reason the diet should follow very much the lines adopted for gouty patients. Besides avoiding foods rich in purins, an adequate supply of vitamins should be ensured. This is of prime importance, because osteo-arthritis is undoubtedly associated with the absorption of toxins from a sluggishly acting bowel. Good results frequently follow measures directed towards changing the character of the intestinal flora, either by the use of Bulgarian soured milk or by such a preparation as lacto-dextrin (supplied by the Battle Creek Company).

Drugs

So far as drug treatment is concerned, the old-fashioned "Chelsea pensioner"—compound confection of guaiacum—or its more modern prototype—tabloid guaiacum and sulphur co.—is of distinct value. It probably acts as an intestinal disinfectant. Lugol's solution finds favour with many prescribers. In certain forms of glandular deficiency associated with the menopause, thyroid medication is clearly indicated. For the local treatment of the synovitis accompanying arthritis of the knee, nothing beats a Scott's dressing. Although no spas can claim anything of the nature of a specific in the treatment of osteo-arthritis, many patients undoubtedly derive benefit from a visit. This is probably accounted for by the change of air, regulation of diet and exercise, and the placing of the patient in such an environment that the *vis medicatrix naturae* can act to the best advantage.

Physical Methods

In addition to the general measures briefly outlined above, there are certain physical methods of treatment which are of the greatest value in restoring movement to stiffened joints and muscles and in the relief of pain.

For the first of these the deep pool bath is extensively used. It is of a sufficient depth to allow a patient to stand upright and to walk a step or two, and wide enough to permit exercises. Its temperature is kept at about 100° F. Combined with the pool is an underwater douche at a temperature of about 10° above that of the bath. This has a powerful effect on the skin circulation, and in itself constitutes a very efficient form of massage, as well as relieving pain. As all objects weigh less in water than in air, a limb immersed in water can be moved with much less fatigue than in ordinary circumstances. The water supports the limbs, and movements are permitted that would be otherwise impossible. In addition to the actual mobilization of a stiffened joint, the fact that movement is possible at all has an excellent mental effect on the patient, and he is thereby encouraged to persevere in his efforts. For the relief of pain, heat in some form or another is a sovereign remedy. To be effectual it should be intensive, or as hot as can be borne. It may be applied in various ways—the hot immersion bath with an underwater douche 10° higher than the bath, radiant heat, or the high-frequency current (diathermy). In deep-seated parts, such as the hip, diathermy is the method of choice. For local applications to more accessible parts the hot pack of peat, mud, or paraffin wax is of value. As, owing to the immobilization of the affected joint, the muscles which control it are apt to waste, underwater massage and manipulation—given by either the Aix or the Vichy system—will restore their tone, and at the same time remove effusions that are liable to form owing to the sluggishness of the blood and lymph circulation.

Active and Passive Movements

Keeping in mind the dictum that no joint can possibly be healthy unless it is moved, or, in other words, unless it is functionally active, the question naturally arises as to whether osteo-arthritic joints are to be kept moving. So far as possible movement should be maintained, but it should be more passive than active. The degree of pain

that attends such efforts is the best guide. It has been wisely said that in osteo-arthritis one should train up the osteophytes in the way they should go. This is not to say that in the acute stages of joint inflammation movements are to be forcibly carried out. At this period rest with soothing applications is essential. When, as frequently happens, walking sets up intense pain and interferes with the patient's general health, the application of a calliper splint must be considered. Properly fitted, such an appliance will save untold pain. It is inconvenient, cumbersome, and much disliked, but the assurance can be given that in time it can be dispensed with. In the case of the hip, with the cessation of the constant grinding of eburnated bone surfaces one upon the other, the osteophytes interlock, and the periarticular structures become fibrosed and add to the stability of the joint. Mobility is seriously interfered with, but pain disappears, and although the patient walks with a limp, he is able to live in comparative comfort. The knee is somewhat different. Its strength lies in its ligaments, and osteophytic outgrowths do not interfere to such an extent with the apposition of the articular ends of the bones concerned as is the case with the hip. They do, of course, limit movement, but a patient can walk quite well with very little play between the two bones. After wearing a calliper splint for the knee for some time, it is often found that on leaving it off there is still enough movement at the joint to permit walking without a perceptible limp. By cautious manipulation and the judicious employment of one or other of the methods of physical treatment briefly referred to above, the range of movement may be considerably increased.

