aurothysin (Anglo-French) used intramuscularly.

The indications for their use are as for other gold compounds generally. Many of these are not available.

Toxic reactions.—Certain toxic reactions may be encountered during chrysotherapy and upon their prevention depends the success of the treatment. These are the result of either an overdosage, idiosyncrasy or sensitisation to the metal. From their long list, it should not be inferred that they are of common occurrence. On the other hand, these are quite rare nowadays, and the more serious complications can usually be prevented by carefully controlled dosage, and closely observing the patient, where further administration of the metal can be stopped, suspended or modified, as soon as the slightest signs of intolerance are detected. For the sake of making this article complete, I give below all the reactions that can possibly occur in chrysotherapy.

REACTIONS	TREATMENT
1. *Focal.*—The symptoms of the disease may become more marked for some time after the injection. These include—	(Mostly symptomatic).
(*a*) Slight rise of temp. for a few hours.	Diaphoretic mixture or a dose of Aspirin.
(*b*) Fever 3 or 4 days with or without rigour or malaise.	Same as above. Reduce the dose at the next injection and prolong interval.
(*c*) Persistently raised temp. for two or 3 weeks. Rare.	Stop gold.
2. *Shock*:—May follow intravenous administration.	Inject slowly. The patient should rest for a few hours after the injection. ½ grain of Ephedrine Hydrochlor given an hour

	before the dose may prevent shock. Treatment consists in administration of Adrenalin ½ to 1 c.c. Intramuscular route should be substituted if shock recurs every time.
3. *Dermal*:—(*a*) Mild and temporary urticaria, pruritis or erythema.	Use Calcium Gluconate 10 per cent, or Thiosulphate of Sodium or Calcium 10 per cent as solvent for Crisolbine or Sanocrysin. (These are not compatible with myocrisin). Locally use soothing applications like Calamine lotion with 2 per cent Carbolic, or Colloid bath. For the relief of itching inject Adrenalin, Pituitrin or Calcibronat. Small doses of luminal or ephedrine may be given.
(*b*) Generalised erythema, pityriasis rosea, vesicular macular or pustular eruptions which may lead to severe desquamative dermatitis or exfoliative dermatitis if neglected. Uncommon.	It is better to stop gold. Daily injection of 10 per cent 10 c.c. Sodium or Calcium Thiosulphate and Contramine gr. 2 in 1 c.c. Potassium Permanganate bath and suitable local applications.
(*c*) Exfoliative dermatitis is a very serious complication but rare. Runs a prolonged course. Pre-existing hepatic damage predisposes to it.	Same as above. Stop gold. Plenty of fluids and Glucose. Liver Extract orally or by injection. Locally use tannafax. Thoroughly investigate the case, but don't attempt to remove the septic foci immediately.
(*d*) Purpuric spots indicate damage to hæmopoietic system.	Stop gold at once and thoroughly investigate the case.
(*e*) Erythema nodosum, lichen planus, etc.	Ditto.
(*f*) Chrysopigmentation or chrysiasis is sequel, which may appear long after the administration has been stopped. It is due to the deposition of the metal in the skin and appears as black patches on exposed parts.	These disappear eventually and call for no treatment. Thiosulphate of Calcium or Sodium may, however, be administered.
4. Alimentary system—(*a*) Stomatitis and gingivitis may be	Deal with septic foci in the mouth. Antiseptic and soothing

