

Sulphadiazine and sulphamerazine qualify for first and second place, respectively, as mixture components. Sulphathiazole, sulphapyrazine, sulphamezathine, and sulphacetamide deserve attention as possible third and fourth members of a combination. Although sulphathiazole has fallen into disfavour in the U.S.A. because of its high clinical toxicity, mixtures containing this drug have shown a low overall toxicity. Sulphapyrazine, the most insoluble of these compounds, induces frequent renal and allergic reactions and therefore offers no advantages over sulphathiazole. Sulphamezathine has adequate solubility and low toxicity, but is subject to substantial conjugation and plasma-binding, which diminish its therapeutic efficiency. Sulphacetamide retains the high solubility of sulphanilamide and shares with the parent compound the improbability of renal concretion formation and the ready diffusibility into all tissues. In addition, it shows low figures for conjugation, plasma-binding, and sensitization.

The mixture sulphadiazine-sulphamerazine-sulphacetamide (equal amounts) revealed low toxicity in animals as well as excellent bacteriostatic activity *in vitro* and in experimental infections of mice. After oral administration, blood and spinal-fluid levels were similar to those from equal doses of sulphadiazine or sulphamerazine. Clinical trials of this mixture in 170 patients with acute systemic infections showed a high curative value and low toxicology.

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## MEDICAL TREATMENT OF HYDATID CYSTS OF LUNG\*

BY

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Pulmonary hydatid cysts, apart from the rare cases which heal spontaneously after a single or repeated expectoration, are exclusively in the domain of surgery, varying only in the details of technique suited to each case.

Encouraged by the good results obtained in severe broncho-pulmonary suppurations, both localized and diffuse, by our method of transthoracic intrapulmonary injections of sulphonamides, antibiotics, and other drugs, we extended this treatment to suppurations due to the retention of hydatid membranes—that is, to suppurating cysts of the lung with incarcerated membranes. A few years later, in view of our favourable experience with infected cysts, we applied the same method of treatment to clean uninfected hydatid cysts.

Without exaggeration, and on the basis of our case records, we can now say that some cases can be treated medically. The importance and scope of this treatment remain to be established by further experience. Whilst the results in cases followed up have so far been successful, their number is too small to warrant definite conclusions. Nevertheless, we are optimistic, since we cannot believe that only the favourable cases came into our hands.

These cases fall into three categories: (1) suppurating pulmonary hydatid cysts, with retained membranes; (2) ruptured pulmonary hydatid cysts, with loss of fluid content and persistence of the parasitic cavity, whether air-containing or not; and (3) hyaline hydatid cysts—that is, closed and non-infected. We will outline the therapeutic procedures employed in each category, and give a single example of each kind to show the more salient clinical features.

### Suppurating Pulmonary Hydatid Cysts, with Retained Membranes

These cases present two problems: broncho-pulmonary suppuration and the retention or incarceration of the parasitic membranes. The first problem is really a consequence of the second, since the membranes, except in rare instances of clean encystment or of calcification, behave as true foreign bodies, leading sooner or later to pus formation in the surrounding parenchyma.

We treat pulmonary suppuration locally by means of transthoracic injections of sulphonamides and antibiotics, choosing the drug according to the organism isolated, whenever possible, from the material aspirated, and adapting the dosage, interval of administration, etc., to the clinical and radiological progress of the patient.

The complete expulsion of the membranes, which is essential to end the suppuration, is achieved by a purely mechanical effect. The local congestion, partly hydrostatic and partly biochemical, created by the transthoracic injection provokes intense and repeated bouts of coughing, which directs the fluid current towards bronchi already dilated as a result of the suppuration. This flow carries along with it fragments of endocyst which have been

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Over 200 Scottish nurses had their names added to the Register of the General Nursing Council for Scotland on June 21. New rules made by the Council provide for the transfer of these nurses from the 1943 Nurses' List to the Register without application or payment of fee. This allows these nurses, who have hitherto been known as State-listed nurses, to be classified as State-registered in the branch of nursing in which they are qualified. It also grants them the right to vote in the forthcoming elections for the new General Nursing Council. The rules provide that persons who would have been eligible for admission to the 1943 list but who did not apply within the prescribed period may also be admitted to the Register. In their case, however, application for admission must be made to the registrar of the council.

