been shown that bodies suspended in a watery solution run into rouleaux only when possessed of a fatty covering. The absence of this phenomenon in pernicious anaemia may be due to a defect in the stroma of the red blood corpuscles, in the lecithin and cholesterin elements, which though not true fats are yet of a fatty nature. The condition of poikilocytosis and abnormal staining of the red cells, sometimes present in pernicious anaemia, may be due partly to the same defect. On such a hypothesis of the blood defect in pernicious anaemia, the results of its somewhat empirical treatment may possibly be explained. The giving of bone marrow recommended by Fraser may be merely a method of supplying to the blood-forming organs those constituents of stromae which they lack. Lecithin is certainly known to exist naturally in the bone marrow. Arsenic, which, since its introduction by Byrom Bramwell in this disease, has been found to benefit a certain number of cases, may act on the stroma of the red blood corpuscles in such a way as to remedy this defect and increase their resistance. Indeed, lecithin has been found to increase the number of the red cells, and some experiments which I have made with regard to the action of arsenic on these cells have gone to show that it increases their resisting power. Nor is there any inherent reason, if a deficiency of iron, for example, or of calcium can cause morbid conditions, why disease may not also be set up by a lack of such necessary constituents as lecithin or cholesterin."

The main contention was that pernicious anaemia is due to a lack of "those materials which go to form the stroma of the red blood corpuscles." Not only this conclusion, but the premisses upon which it was based, seem to resemble very closely those which have later been admitted. For example, Whipple² wrote in 1922:

"Our conception of pernicious anaemia is that there is a scarcity of stroma-building material or a disease of the stroma-forming cells of the marrow which limits the output of red cell framework. There is plenty of pigment material (an excess in fact) as evidenced by the high colour index or the saturation of the red cells with haemoglobin."

It is unnecessary here to attempt to recapitulate the recent advances in knowledge of pernicious anaemia, which furnish one of the most brilliant successes of therapeutics. The value of liver diet and of liver extracts has been firmly established. As to what the substance is which, occurring in various organs, seems to supply the material lacking for stroma formation, there is still doubt—a doubt which may soon be dispelled. There is a good deal of evidence to show that more than one substance, and possibly not always the same substance, may be lacking. My original conjecture that the failure to produce red cells in pernicious anaemia might be due specifically to lack of lipid material seems to have been disproved. At any rate, this cannot be the sole factor, so far as one can judge from the evidence of liver extracts.

A SUGGESTION PUT FORWARD

My object in publishing this note is, however, not to derive a melancholy satisfaction from the fact that I was nearer the mark than the authorities of my early days were willing to allow, but to make a further suggestion. As Whipple says in the paper already quoted: "hypotheses are of some value for further work, even if there be little or no truth in them." Having formulated this hypothesis of the causative factor in pernicious anaemia, I attempted in 1908 to proceed to the next obvious step, which was to administer the separated stroma material in pernicious anaemia. I tried to obtain this by haemolysing defibrinated ox blood and separating the stroma by centrifuging. Having at my disposal only a very small centrifuge, I obtained only an insignificant amount of stroma material. Having also no facilities for testing this material clinically, even if I could obtain a sufficient quantity of it, and

having little hope of persuading anyone to test the fruits of a discredited hypothesis, I gave up the work, discouraged. During recent years, when opinion has come round in the direction of believing that pernicious anaemia is due to some lack of stroma-forming substance, I have wondered that no one has done the experiment I originally contemplated, and which still seems to me a crucial experiment. It may have been done and escaped my notice. In the belief that it has not been tried, I venture to put forward the following considerations in the hope that someone who has the requisite plant and facilities will hazard the gamble.

If pernicious anaemia is due, partly or wholly, to a lack of the materials (in the widest sense) necessary for stroma formation, it would seem that the most direct and complete method of supplying this deficiency would be to administer the actual stroma material as a whole and unchanged. Presumably all the materials necessary for the ultimate stages of stroma formation are there present. As it is impossible to foretell to what extent, if any, the stroma constituents may be destroyed by digestion, a saline suspension of stroma might first be tried intramuscularly. It is more than probable that, if this were to be effective at all, it would act quickly in pernicious anaemia.