encountered especially in patients with septic teeth or faulty dentures. Multiple painful ulcers form.	mouth washes and use of Planacrine lozenges for prophylaxis and treatment. Reduce the dose of the metal, and if the condition is persistent suspend treatment for a few weeks.
(*b*) Nausea, vomiting, colic and diarrhœa. Uncommon.	Symptomatic treatment. If severe, suspend administration temporarily. If recurrent, stop gold.
(*c*) Proctitis, dysphagia and purpuric spots on the mucous membrane are rare.	Stop gold and attend to the condition.
(*d*) Jaundice of any degree indicates hepatic damage. Usually transient and mild.	Stop gold and treat on general lines.
5. *Urinary*:—(*a*) Mild and transient albuminuria for a day or two.	Reduce the next dose.
(*b*) Rather persistent albuminuria with or without erythrocytes and casts.	It is better to stop gold.
(*c*) Toxic nephritis is extremely rare nowadays and is preventable.	Withdraw the metal at once and treat on general lines.
6. Blood dyscrasias are the most serious complications but are very rare.	Stop gold at the just sign. During chrysotherapy the blood should be frequently tested for any evidence of thrombo-cytopenia, leucopenia eosinophilia, punctate basophilia.
(*a*) Agrannlocytic angina or marked leucopenia.	Stop gold. Pentnucleotoid 40 c.c. I.M. daily. Blood transfusion. Liver Extract. Yellow bone-marrow concentrate (Armour) one dram every 4 hours. Appropriate local treatment.
(*b*) Purpura hæmorrhagica manifested by purpuric patches, spontaneous bruises, menorrhagia, etc.	Blood transfusions. Later on liver extract, iron, vitamin C, etc.
(*c*) Alenkia hæmorrhagica is a grave but extremely rare complication.	Repeated blood transfusions may help.

7. Nervous complications are the rarest and include muscle spasms, neuritis, psychotic disturbances and deranged cutaneous sensation.	Stop gold. Treat the symptoms.

8. *Others*:—Bronchitis, vulvitis, conjunctivitis, etc. Rare.

How to prevent reactions.—The more serious reactions can generally be prevented by employing carefully controlled dosage and constant clinical supervision.

1. Before commencing the gold treatment thoroughly investigate the case.

(*a*) Take complete history, especially for hæmorrhagic tendencies (subcutaneous or hæmorrhages, frequent epistaxis, bruises spontaneous or from slightest trauma), previous attacks of exfoliative dermatitis and other dermatoses, chronic alcoholism, marked hypertension, gross hepatic, renal or cardic disease, etc.

(*b*) Thorough clinical examination in order to (i) judge that the type of tuberculosis is such as is likely to derive benefit from chrysotherapy, (ii) detect any existing absolute or relative contra-indications.

(*c*) The following biochemical tests should be carried out.—

(i) Test the urine and perform kidney-function tests. Polyuria, or urine with persistently low specific gravity with normal intake of fluids, or slight albuminuria indicate lowered function and gold may aggravate this.

(ii) Make blood counts. Cases with marked leucopenia or thombocytopenia are bad risks as agranulocytosis or purpura hæmorrhagica may develop in such cases. Eosinophilia and moderate anaæmia call for caution. Punctate basophilia is also a sign of intolerance. Erythrocyte sedimentation rate, coagulation and bleeding time may be recorded.

(iii) Perform hepatic function tests and fractional meal test.

(iv) Record blood pressure.

(*d*) Eradicate septic foci as far as possible.

2. During chrysotherapy constant clinical supervision is necessary to detect any signs of intolerance. Keep a temperature chart. Test urine daily for albumin, erythrocytes and casts. Blood should be tested frequently. A moderate fall in the number of platelets or leucocytes calls for interruption of treatment. Punctate basophilia also necessitates suspension of chrysotherapy. Exercise caution if there is eosinophilia above 8 per cent. Progressive fall in erythrocyte sedimentation rate occurs in favourably reacting cases. Keep a watch for other reactions.

The following general rules should be observed.—

(*a*) Don't inject after a meal or during or immediately preceding menses. Ambulatory patients should rest for a few hours after the dose.

(*b*) Shock can usually be avoided by injecting slowly and administering ½ grain of Ephedrine an hour before the dose.

(*c*) Diet should be rich in protective elements. Plenty of glucose (with or without small doses of insulin), vitamins especially ascorbic acid, liver extract by mouth (or by injection), hydrochloric acid to cases with hypo or achlorhydria, lessen the risks of toxic reactions.

Attend to oral hygiene.

Sanocrysin may be dissolved in calcium gluconate 10 per cent or thiosulphate of calcium or sodium 10 per cent with advantage. It is better to avoid oily suspensions. Simultaneous arsenotherapy should be avoided.

Lastly gold should not take the place of other therapeutic measures, but should form only an adjunct to usual treatment in suitable cases.

NOTE:—I am indebted to the various writers for the many quotations and ideas extracted from their writings—*The Antiseptic* March 1947.