detached as much by the intense cough as by the proteolytic ferments of the pyaemic organisms. The insertion of the needle into the parenchyma, as well as the jet of solution, helps to break up the membrane and facilitate its expulsion. It is noteworthy that in most cases cyst remnants thus ejected were expelled during or shortly after injection; this seems to establish a cause-and-effect relationship between the local influx of the drug and the expulsive action that follows it. In our cases the mechanical action achieved by the intrapulmonary injection has shown itself to be superior to bronchoscopic suction, which proved completely ineffective in all our cases, though performed by an experienced operator several times on one patient.

When all parasitic remains have been expelled and the broncho-pulmonary infection has died down, healing occurs rapidly; this includes the whole bronchial tree draining the affected area, as demonstrated by clinical and radiographic examination. In some cases a slight increase in pleural opacity remains, with deformity of the diaphragm and obliteration of the costodiaphragmatic recess in the case of basal cysts, sequelae which do not affect the working capacity of the lung or the efficiency of the patient in carrying out normal activities.

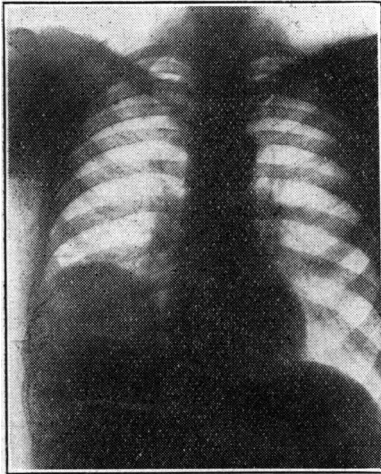


FIG. 1.—Case 1. The opaque cyst occupying the base of the right lung. A slight reaction is present.

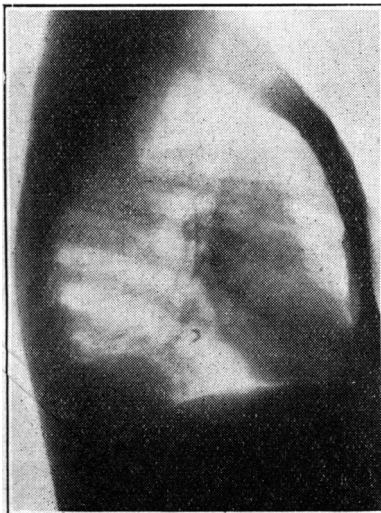


FIG. 2.—Case 1. The cystic shadow is in the lowermost segment of the right lower lobe.

**Case 1**

A single labourer aged 41 was suffering from a suppurating hydatid cyst in the right lower lobe (Figs. 1 and 2). He was treated in the outpatient department and was thus able to remain on light work throughout treatment.

In view of the long history and the size and superficial location of the cyst, it was punctured at once at its most accessible point, which corresponded to the postero-inferior region of the lobe.

Hydatidocentesis was carried out without the slightest inconvenience, immediate or remote. The first punctures yielded a small quantity of very thick pus and were then followed by 27 intrapulmonary injections. The first contained 200,000 units of crystalline sodium penicillin in 20 ml. of isotonic glucose saline; most of the others contained 100,000 units in the same volume. Two injections consisted of an ampoule of "prontosil" mixed with an ampoule of "cibazol," and the last two injections consisted of 100,000 units of penicillin and an

ampoule of cibazol and an ampoule of prontosil respectively. Treatment began on June 13, 1947, and ended on August 23 of that year, the intervals having varied from one to three days at the beginning and from four to twelve days towards the end. The cyst membrane was expelled in fragments during the course of the treatment. The good result obtained is clearly shown in Figs. 3 and 4.

**Hydatid Cavities, Whether Air-containing or Not**

In these cases, after rupture of some cysts, treatment is aimed essentially at removing the retained parasitic membrane which lines the cavity. This is achieved over a certain time, usually several months, by injection of digesting solutions containing hydrochloric acid and pepsin. Hydatid membrane, when exposed to these substances, becomes appreciably thinned and can then be coughed up without great efforts. This structural change is easily demonstrable by comparing the eliminated fragments with membrane which has not been exposed to digestive action. Patients show complete tolerance to the digestive solution, and this allows the frequent injections rendered necessary by the fact that the solution acts only for a short time because of rapid elimination, reabsorption, or both, and because of its dilution.