If it did act, it might be easier to obtain the active principle from stroma material than from liver or other organs, because the chemical structure of the stroma must almost certainly be less complicated than that of liver. The stroma is only a box, while the liver has many functions to perform other than those concerned with blood metabolism. It is possible, however, that, even if the supposition be correct (that pernicious anaemia is due to lack of stroma-building material), the administration of completed stroma material will not supply the deficiency, because the blood-forming organs may deal with the precursors of that material and may not be able to avail themselves of the material in the full and final stage of its synthesis. This possibility is, however, not sufficiently deterrent to oust the propriety of trying the administration of stroma material in pernicious anaemia. If this proved successful, it might provide a therapeutic agent, cheaper and more concentrated than liver extract, it might furnish a simpler matrix for extracting the active principle, and it would certainly provide further direct evidence as to the aetiology of pernicious anaemia.

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CRYPTO-EMPYEMA

BY

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By crypto-empyema is meant an empyema that cannot be diagnosed by repeated needling, even under an anaesthetic. The term is useful, if for no other reason than that it reminds the practitioner that empyema ought to be diagnosed and treated, on occasion, when pus cannot be found by the exploring needle.

Three cases of this condition that have come under my care may be briefly related.

CASE I

A public school boy developed a left empyema nine days after the onset of pneumonia. Temperature was 103°, pulse 100, respirations 30. A large empyema was evacuated by rib resection after locating the pus with a needle. It contained streptococci and saprophytes. For a few days he did well, then the temperature rose again, and the boy looked

very ill. Twelve days after the first operation an anaesthetic was given and the residual empyema searched for by needle, but it could not be found. Four inches of the posterior part of the fifth rib, and two inches of the fourth were resected, and the whole hand was put in to explore. On breaking down a long stretch of adhesions posteriorly a cavity containing one ounce of foul pus was opened at the back of the root of the lung. The original empyema cavity was quite clean. A tube was inserted. After a long illness the boy made a perfect recovery.

CASE II

A gentleman, aged 45, was referred to me by Dr. J. A. Nixon and Dr. Dyer. He had been ill five weeks with influenzal pneumonia; the temperature was still 99° to 100° every night, there was dullness at the right base, and the patient looked ill. A skiagram showed opacity of the right base. A needle had been put in three weeks before, but found no pus. Under ether, I needled in five places but found no pus. A piece of the ninth rib was resected in the posterior axillary line, and the pleura opened; it was clean and non-adherent. The lung was adherent further back and felt firm. The clean pleura was closed, more rib removed posteriorly, and adhesions separated by the finger. Two small loculi of pus were found, one alongside the vertebral column, and another between the lobes of the lung. A bifurcated tube was put into these, the chest wall sewn tightly around it, and the projecting end clamped. Twice a day the discharge was drained off under the surface of carbolic lotion. In ten days the empyema had healed.

CASE III

I was called by Dr. C. Bernard to see a man, aged 60, who had appeared to recover from influenza in the epidemic of January, 1933, but after being up a week had to go back to bed with fever, shortness of breath, and dullness of the base of the right lung, with absent breath sounds and diminished vocal fremitus. The heart was not displaced. A needle was inserted in two places, but no pus was found. He was removed to the Bristol Royal Infirmary, a very sick man. Under an anaesthetic the chest was repeatedly needled, but no pus was found. A piece of rib was resected posteriorly, and clean, non-adherent pleura opened. This was closed again, and adherent pleura separated back until an abscess containing several ounces of foul pus was opened between the base of the lung and the dome of the diaphragm far in. It was treated as in Case II, and an excellent recovery followed.

The main lesson to be learned from these cases is that one must not be dissuaded from diagnosing empyema because repeated needling fails to strike pus. In a patient who has suffered from pneumonia, and especially influenzal pneumonia, if the temperature keeps up for more than three weeks, if dyspnoea and sweating are present, and dullness is found at the base of the lung with diminished breath sounds and vocal fremitus, that is enough to warrant an exploratory operation and a determined effort to find pus with the finger, or if necessary the whole hand, inside the chest, even if the heart is not displaced. A skiagram is useful; it will show some opacity, but it cannot be relied on to tell us exactly where the abscess is. The loculi of pus may be small, but they are likely to lead to a long and serious illness if not evacuated.