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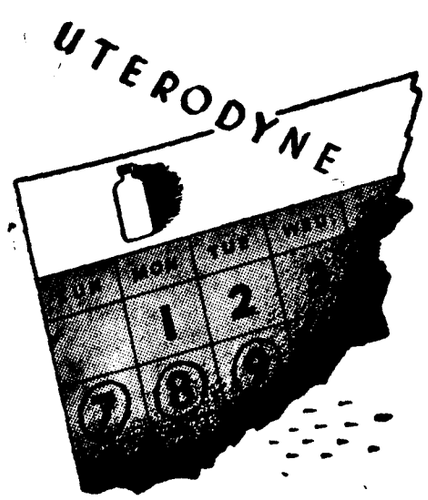

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Printed by Mr. S. Sundaresan, L.P.T., for the C.O.P. Works, Ltd., 1/17, Mount Rd., Madras.

MEDICO-SURGICAL SUGGESTIONS

Vol. XVI. JUNE 1947. No. 6.

MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVI JUNE 1947 No. 6

LIVER ABSCESS

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Liver abscess is the commonest complication of amœbic dysentery. Though in a large majority of cases the diagnosis is very easy, at times the symptoms and signs are misleading. One must be on guard not to miss the possibility of liver abscess in such obscure cases.

In my opinion the predisposing factor in abscess liver seems to be an alcoholic habit. In the series of my cases which I have studied for this paper, out of 32 cases I came across two cases of liver abscess in non-alcoholics. Even at the expense of being considered as overstressing. I should like to say that I consider liver abscess—case proved by aspirating chocolate coloured pus—is exceedingly rare in a non-alcoholic. Alcoholic habit seems to devitalise the liver resistance to amœbic invasion. I am quoting three cases just to show the importance of alcoholic habit. In my first case liver abscess was diagnosed in an old man. We aspirated him once and put him on Emetine. In spite of that he was sinking. Finding that he was not improving, we asked him as to what he wanted. He wanted a pot of toddy to drink and he was given the same as his general condition was too poor. In a day or two he died and partial autopsy showed a big liver abscess containing a small amount of pus and the rest of the abdominal visceral healthy. In the second case a man was admitted with abscess liver. He was aspirated 18 years ago and we aspirated again typical chocolate coloured pus. The liver had shrunk and he was afebrile. At this stage he took leave to attend his daughter's marriage, went out, drank heavily at the wedding and in a week's time he was back in the hospital with the recurrence of symptoms and liver again palpable four fingers breadth below the costal margin. We again aspirated about 10 oz. of pus and warned him not to indulge in alcohol. He was reporting himself once in a way for two or three years when he was found to be maintaining his health. Later he joined the Military in 1942 and by 1945 started to take alcohol and

in 1947 reported sick with hepatitis. This time we did not strike any pus and the hepatitis responded to Emetine treatment.

I have come across liver abscess only twice in women. In the second case which occurred in December last year when I inquired for alcoholic habit the women actually said brandy was very welcome. This woman was aspirated twice and she was a heavy alcohol addict. It is well known that liver abscess is comparatively infrequent in women. Even amœbic dysentery is less common in women than in men. This might be due to the more sheltered life that they have. But the liver abscess as a complication in women is almost a curiosity. I presume it is so because they do not indulge in alcohol. For the same reason liver abscess is very rare in children. The youngest age recorded is by Biggam A. G. in 1932 of a case of amœbic dysentery in an Egyptian child three months of age who had also amœbic abscess of the liver. Child died of broncho-pneumonia and autopsy showed amœbic ulcers in the bowel.

Pathology of liver abscess.—Entamœba histolytica reach the liver from the dysenteric ulcers in the colon through the portal vein in large numbers. At this stage it can be compared to an army on the march and amœba are scattered in the liver and cause a diffuse inflammation or hepatitis At this stage if a needle is put into this enlarged liver only blood is drawn. This condition improves dramatically with Emetine, If the amœba meets with devitalised liver cells and gets a hold it multiplies and by a process of co-agulative necrosis causes destruction of the liver. This occurs in various centres and these spread, and by a confluence lose their individuality and constitute a large abscess. Thus the pus inside is actually a liquefied liver and not due to suppurative process as in a coccal infection. Hence culture of this pus is always sterile unless secondary infection has taken place. The abscesses may fail to coalesce and then we get multiple liver abscesses. The pus when secondarily infected is no longer chocolate coloured but is greenish or yellowish depending upon the organism. The commonest secondary organism seems to be B. coli.