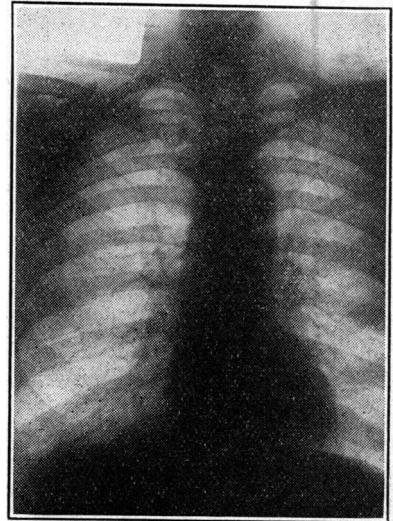


FIG. 3.—Case 1. Disappearance of the cystic shadow, and absence of any remnant of membrane.

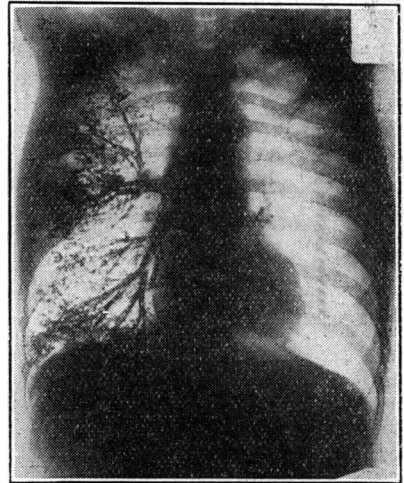


FIG. 4.—Case 1. Bronchogram showing the normal bronchial tree in the area previously occupied by the cyst.

**Case 2**

A single labourer aged 34 had a ruptured hydatid cyst with air in the residual cavity situated in the left postero-inferior lobule. He was given intracystic injections of 10 ml. of a solution of pepsin in hydrochloric acid, the concentration of pepsin varying between 5 and 20%, and the HCl from 0.05 to 0.15%.

After 30 injections over a period of three months, and following complete expulsion of the parasitic membrane and consequent obliteration of the cavity, he was discharged healed. The digestive action had visibly affected the chitinous membrane, the expelled fragments being reduced to thin wafers which had lost their characteristic tendency to form cylinders. Erosion of the membrane facilitated its fragmentation and subsequent expectoration.

### Hyaline Hydatid Cysts

These are referred to as clean, because they are closed and non-infected; they require a more complex treatment as follows: (1) Desensitization of the patient by injection in increasing doses of hydatid fluid and of its antigen, along the lines suggested by its discoverer, Dr. B. Calcagno. This is to prevent anaphylactic shock which, as is known, may be severe or even fatal. According to Calcagno this measure brings on death of the hydatid and so deprives it at the time of opening of its toxic properties on absorption of the hydatid fluid. (2) Fixation of the cyst to the chest wall, if this has not already occurred. This requires: (a) the induction of a pneumothorax; (b) irritation of the pleura by the use of substances such as hypertonic glucose or saline solutions, cibazol, 5% sodium morrhuate or ricinoleate urethane, etc., after previous injection of about 2 ml. of 0.5 to 2% procaine to allay pain and prevent reflex manifestations; (c) re-expansion of the lung; and (d) confirmation of pleural adhesion over the area by the failure of repeated attempts at fresh pneumothorax. (3) Puncture of the cyst, or hydatidocentesis. (4) Gentle aspiration of part of the hydatid fluid. (5) Chemical sterilization of the cyst by instilling some 10 to 20 ml. of 2% formalin and allowing it to stand for ten minutes. (6) Complete evacuation of the cyst.

There are now two alternative courses. One is similar to the treatment of a hydatid cavity and relies on the use of digesting substances. The other, which is much longer, is to await suppuration as a result of the retained membranes, or to induce it by such means as injection of terebene oil; induction of suppuration, however, is difficult to achieve because of the diffusion and absorption of the injected fluid. When suppuration is established, treatment is carried out as for the first category, in which infection pre-existed.

