Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Haematological Applications of A.C.T.H. and Cortisone

SIR,—While I have no clinical contribution to offer in the controversy concerning the haematological applications of A.C.T.H. and cortisone, some of the experimental findings of my colleagues and myself in studies of animal bone marrow may be relevant. Our work started in 1944[1] when, in an attempt to solve the mystery of the large numbers of lymphocytes daily leaving the blood, we began to apply quantitative methods to the study of the cell content of bone marrow. We used the costal marrow of the rabbit. The technique was unsatisfactory in several respects, but, taking all these into consideration, we concluded at that time that the number of lymphocytes normally present in the bone marrow was of the same order as the number daily leaving the blood.

In the meantime, Dougherty and White[2] had reported that A.C.T.H. and 11-oxysteroids exerted a lymphoclasic action. Though unable to confirm their results in either blood or lymphoid tissue,[3] and though with cortical extract in the dosage employed we actually induced a lymphoid tissue hyperplasia, we nevertheless felt that without accurate knowledge of the bone marrow it was difficult to assess changes in the circulating blood, such as eosinopenia or lymphopenia. Accordingly, after numerous trials, we found that the bone marrow of the guinea-pig humerus lent itself much more effectively to quantitative study, and we proceeded to investigate the effects of single doses of A.C.T.H. and cortical extract ("eschatin," Parke, Davis & Co.) on the bone marrow.[4] We found no marked change in the marrow eosinophils, but, somewhat to our surprise, a significant increase in the marrow lymphocytes instead of the anticipated decrease. This seemed worth following up, and accordingly we treated a further batch of guinea-pigs with daily injections of A.C.T.H. for 7 days.[5] This time, though there was a slight increase in the lymphocytes and no definite change in the eosinophils, there became evident an increase in both the myeloid (neutrophil) and erythroid cells of the marrow.

However, one injection of A.C.T.H. daily did not seem to be the best way of giving this substance. Furthermore, it was thought that more precise information might be obtained by using individual steroid compounds. Accordingly, together with Drs. Ancill, Holt, and Owen Smith, we gave daily injections of cortisone (5 mg. per injection) for 7 days to 30 young male guinea-pigs. A detailed account of these experiments is at present being prepared for publication, but in view of the correspondence in your columns a brief summary of the results may be of interest to your readers.

As compared with 30 control animals—and despite what our endocrinological colleagues told us about the relative refractoriness of the guinea-pig to cortisone—there is a statistically significant increase in the absolute count of the nucleated cells of the bone marrow, so appreciable that it is reflected in an increase of the specific gravity also. The change affects both the myeloid (neutrophil) and erythroid cells, but more especially the latter, to such an extent that one is tempted, even apart from the present controversy, to speculate on a possible function of steroid compounds as erythropoietic stimuli.

Ten experiments with hydrocortisone (free alcohol) gave similar results. Seven experiments with compound A appear to give evidence of increased transformation of reticulum cells to granulocytes, with what may be a short-circuiting of the typical myeloblast stage. However, neither the eosinophils nor the lymphocytes of the bone marrow underwent any striking changes, and the mystery of the latter remains as elusive as ever.—I am, etc.,

Bristol. J. M. YOFFEY.

REFERENCES

1 Yoffey, J. M., and Parnell, J. (1944). *J. Anat., Lond.*, **78**, 109.
2 Dougherty, T. F., and White, A. (1944). *Proc. Soc. exp. Biol., N.Y.*, **53**, 132
3 Yoffey, J. M., and Baxter, J. S. (1946). *J. Anat., Lond.*, **80**, 132.
4 —— Metcalf, W. K., Herdan, G., and Nairn, V. (1951). *British Medical Journal*, **1**, 660.
5 Hudson, G., Herdan, G., and Yoffey, J. M. (1952). Ibid., **1**, 999.

The Perennial Peptic Ulcer Palaver

SIR,—May I express my pleasure in reading Sir Robert Hutchison's grand remonstrance on peptic ulceration (August 30, p. 513)? It is an honour to have one's breeches taken down by such a master of the art. I have received verbal chastisement at the same hands before, but never so pleasantly phrased.

In framing my reply, my chief difficulty is that I agree with everything that Sir Robert wishes to say to me. I always seek surgical advice for patients with chronic ulcers, both before and after haemorrhage, though my confidence in this course has been slightly shaken by a sideways glance at that part of the letter addressed to the surgical Ogilvie (in the light of whose reputation the lesser Ogilvies shine with reflected glory).

In conclusion may I, through you, Sir, tell Sir Robert of the keen pleasure which it has given to his many friends in Newcastle to read a letter from him composed in the old authentic style. We can almost hear him saying, "Hoots, toots," once more.—I am, etc.,

Newcastle-upon-Tyne. A. G. OGILVIE.