The abscess may slowly work its way to the surface and may even rupture into the adjacent portion as into the pleural cavity, pericardial cavity into the peritoneum or rarely into the surface by a sinus. In chronic abscesses the pus may be well walled off by a wall of connective tissue. In these cases, signs and symptoms are apt to be misleading. If as a result of treatment, the amœba are destroyed, calcification of the abscess wall may take place. Amœba themselves are not usually seen in the liver abscess pus. They are only seen in the scrapings from the wall of the abscess cavity. Cysts are never found in the liver abscess pus.

Liver efficiency tests are likely to show greater deficiency of the liver in the hepatitis stage, and in a chronic abscess liver in

which the abscess is well walled off, the liver efficiency may be normal.

Symptomatology.—There are few diseases with such varied symptomatology. Even the best of clinicians have missed abscess liver and diagnosed one when it was not there. In a typical case patient complains of pain over the side of the chest over the liver area or over the shoulder. The pain is fairly severe, with fever coming on in the evenings. At the onset of the fever, there may be rigor but there may or may not be further rigors but occasionally there may be daily rigor. On examination there is bulge on the right side of the chest over the liver area and also over the right hypochondrium. The liver is enlarged and tender. The enlarged liver is smooth aud not nodular. It may be moderately firm or even very hard. Quite a few cases have even been misdiagnosed as cancer liver because of the hardness of the liver that might occur in some cases. In most of the cases over the right base of the lung percussion note is impaired and the breath sounds may be feeble or even absent with fine rales. This may be due to either the upward enlargement of the liver in the right upper quadrant or associated pneumonitis in the right base or to pleurisy with or without effusion in the right side. This pleural effusion may be clear straw coloured fluid showing that the pleura is being irritated or in some cases the liver abscess may burst in the pleural cavity. When liver abscess bursts into pleural cavity—if the lung itself is not adherent to the diaphragm—it may behave like pleural effusion due to any other cause. If. on the other hand, the lung is adherent to the diaphragm, then the patient may cough out liver abscess pus, and the liver might suddenly shrink. I can now recall a case. A wandering Sanyasi was admitted with what appeared like an oval tumour filling up the right hypochondrium, right loin and almost reaching the right iliac fossa. No definite diagnosis could be made. The tumour was found to be moving with respiration and looked as though in continuity with liver dullness. The man gave a history of dysentery some years ago and was an alcoholic. He was complaining of pain and was also running a temperature between 102° to 103°. Though we were not certain of the diagnosis we put the patient on Emetine I. M. daily and on the 2nd day the patient said he was feeling giddy and vomited about a pint of chocolate coloured pus and in the course of the next few hours the tumour disappeared under our very eyes. He was spitting bile stained saliva for a few more days and this man made an uneventful recovery.

In a typical case the abscess may actually point in various parts of the chest or even in the back. In one of my cases, our surgeon even thought it might be abscess of adominal wall. In another case the abscess had worked its way into the anterior abdominal wall and presented as a small ball-like structure in the

anterior abdominal wall. Only on the table it was realised that it was a case of liver abscess which had worked its way into the rectus sheath. In another case the abscess had worked its way into the small of the back and was diagnosed as perinephric abscess. This case again was properly diagnosed only by operation. In another case a man came complaining of pain over the area of right kidney and intermittent type of temperature. Fever used to be coming on with rigor. There were not positive clinical findings except slight tenderness over the small of the back on the right kidney region and very slightfulness. Urine did not show any change and urine culture was sterile. All the same he was put on alkaline diuretic mixture for a few days with no benefit. One day the patient complained of a severe pain and said that something had given way deep in his chest and in a few minutes he was in a state of shock with profuse perspiration and fast and feeble pulse. Clinical examination showed signs of pleural effusion right base and a chest picture taken in the next few hours confirmed the diagnosis. In view of the fever and the abrupt onset of effusion liver abscess bursting into the pleural cavity was thought of and a needle was put into the pleural cavity and chocolate coloured pus was aspirated. Patient was immediately started on Emetine therapy with considerable improvement. In this case the liver abscess must have been situated posteriorly and pressed upon the kidney, causing a slight amount of fulness over the loin and stimulated pyelitis.