Expectoration of the intact membrane after emptying the cyst by puncture remains for us only a theoretical possibility, since we have never seen it happen. This could be explained by the disparity between the size of the membrane and that of the bronchial lumen, so that passage of the former is impossible even in the most severe bouts of coughing, whether or not induced by intrapulmonary transthoracic injection.

On the other hand, expectoration of the endocyst occurs reasonably easily and within a relatively short period after intrafocal medication when pulmonary suppuration is present, since the latter dilates the bronchial lumen at the same time as it fragments the parasitic membrane.

#### Case 3

A married woman aged 30 had a hydatid cyst in the left postero-inferior lobule. Pneumothorax was first induced, later followed by the intrapleural injection of 25 ml. of 50% glucose solution containing one ampoule of cibazol. Another sclerosing solution, "neo-varisclerin," was run in on three subsequent occasions, and the lung was then helped to re-expand by aspiration of the pneumothorax. All this took four months, during which time the patient was also undergoing desensitization with an antigen prepared by Dr. Pirotsky, following Dr. Calcagno's method, according to whom this procedure should kill the cestode.

Failure to reinduce pneumothorax having demonstrated the pleural adhesion, the cyst was punctured without mishap. Then 20 ml. of fluid was drawn off and replaced by 10 ml. of 2% formol. Ten minutes later a similar amount was extracted and a further 10 ml. of 2% formalin was run in. As a final step, total evacuation of the cyst was attempted by carrying out injections into the cavity, some of penicillin and some of sulphonamides ("rubiazol" and prontosil), over a period of two

months. After an interval of air-distension, the cyst collapsed and incarcerated the membrane.

Months later, since the patient had not managed to cough up the membrane, suppuration of the surrounding lung parenchyma was induced by the injection of terebene oil and the patient was temporarily discharged until the suppuration had become established some six months later. At this stage amounts of 20 to 40 ml. of physiological saline were injected into the area to act purely mechanically by causing coughing and subsequent expectoration. Five injections in six days were enough to achieve the complete expulsion of the parasitic membrane followed by the almost immediate subsidence of the pulmonary infection despite the fact that no active therapeutic substance had been used. This supported the belief that the pulmonary suppuration was caused mainly by the retained endocyst acting as a foreign body.

### Conclusion

We consider that this method of bloodless treatment which we have devised is worthy of trial in strictly selected cases of hydatid cyst before deciding in favour of surgical intervention, which should remain a last resort.

The advantages of the method are: (1) It can be completely effective. (2) It does no injury to the body, whether locally or systemically. (3) It does not hinder the recovery of the affected broncho-pulmonary area. (4) It carries less risk than operative methods, which involve loss of blood and some mutilation. (5) It can be carried out on out-patients, to the advantage of either the State or the individual, who is spared the expense, and of the family, whose breadwinner can with care engage in some forms of light work without prejudicing his recovery. This double advantage of ambulant treatment would compensate for the longer time that is sometimes required for medical treatment as compared with surgical methods, particularly since the latter may also occasionally be prolonged by unfortunate complications. (6) It is no bar to subsequent operative treatment, which should be held in reserve in case of failure of this bloodless method.

## RECENT ADVANCES IN OUR KNOWLEDGE OF THE MALARIA PARASITE\*

BY

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The demonstration by James and Tate (1938) of the essential part played by the exo-erythrocytic forms in the life cycle of *Plasmodium gallinaceum* started an intensive search for similar forms in the case of mammalian and human malaria parasites. The subsequent demonstration of the pre-erythrocytic forms of this parasite (Mudrow, 1940; Shortt, Menon, and Iyer, 1940; Huff and Coulston, 1944) intensified the search for similar pre-erythrocytic forms in simian and human malaria.

The investigation was taken up by malariologists in Europe, America, Asia, and Africa, and various findings were reported, none of which secured general recognition. A critical survey of these results was made by Angelini (1947), who came to the conclusion, subsequently justified, that none of the claims had been substantiated. This was the position when Fairley (1945, 1947) described the results of his classical experiments at Cairns with human volunteers infected with *P. vivax* and *P. falciparum* by the bites of

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