SIR,—I am without an answer to Sir Robert Hutchison's gentle banter (August 30, p. 513), except to particularize Arthur Hurst's remark by saying that the worst thing that happened to gastric surgery was the remarkable success of a usually unsuccessful operation in the case of the President of the Royal College of Physicians.

Dr. H. Maitland Moir (p. 514) is not alone in regarding the stomach purely as a producer of acid. Meulengracht and others have shown that the cardiac glands and the glands of the pars pylorica secrete an alkaline fluid rich in mucus, and more recently J. N. Hunt has studied the alkaline factor in gastric secretion: in the summary of a recent paper[1] he says: "A reduction in the concentration of acid in the gastric contents does not necessarily mean a reduction in the amount of acid secreted. Duodenal regurgitation is of only minor importance in neutralizing the acidity of the gastric contents. Most of the alkali is secreted by the stomach."—I am, etc.,

London, N.W.8. HENEAGE OGILVIE.

REFERENCE

1 *Guy's Hosp. Rep.*, 1949, **98**, 185.

A Gastric Gossip

SIR,—Mr. Peter Konstam, having added (September 13, p. 614) some interesting facts from West Africa to the discussion of Sir Arthur Porritt's gastric gossip, emboldens me to produce a few from East Africa. There we find a considerable variation in the diseases amongst the tribes for very similar reasons to those quoted for West Africa by Mr. Konstam. In Uganda, with which I am most familiar, besides the tribes of the territory we have a considerable number of immigrants from the Belgian Congo.

Up to recent years the incidence of peptic ulcer in Uganda appeared to be very small. In a review of 1,020 necropsies done at the Kampala Government hospital prior to 1949 evidence of gastric ulceration was found in only 3 cases. These figures are not easy to understand, as my colleagues just over the border in the Belgian Congo have been operating on peptic ulcer patients for more than 10 years.

In June this year, in Uganda, I reviewed patients treated by us in the previous four years at Mengo Hospital, Kampala, and out of a total of approximately 10,000 in-patients

(medical and surgical) treated in that time there were 41 cases of proved peptic ulceration and 7 of carcinoma of the stomach, most of these latter arising in an ulcer. It is true that these are few, but this year the numbers admitted for peptic ulceration have increased markedly. The type of patient in whom it occurs is still the same, mostly of the peasant class, though more of the "chief" class and clerks are being seen. I am not sure yet whether the incidence is rising, or whether successful treatment encourages others to come.

Most of the ulcer patients come from tribes who make a habit of indulging in one vast meal at the end of the day, and take practically no food the rest of the day. A good many of them are steady pipe-smokers and many are of the highly strung type. The 48 cases are too few to be significant, but they are proved cases of peptic ulceration and carcinoma of the stomach. It is said that 10% of the British population suffer from peptic ulcer, but in East Africa it would be difficult as yet to assess the figure. The numbers passing through our hands so far do not suggest anything approaching this high figure, but we have not got a practitioner in every village. However, it was interesting to find that even in this very short series the ratios of duodenal ulcer to gastric ulcer, and the sex incidence, are almost identical with the average of the United Kingdom.—I am, etc.,

Kampala, Uganda. C. J. S. SERGEL.

Cardiac Arrest During Operation

SIR,—The authors of "Acute Circulatory Failure During Surgical Operations" (September 6, p. 533) rightly emphasize the difference between cardiac arrest due to anaesthetic hazards, such as asphyxia and chloroform poisoning, and heart failure due to surgical hazards such as blood loss and traumatic shock. The cardinal feature of the latter group is lack of venous return to the heart, and the futility of treatment by cardiac massage is brought home to the surgeon who palpates the heart in these cases. The heart is a flabby empty bag which is in urgent need of blood both to stimulate it to beat and to nourish it. Alexander and Hewer in their medical memorandum on "A Treatment of Cardiac Arrest" (September 6, p. 546) touch on the vital factor—namely, the need of the heart for a volume of fluid—and suggest the intraventricular injection of saline as a first line of treatment. A recent experience suggested another way of rapidly restoring the circulating blood volume. Esmarch's rubber bandages are rapidly applied in tight overlapping spiral turns from the toes to the groins of both lower limbs. In this way a considerable volume of blood and lymph is transferred in a very short time to where it is urgently needed.

Case History.—Mrs. C. B., aged 74, admitted with fracture of the neck of the femur. A Smith-Petersen nail was inserted under a low spinal analgesic. During the later stages of the operation she became restless, with sighing respirations, and, while the nail was being driven home, the anaesthetist reported cardiac arrest. Artificial respiration with oxygen and intracardiac injection were tried unsuccessfully. Cardiac massage was resorted to, and two fingers were inserted through an opening in the diaphrgam. The heart was felt to be empty and lifeless and did not respond to massage. As a last resort Esmarch's bandages were wound tightly from toes to groins and then further tightened to occlude all circulation in the lower limbs. Almost at once the heart began to beat strongly. After a rapid infusion of fluid into an arm the bandage tourniquets were removed at intervals and the patient returned to the ward. The pulse remained good until the patient died in cerebral coma 12 hours later.