Jaundice does definitely occur in the course of liver abscess, Failure to bear this possibility in mind has been the cause of missing at least quite a number of cases by clinicians. In one of my cases a man came with jaundice, enlarged spleen and liver and intermittent type of fever. Jaundice was of the obstructive type. He gave a history of alcoholic habit and also of having had dysentery some years ago. We put him on a course of Emetine and aspirated about 8 ozs. of pus and the jaundice promptly cleared. A few days later he was admitted again with jaundice. He was aspirated again and the jaundice cleared within a day or two. In this case jaundice showed unmistakable relationship to the abscess liver. In another which I happened to see was in an old man past 55 or even more. This man was toxic and deeply jaundiced with a very big liver which was nodular and very hard to the feel? Primary carcinoma liver was the diagnosis made. At the autopsy it proved to be a case of liver abscess and the nodularity felt in the wards turned out to be due to the abscess wall bulging through the healthy liver. In this case the age of the man, the nodularity of the liver and the hardness of the liver completely misled everybody and but for the autopsy this would have been completely missed. So it is worth bearing in this factor in mind. An enlarged liver with fever and

jaundice means the posibility of a liver abscess. Another of my case, again an old man, was admitted with what looked like a case of congestive heart failure. The patient had œdma of the legs and arms with slight puffiness of the face. He was deeply jaundiced and an abscess pointing in the anterior abdominal wall. It looked as though the abscess would burst any minute I put him on Emetine and showed him to our surgeon. He was operated on immediately and about a pint of pus was drained. Left to me I would not have advised operation at that stage but my surgeon was afraid that the abscess might burst and thus might become an emergency. He had to be aspirated two or three more times before he recovered completely. In this case by the 3rd day the œdema of the legs and arms cleared up and in a week's time the jaundice also cleared up but he developed broncho-pneumonia for which he was put on Sulphathiazole and was fully recovered at the time of discharge. In this case there were several features which were misleading in arriving at a diagnosis. The patient having congestive failure symptoms and abscess pointing almost like a tent in the anterior abdominal wall and deep jaundice. My chief called my diagnosis a bold one. This case illustrates the type of cases that come with symptoms of congestive heart failure. I have seen another case with symptoms of heart failure and generalised scabies. In this case for a time at least the liver abscess was missed. Text books do not mention this type of cases The problem in this type of case in Emetine therapy. I am of opinion that the heart failure is only secondary to abscess liver and it can only be cured by drainage of the abscess and Emetine therapy. I advocate Strychnine or Coramine or any other cardiac stimulant may be given along with Emetine. I will refer to this point later when I come to the treatment.

In only a very small group of cases we get the abscess liver and dysentery being present at the same time. In my series of cases in only two cases were the amœba seen in motion. Motion examination may more advantageously be done for cysts but it is not easy to spot them. In the analysis of 32 cases in only two cases were E. H. seen. It is easier to look for such indirect evidence as thickening of the ascending or sigmoid colon. It is very exceptional for the transverse colon to show any evidence of thickening.

Rarely it is the complication that occurs in the course of the abscess that is likely to draw attention to the existence of the liver abscess. The abscess might burst into the neighbouring structures. By far the common sites for rupture of the abscess are into the pleural cavity and peritoneal cavities. I have seen one case in which the abscess burst on to the skin. The case in which it burst into the pericardial cavity was a middle aged man. He was first seen by me in a mild state of shock with

thready pulse and cold sweat. He complained of severe pain in the epigastric region. Examination showed liver enlargement two fingers breadth below the costal margin. I admitted this case as hepatitis. In the wards he got over the state of shock and was quite all right in about three hours time. At this stage he gave a history of periodic attacks of pain coming on two or three hours after food and being relieved by taking a little food. In view of the history I thought I was dealing with a case of duodenel ulcer. Fractional test meal showed low acid and barium meal series failed to reveal any defect in the duodenal cap. I thought of the ulcer with perigastric adhesions. By this time again for no reason while he was at perfect rest he went into a mild state of shock. This only further favoured my suspicion of perigastrie adhesion causing sympathetic disturbance and our consulting surgeon suggested that it might be only liver abscess and took over the case. He put the patient on Emetine ½ gr. I M daily. After three injections were given patient again developed a state of shock but this time it ended fatally. At autopsy it was found to be a liver abscess that had burst into the pericardium. In this case we had two misleading features. One was the periodicity of pain in relation to food simulat ng duodenal ulcer (subsequently I have elicited such a history in a number of cases). Probably it is the distension of the duodenal cap pressing on the inflamed liver that causes the pain). The second misleading thing was periodic cold sweat and a state of shock from which the patient recovers in the course of a few hours. Very rarely the abscess might burst into the perinephric tissues.