There are two exceptions to the rule just laid down. If tubercle bacilli have been demonstrated in the sputum a diagnosis of crypto-empyema would be precarious. If the patient is very toxic, bringing up quantities of putrid expectoration, and especially if it contains elastic fibres, there is probably an open abscess or gangrene of the lung, and operation would be too dangerous. A closed abscess of the lung might well be confused with crypto-empyema, and if the pleura was found non-adherent, it would be safest to make a two-stage operation of it, packing off with gauze at the first intervention so as to promote adhesion of the lung to the chest wall. Probably some cases of abscess of the lung are better left alone.

It may be objected that the surgeon following this principle will often find himself meddling with an

"unresolved pneumonia." We do not agree. When from the so-called "unresolved pneumonias" with fever and physical signs persisting for three weeks there have been deducted the tubercles, the pleuritic effusions, the empyemas, and the abscesses, there is little if anything left.

SODIUM SONERYL AS A BASAL HYPNOTIC A REPORT OF 150 CASES

BY

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Sodium soneryl is the sodium salt of butyl ethyl barbituric acid, and has been used as a basal hypnotic before general anaesthesia in 150 cases at St. Bartholomew's Hospital between January 30th and April 14th, 1933. Chemically sodium soneryl resembles nembutal, which is sodium ethyl (1-methyl-butyl) barbiturate; clinically it is of lower toxicity, and is administered in larger doses. The presence of a methyl group may be the cause of the greater toxicity of nembutal. The series of cases includes patients whose ages varied from 6 to 70 years, and operations were performed for diseases of the ear, nose, and throat (45), the abdomen (39), the uro-genital tract (36), bone (11), the breast and neck (10), and for hernia (9). In every case the anaesthetic was administered by means of Boyle's nitrous-oxide-oxygen-ether apparatus. In the ear, nose, and throat cases, and in nearly all the abdominal ones, the anaesthetic was given by the endotracheal route, comprising in all eighty-five cases.

Sodium soneryl was taken by the oral route, in capsules containing 0.15 gram each. In the first eleven cases the dosage was as follows. Two capsules (0.3 gram) were given at 8 p.m. the day before operation; this ensured a good night's sleep, though in four instances the patients were found to be sweating the next morning. On the day of operation sodium soneryl was given one hour before the induction of anaesthesia, this dose being regulated according to the weight of the patient. Thus from 6 to 8½ stone 0.45 gram (three capsules), from 8½ to 10½ stone 0.6 gram (four capsules), from 10½ to 12½ stone 0.75 gram (five capsules), and above 12½ stone 0.9 gram (six capsules) were administered. Gynaecological operations were performed on six of these patients, and it was found that they were still drowsy on the morning of the operation, so that enemas were imperfectly returned; on this account the evening dose was discontinued. Doses of 0.45 gram were generally found not to produce sleep in adults, and the dosage was therefore again simplified, the following scale being adopted for the majority of the cases in the series: below 10 stone, 0.6 gram; between 10 and 12 stone, 0.75 gram; and above 12 stone, 0.9 gram. In children (below 12 years) 0.3 gram was given, followed by a further dose of 0.15 gram if the child was not asleep or drowsy after half an hour. The capsules were given one hour, and atropine (grain 1/75) fifteen to thirty minutes, before operation. No morphine was given except in three cases.

EFFECTS OF SODIUM SONERYL

The following effects were noted: in ninety-seven cases the patient was asleep on reaching the operating theatre; in forty-six the patient was very sleepy; in five no definite effect was noted; and in two the patient was excited. All arrived in the theatre breathing naturally, with no trace of cyanosis and no stertor. Sleep was commonly produced in thirty to forty-five minutes. The induction of anaesthesia was very smooth, the length of time taken being the same as in non-premedicated patients, averaging about six minutes for moderately deep anaesthesia by nitrous oxide, oxygen, and ether. In the majority of