No originality is claimed for this modification of an ancient method of treating shock, but I do not know if it has been tried before in cardiac arrest under anaesthesia. I am sure this patient would have survived if I had tried exsanguination of the limbs first instead of fussing about with injections. It is not my intention to advocate a trial of this treatment in all cases, but only where there is reason to believe that there is a failure of venous return. Even in these cases there should be no delay in preparing for cardiac massage.—I am, etc.,

Winford, nr. Bristol. A. W. FOWLER.

Sensitivity to Streptomycin and P.A.S.

SIR,—Surgeon-Lieutenant D. G. Julian (August 30, p. 476) described a case, claimed to be the first reported, of simultaneously acquired sensitivity to streptomycin and to sodium P.A.S. in a patient suffering from pulmonary tuberculosis. The following is a report of a case of simultaneously acquired sensitivity to streptomycin and to P.A.S. in a patient suffering from renal tuberculosis.

A man aged 34 years, suffering from unilateral renal tuberculosis, was admitted to hospital in May, 1952. Prior to a nephrectomy, a preliminary course of streptomycin, 1 g. daily, and P.A.S., 20 g. daily in four doses, was commenced on July 15, 1952.

On August 15 he developed symptoms of shivering, headache, and generalized aching, suggestive of impending influenza, although the temperature remained within normal limits. On August 19 he developed an erythematous rash on the legs; the temperature averaged 100° F. (37.8° C.) and the pulse rate 120 per minute. By the following day the rash had extended to cover the whole body and was extremely itchy. Chemotherapy was discontinued and "benadryl," 100 mg. twice daily, commenced. By August 22 the symptoms had subsided.

In order to determine to which of the agents he had become sensitive it was decided to withhold the benadryl and use one drug only. The patient was sure that streptomycin had been the cause, and in the absence of a better reason it was decided to try P.A.S. first. Shortly after he had received the second dose an itchy erythema appeared again on the legs and he complained of intense headache. No further P.A.S. was given and benadryl was recommenced. The symptoms had subsided completely by the next day (August 23). Benadryl was continued, and on August 24 P.A.S. was restarted in half-strength doses. After the third dose the erythema and headache returned.

The patient had now changed his mind as to the cause of his symptoms. However, he was a little apprehensive, so on September 8 he was given 1 ml. of sterile water, under the impression that it was streptomycin. On September 9, at 10 a.m., he was given streptomycin 1 g. By 5 p.m. the itchy erythema was again present on the legs and the head ached. On September 10 10% of the total white cell count of 6,400 per c.mm. were eosinophils.

There is no question of accumulation of the drugs in the body due to impaired renal function, as all the subsequent reactions occurred on the first days of the test doses. The blood urea estimations were normal before, during, and subsequent to the sensitivity reactions. It is noteworthy that the patient had not expected a reaction from the first trial of P.A.S. and that his slight apprehension of a trial of streptomycin had been completely allayed after the first day when sterile water had been substituted.

The conclusion is that sensitivity reactions to streptomycin and P.A.S. may be identical and that in this case the occurrence of a state of sensitization to both drugs developed simultaneously.

I wish to express thanks to Mr. W. M. Borthwick for his help and criticism and to Dr. M. A. Foulis, physician-superintendent, Robroyston Hospital, Glasgow, for his permission to publish this case.—I am, etc.,

Millerston, Glasgow, E.1. PETER MACPHERSON.

E.C.T. for Prolonged Stupor

SIR,—Dr. P. H. Mitchell's interesting article (September 6, p. 535) shows the need for further investigation of the causes and treatment of cases of stupor. Some of these cases can be fatal within a short time, and it is not generally realized that early and energetic treatment can often effect an early recovery. It may be beneficial to carry out a preliminary diagnostic test. The intravenous injection of about 0.3 g. of sodium amytal in a 2.5% solution will often enable a patient to speak to the psychiatrist. Sometimes a patient talks quite rationally and asks if the doctor thinks he can cure him, while at other times the patient refers to his delusions and appears to be mentally deteriorated. Twenty per cent. of carbon dioxide in oxygen has also enabled a man who has been stuporous for some months to speak rationally for 20 minutes. Fasting blood sugar should also be estimated to exclude hyperinsulinism.

Professor Lopez Ibor at the World Congress of Psychiatry in Paris, 1950, in summing up the indications for the various