The aids to diagnosis are examination of blood, a skiagram of the chest and finally aspiration of the enlarged liver.

Blood shows leucocytosis in the hepatitis stage and in the acute stages of the liver abscess. In some of the chronic cases when the abscess in well walled off by fibrous leucocytic does not occur. In one of the cases leucocytic count done three times showed only 4,000 per cm m. The liver was enlarged to such an extant as to almost completely fill the entire abdomen, leaving only a very small area free between the margin of the liver and symphisis pubis. On opening the abdomen was occupied almost completely by the liver and on incising the liver 7½ pints of pus was drained and scrapping from the wall showed motile amœba. This patient was put on Emetine with complete recovery. A few days later at the time of discharge liver was only just palpable.

X-ray of the chest is a very valuable procedure. It may not be of any value when the abscess enlarges downward or is situated in the left lobe. It is of the greatest value when the abscess is situated in the right upper quadrant. In a few cases in which effusion right base is suspected X-ray chest has shown only raising of the dome of the diaphragm without any displacement of the heart. In

two cases where the patients were very markedly emaciated and complained of pain in the abdomen with doughy feel they were suspected in one as tuberculous peritonitis with a just palpable liver and in the other as tuberculous pleural effusion right side. In both cases X-ray chest showed that we were dealing with liver abscess. Screening shows absence of diaphragmatic moving on the right side in a large number of cases but where the abscess does not progress in the upper quadrant diaphragm might freely move with respiration.

Aspiration of the liver clinches the diagnosis and is also part of treatment. Once a needle is put in and pus is drawn, aspiration should be done straightway. I very well remember a physician putting in a needle and demonstrating to a batch of students the presence of pus in the morning. By night the patient developed acute abdomen and laparotomy showed nearly a pint of pus had collected into the peritoneum. In the liver abscess the pus is under tension and a needle track affords sufficient passage for the pus to leak.

Differential diagnosis in liver abscess.—As I said at the very beginning a number of conditions may be mistaken for liver abscess. The common conditions which have to be differentiated are primary carcinoma liver and a liver riddled with secondaries. The liver that is the seat of malignancy has many factors that are likely to present misleading features. It is likely to show a low temperature, hard liver which might also be tender and moderate leucecytosis and skiagram may also show elevation of the right dome of diaphragm. Aspiration might show blood stained material and if the needle passed through a portion of the liver bearing malignant deposit or malignant changes, then the aspirated material shows malignant cells as in one of my broncho-genic carcinoma cases with extensive secondary deposits in the liver. In another case, with primary growth in the gall bladder, with plenty of secondaries in the liver, it failed to show any malignant cells. Therapeutic response to Emetine may also be tried.

The other conditions to be thought of are pneumonia right base; pleural effusion right base, tuberculous peritonitis, peptic ulcer, typhoid and other long continued fevers, gumma of the liver, hydatid of the liver, perihepatitis occurring in cases of kala-azar and malaria cholecystitis both acute and chronic and also adenocarcinoma of the gall bladder. Perinephric abscess and pyelitis and malignant tertian malaria and early cases of cirrhosis liver. I do not say I have completely exhausted all the possibilities. There are many conditions not mentioned by me but I have mentioned the common ones.

A Hindu, male, aged 16, was admitted for pain in the legs and abdomen and night blindness of two months duration.

Previous history :—History of dysentery 4 years ago. History of venereal sore 5 years ago. Habits: Occasionally takes alcohol, non-vegetarian.

History of present illness :—Two months ago patient had fever for ten days. This was followed by pain in the right hypochondrium.

This patient was an emaciated young man with œdema of the feet. Pigmentation of the palate, sclera and icterus. Abdomen: liver enlarged, more the left lobe and soft. No tenderness, palpable —3 fingers breadth below the right costal margin and 5 fingers breadth in the epigastrium. The other systems were normal.