Operative Measures

There will still remain, however, a certain number of cases in which neither physical methods of treatment nor fixation will relieve the intolerable pain. The question of operative intervention will then have to be considered. Such procedures have for their object either the correction of deformities by osteotomy or the removal of some inter-articular cause of arthritis—such as a misplaced semilunar cartilage or a loose body—or they may be designed with the aim of enabling the joint to be used without pain. This might entail the removal of osteophytes, and an excision of the joint or an arthrodesis to secure bony ankylosis. In this connexion it must be remembered that cases of osteo-arthritis are by no means ideal subjects for extensive operative measures.

A CASE ILLUSTRATING FAILURE OF INTRAVENOUS LIVER THERAPY IN PERNICIOUS ANAEMIA

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It appears justifiable, in view of the prominence recently given to the value, in certain cases of pernicious anaemia, of liver preparations suitable for intramuscular or intravenous injection^{1 2 3 4 5 8 10 12}, to record a single case in which this mode of therapy proved ineffectual, though it is admitted that the data furnished are not sufficient to enable completely definite conclusions to be drawn.

CASE RECORD

Female, aged 62, married. Admitted to the Royal Infirmary, Edinburgh (under the care of Professor W. T. Ritchie), on February 2nd, 1932, complaining of "bloodlessness and pains all over" of three years' duration, "breathlessness" for one year, and "loss of appetite" for about two months.

No satisfactory medical history was available, but it appeared that the patient had not been in good health for three years. She had noticed oedema of the feet and ankles, especially in the evening, during that period. Intermittent pain and stiffness in various situations—notably the back, heels, and limbs generally—had made it difficult for her to get about, but these symptoms had not been so prominent during the six weeks immediately preceding admission, as severe breathlessness on exertion had rendered the patient practically bed-ridden. For about two months towards the end of 1931, "pain across the stomach," relieved by vomiting, had been present; the appetite thereafter became poor, but pain and vomiting ceased. Soreness of the tongue was not complained of. There was no history of haemorrhage. The patient stated that she had lost weight. She gave a history of an operation for "ovarian tumour" forty years previously, and of "gall-stones" twenty years previously, but in general appeared to have been a healthy woman up to the time of onset of the symptoms already described.

Apart from the fact that the patient was one of a family of fifteen, of whom eleven "died young," the family history revealed nothing of note.

Physical Examination

General nutrition poor, but no gross emaciation. Some oedema of the feet present. Patient very pale, with a "lemon yellow" tint. Van den Bergh reaction, positive delayed direct. Icterus index, 14. Pulse rate, 108 per minute: blood pressure, 114/64. Heart not enlarged; blowing systolic murmur audible all over praecordia, loudest in pulmonary area. Marked muscular weakness in lower extremities, but reflexes normal, and sensation (including vibration sense) unimpaired. Tongue: very pale, clean, and smooth; no ulceration, and no subjective soreness. Abdomen: scars of former operations present, otherwise nothing abnormal detected. On account of the patient's great weakness, examination of the gastric juice was not carried out. Stools: no abnormal appearances; benzidine reaction for occult blood, negative. Urine: healthy. Respiratory system: no abnormal signs detected.

Blood Examination

Red blood cells, 885,000 per c.mm.; haemoglobin, 18 per cent. (Haldane); colour index, 1.06; white blood cells, 2,660 per c.mm. A second count gave the following figures: red blood cells, 813,000 per c.mm.; haemoglobin, 20 per cent.; colour index, 1.25. Reticulocytes, 3.4 per cent. Anisocytosis was marked, megalocytic forms being prominent, many having the oval shape emphasized by Davidson and Gulland.⁶ A Price-Jones curve was not constructed, but careful inspection of the film left little doubt that this would have been of the typical broad-based variety, with deflection of the summit to the right. There was some poikilocytosis. A few cells showed punctate basophilia: polychromasia was not seen. No nucleated red cells were observed, even after extensive search. Platelets were obviously diminished, such as were present occurring singly rather than in groups. A differential count of 100 leucocytes gave the following result: neutrophils, 64 per cent.; lymphocytes, 35 per cent.; monocytes, 1 per cent. In view of the unexpectedly high proportion of neutrophils, considering the leucopenia, another count was made by an independent observer on another film, when practically identical figures were obtained. Many of the neutrophils showed hypersegmentation of the nucleus, indicating a "shift to the right" of the polynuclear count.