Blood W.R. was positive strong. Total W.B.C. 6,000 per cm.m. By liver aspiration through the right 8th inter-space only blood was drawn. No pathogenic organisms were seen. X-ray chest showed moderate elevation of right dome of the diaphragm.

Patient was admitted as amœbic hepatitis. He was given a course of Emetine 1 gr. I.M. daily with no benefit. Since the left lobe was enlarged and only blood was drawn in the aspirating syringe left lobe abscess was diagnosed and the case was transferred to surgical side. Under local anæsthesia laparotomy was done. Liver was not adherent to the peritoneum. Liver surface was smooth. Aspiration of left lobe also yielded blood only. Peritoneum sticked to the liver surface and packed with gauze.

In this case patient had no fever to start with and at the end of 7 injections started having fever. After the laparotomy on the 8th day patient started having fever and this responded to lodide by mouth. Eight months later patient developed ascities. He was given mercurial diuretics and milk diet and ascites cleared. In view bf the history of dysentery and enlargement of the liver and emaciation amœbic hepatitis was diagnosed. This should have been revised in view of the left lobe being much more enlarged, leucocyte count being only 6,000 per cm, and the absence of response to Emetine. As a matter of fact the temperature started going up on the 8th day of Emetine injection. With the history of sore on the penis five years ago, blood W.R. should have been done at the very first instance. This type of diffuse involvement of the liver by a syphilitic process is not common and is likely to be mistaken for an abscess liver.

For every one of the conditions that has to be borne in mind can cite illustrative cases and I am sure you would also have seen cases of a similar nature.

Treatment in this condition, that I adopt as a routine is to put the patient on Emetine 1 gr. daily I.M. for 9 days. If there is no urgency then I prefer to aspirate at the end of course but where the pain is severe and abscess is bulging and threatening to perforate I aspirate at the end of 3 grains of Emetine but where the symptoms are very urgent and where delay might mean rupture of the abscess any minute I aspirate immediately after giving 1 grain of Emetine. But I always prefer if conditions permit to allow the patient to have at least three injections of Emetine 1 grain each daily, before I aspirate. This much of Emetine is enough to kill the active forms at the surface and aspiration tract is not likely to act as a passage for the amœba to spread.

Most of the symptoms clear up by the third or fourth injection. If a patient is markedly emaciated and general condition too poor, I do not prefer to give a lower dose of Emetine but I give Emetine gr. 1 and Strychinine or Coramine along with Emetine. If the patient is febrile he becomes afebrile by this time. I do not find any advantage in putting Emetine locally into the abscess cavity and I do not adopt that procedure. The aspiration with potains aspirator is the method of choice when the abscess is in the right side of the liver to let out the pus. I have aspirated by this procedure in two of my cases as much as 64 ozs. But where the abscess is aspirated in the left lobe open operation is the ideal method. Even for this a preliminary premidication with Emetine is of great value in avoiding post operative complications. Aspiration is done if necessary more than once at intervals 4 or 5 days. Where there is urgency I aspirate at the end of three grains of Emetine and repeat the aspiration at the end of 9 grains of Emetine.

After a course of Emetine the patient is put on E.B.I, 2 grains at bed time for 12 nights.

I prefer to have the bowels regular and from the start I put my patients on Oleum Recini emulsion. By the time they have had about 6 grains Emetine I shift over to Shark Liver Oil emulsion so that these emaciated patients may put on some weight.

Prognosis is these cases is good if the abscess is aspirated or drained well and if the patient has not gone down in general condition too far. It is surprising how even very advanced cases respond to aspiration and Emetine.

In my analysis of 32 cases only 2 deaths occurred. Abscess liver is likely to recur if the patient takes to drinking alcohol again. This is one of the few conditions where under our very eyes with proper treatment a patient gets remarkably better in the course of a few days. (*The Antiseptic, May 1947.*)

Extract.

USE OF PENICILLIN IN SURGERY.