TREATMENT AND PROGRESS

From February 3rd to 9th (inclusive) the patient was given daily intravenous injections of 5 c.cm. of a liver preparation which has recently been the subject of favourable comment in the literature.^{1 2 4 10 12} The 5 c.cm. dose is said to contain the active principle derived from 100 grams fresh liver. No undesirable effects appeared to be associated with the injection, but there was no improvement in the patient's general condition, and no reticulocyte reaction occurred. As already noted, the reticulocyte level was 3.4 per cent. on admission. On the second day of treatment the figure was 5 per cent., but thereafter a fall occurred, the reticulocyte percentage varying from day to day between 0.5 and 1.5.

On February 10th, the patient's condition being obviously one of extreme danger, a blood transfusion was decided upon. Both the patient and the daughter selected as donor belonged to Group IV (Moss); the bloods were directly tested for incompatibility, and no agglutination was found. Shortly after the commencement of the operation, however, the patient became extremely distressed, restless, and dyspnoeic. The transfusion was stopped immediately and stimulants given, but the patient died one hour later.

Post-mortem Examination

This was carried out on February 11th, thirty-one hours after death, and the appearances typical of pernicious anaemia were found. There was a slight generalized yellowness of the skin, and the legs showed some oedema. The serous sacs contained a small quantity of clear yellowish fluid. The heart was slightly enlarged and globular in shape, the myocardium being pale and flabby, and showing, in the region of the right ventricle, considerable fatty infiltration. There was a slight increase of bright yellow subepicardial fat. The lungs were oedematous, particularly at the bases. The mucosa of the stomach had a very atrophic appearance. The liver was enlarged and pale in colour. The spleen was enlarged, soft, and bright red. The kidneys presented a pale yellow appearance. Apart from some oedema, the brain showed no abnormality. In the centre of the shaft of one femur, fat had been completely replaced by bright red erythroblastic marrow, of diffuent, almost creamy, consistency; there was considerable erosion of cancellous bone. The first ribs also showed a marked erythroblastic reaction. The liver showed a definite Prussian blue reaction, the spleen and kidneys a fainter one.

Microscopical examination of the bone marrow revealed the presence of very active haematopoiesis, this having the characters described by Davidson and Gulland⁶ as typical of pernicious anaemia. The erythroblastic areas showed definitely a megaloblastic reaction, many cells of very primitive type being seen. Equally characteristic was the large amount of leucopoietic tissue present; in these areas, the predominant cell was the myelocyte; polymorphs were scanty, and megakaryocytes also much reduced in numbers. The liver showed extensive fatty changes; the spleen, packing with red corpuscles; and the kidney, slight arterio-sclerotic changes, together with marked degeneration of the tubular epithelium. Professor G. Lovell Gulland was kind enough to consider fully all the facts of this case, including the microscopical sections above described, and as a result had no hesitation in stating the case to have been one of pernicious anaemia.

COMMENTARY

The question arises whether, in this case, the diagnosis of pernicious anaemia may have been wrong, though the opinion of Professor Gulland, quoted above, naturally renders this unlikely.

The clinical and pathological findings are admittedly compatible with this diagnosis. It remains to be discussed whether they are compatible with any other diagnosis. The post-mortem data put any kind of "secondary" anaemia out of court—a "secondary" anaemia of high colour index type, with leucopenia, is in any event a most unusual phenomenon. Leukaemia and acute lymphadenoma can be similarly excluded. Aplastic anaemia was, at the end, the diagnosis favoured clinically, on account of the lack of response to treatment, but, in view of the intensely active marrow demonstrated at necropsy, was proved to be incorrect. The condition which appears most to warrant discussion is that of the "obscure haemolytic anaemia" group referred to by Davidson.⁵ One imagines that certain of these cases would be regarded

by Lord Dawson⁷ as examples of "acholuric jaundice," since he does not consider a normal blood fragility incompatible with this diagnosis, and further states that, while the marrow response in acholuric jaundice is usually normoblastic, it may be megaloblastic, with a high colour index type of anaemia. Though the fragility of the erythrocytes was not investigated in the present case, any such diagnosis appears to be ruled out by the co-existence of a hyperplastic marrow with a low percentage of circulating reticulocytes. In haemolytic anaemia, death may occur in the presence of extensive marrow hyperplasia, if blood destruction runs ahead of even markedly increased blood formation; but, in these circumstances, the circulating reticulocyte percentage is high. Conversely, as emphasized by Lord Dawson,⁷ death may result from diminished marrow output, even though blood destruction may not be excessive; but, in these cases, the small number of reticulocytes in the circulation can be shown at necropsy to have resulted from marrow aplasia. Low circulating reticulocyte percentage and hyperplastic marrow cannot coexist (as they did in this case) unless there is defective maturation and emigration of the marrow cells—the characteristic feature of pernicious anaemia. As already noted, the highly characteristic findings were present in this case, not only of active megaloblastic proliferation in the marrow (with little emigration of new red cells into the circulation), but also of considerable leucopoietic activity (with nevertheless a leucopenia in the circulating blood). The conclusion seems justified that, clinically and pathologically, this case satisfied all the criteria of pernicious anaemia.