Penicillin Versus Sulphonamides in Prophylaxis :—Sulfonamides usually prevent spreading or generalised infections from wounds ; but have no appreciable effect on the local infection. Penicillin alone was found to be quite effective rather better than a combination of penicillin and sulfonamides as sulfonamides produced at times dangerous complications. In 497 cases treated with penicillin locally and parenterally 93.1 per cent of cases showed none or slight infection, in 480 cases treated with penicillin plus oral sulfonamides the incidence was 90.4 per cent, while in 157 cases treated with sulfonamides oral and local the incidence was 73.2 per cent. The value of penicillin in prophylaxis and treatment of wound infection is further confirmed by the study of incidence of anaerobic myositis.

The incidence of this serious infection was high in 1914—1918. Even in desert compaign, the incidence of anaerobic myositis was 3.4 per. 1,000 (Macdenan 1944), in Tunisia 6.7 per 100.

The Value of Penicillin in Surgery : Penicillin has a great value as a prophylatic of wound infection. During 1945 war casualties had marked absence of severe sepsis and incidence of all wound infections. The most dominant factor in this was the use of penicillin. This fact was confirmed by bacteriological investigations as well. In the 1942 Middle East Campaigns "no growth" reports on the first wound swabs, taken after admission of casualties to hospital were most uncommon, a positive culture was obtained in a series of 100 cases at one centre. In the N. W. European (B.L.A) campaign of 1944—5, "no growth" reports were common and phyogenic infections were relatively uncommon (Porritt and Mitchell), 1946. Sterptococci were isolated only in 5 per cent of cases in B.L.A. casualties as against 68 per cent in M. E. F., Staphylococci in 25 per cent as against 58 per cent, Clostridia 2 per cent, as against 28 per cent. coliform 10 per cent, as against 6 per cent. and in Italy not less than 10 per 1000 (Jeffre and Thompson 1944). In N. W. Europe the incidence in Allied troops (Porritt and Mitchell 1945) was only 1.5 per 1,000. The death rate in the N. W. Europe was exceptionally favourable, being 21.5 per cent.

Prophylactic Use : In minor wounds local application alone is usually adequate. Penicillin powder 5,000 units of penicillin per gramme, the diluent being sulfonamides or powdered plasma ; is used. It is dusted on the wound at the first examination. In serious cases local and par enteral use (15,000—100,000 units per injection are used at 3 hourly, 6 hourly intervals) is needed. The dose and frequency of administration depend on the severity of infection.

Value of Penicillin Therapy :—Penicillin treatment by curing sepsis made secon dary sutures, grafts and plastic procedures safe for the patient. Lot of time and suffering of the patient, material and attendance of hospital staff were saved. The work of Florey and Cairns (1943) and others showed that many wounds could be closed safely under the prote ctive action of penicillin. Prophylactic use of penicillin made at least 9 out of 10 wounds clinicallyclean and secondary sutures could be performed successfully in such case.

G. A. G. Mitchell reviewed the results of wound sutures in 4,432 cases treated with various methods. Penicillin therapy gave results with success in 80-86 per cent of cases, success and partial success in 95-98 per cent of cases. These results with sulphonamide therapy locally and parenterally were 62.41 per cent and 83 per cent, with local sulfathiazole and proflavine mixture 54·09 per cent—81.97 per cent. The highest percentage of success was in cases treated

with parenteral penicillin only. Briefly speaking, success in penicillin cases was about 81 per cent as against about 63 per cent in other cases, success and partial success was about 94 per cent in penicillin cases as against about 84 per cent in other cases.

Results of penicillin therapy will appear still far better when it is realised that penicillin therapy especially the parenteral was given to serious and major types of wounds.

B.M. J., G. A. G. Mitchell, January 11, 1947. (Pages 41-45.)

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தமிழ்நாடு அவணக்காப்பக நூலகம்,
எழும்பூர், சென்னை-600 008.

தவணைத்தாள்.

சே எண் : 177615 ப. எண் :

வழங்கிய நாள். (1)	திரும்பிய நாள். (2)	வழங்கிய நாள். (1)	திரும்பிய நாள். (2)

S.F. 259A-6—1,00,000—30-1-84.

Regd. No. M. 2863.

Edited and Published by Dr. P.R. Venkappa, Sai 2/337, Mint Street, Madras,
Printed by Mr. S. Sundaresan, L.P.T, for the G.G.P. S. Ltd., 1/17, Mount Rd., Madras.