The question of whether the lack of response to treatment resulted from the use of an inactive liver preparation, or from the case being truly a "liver-resistant" one, cannot be definitely answered. It can only be said that the particular preparation used has, in the hands of other workers, given apparently uniformly successful results.^{1 2 4 10 12} It is stated that the reticulocytes usually commence to rise within twelve to twenty-four hours of the first injection,¹² and the maximum reticulocyte response should occur on the sixth or seventh day. It would thus appear that in the case under discussion sufficient time was given for the signs of improvement to have appeared had they been going to do so. It is regrettable, alike on humanitarian and on scientific grounds, that no opportunity occurred of noting whether or not any other preparation might have had a beneficial effect. Had such arisen, it would have been strong evidence in favour of the inactivity of the substance first employed. As it is, it can only be said that the conclusion may or may not be justified that the preparation used was inactive. It may be that variations in activity occur even in different samples of the same product, as was recently emphasized by Wilkinson¹³ in the case of stomach preparations, but certainly no case of failure of any sample of this particular product appears to have been reported hitherto.

The possibility exists that this may have been a true "liver-resistant" case. That such cases occur, when oral liver therapy is employed, is admitted by most observers; Naegeli and Gloor⁹ give the figure as 10 per cent. of all cases. The general opinion, however, appears now to be that the lack of response is due to inability on the part of such patients to absorb the active principles when the liver is administered by the mouth, and that no undoubted case of pernicious anaemia should fail to respond to parenteral administration of a suitable liver preparation (Davidson,⁵ Gänsslen⁸). Prior to the introduction of preparations suitable for injection, Davidson and Gulland⁶ had suggested marrow aplasia as a possible cause of failure of liver therapy. While the marrow in the present case was not investigated in many different parts of the

body (as, according to Sheard,¹¹ is, strictly speaking, necessary), the investigation showed that at any rate a large part of the marrow was highly active. Yet the therapy employed should, according to the observers already quoted, have been quite sufficient to initiate a remission. In the absence, however, of definite proof of the activity of the liver preparation employed, it is impossible to decide whether this case was genuinely "liver-resistant" or not.

SUMMARY

1. A case is described which, clinically and pathologically, presented the features of pernicious anaemia.
2. It failed to respond to intravenous injections of a liver preparation which has been found by other workers to be highly effective.
3. It is suggested either (a) that not all samples of this preparation are equally potent, or (b) that the case is an example of "liver-resistant" pernicious anaemia.

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THE NOMENCLATURE OF ECLAMPSIA *

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The text of our paper is the following case:

Mrs. McG., aged 26, a 3-para, had had two normal confinements. She attended the pre-natal department once, in September, 1931, but failed to return. At that time there was no albumin, but the feet were greatly swollen. She was admitted to the hospital on October 5th with a history of having had two fits. She was given morphine 1/2 grain at 11.30 a.m. On examination she was found to be about thirty-three weeks pregnant; general condition good; restless. Pulse 70, tension fair; blood pressure 122/70; semiconscious. Gastric lavage with good results. Colonic lavage, excellent result. Catheter was passed, but there was no urine in the bladder. At 10.45 p.m. the patient was still semiconscious. At 12.30 p.m. colonic lavage with excellent result. Morphine 1/4 grain given on account of restlessness. Submammary saline given; blood pressure 118/70. Still semiconscious. On October 6th, general condition fair, patient in labour; stillborn foetus, 4 lb. 12 oz., delivered spontaneously at ten hours. There were signs of consciousness returning, and patient seemed better; colonic lavage achieved a good result, but the patient relapsed into a more comatose condition; blood pressure 142/70; blood urea 30 mg. per cent. At 6.15 p.m. she had a fit lasting three minutes; morphine repeated. Patient had further twenty-nine fits before 11.40 p.m., totalling 31 in all. She died at 11.47 p.m.

* Read before the Obstetrical Section of the Royal Academy of Medicine in Ireland, March, 1932.