secretion of acid was 40–60% inhibited by the 5-mg. dose given three hours before the test. In 6 out of the 12 persons the secretion of acid was 40–60% inhibited nine hours after a dose of 10 or 8 mg. The output of the alkaline secretions of the gastric mucosa was usually not reduced, but gastric emptying was somewhat slowed. With doses up to 10 mg. there were no troublesome side-effects, the reduction of salivary flow not being noticed by the subjects if it occurred.

Clinical trials of this drug, which in low doses by mouth has a selective action of long duration on the gastric secretion of acid, are now being undertaken with a view to controlling secretion of acid in patients with duodenal ulceration.

We wish to thank our students who took part in the tests; the members of the clinical staff who allowed us to investigate their patients; and Beecham Research Laboratories Ltd. for the supply of IS 449.

REFERENCES

- Acred, P., Bainbridge, J. G., Brown, D. M., Quinton, R. M., and Turner, D. H. (1957). In preparation.
Doyle, F. P., Mehta, M. D., Sach, G. S., and Pearson, J. (1957). In preparation.
Hunt, J. N. (1954). *Guy's Hosp. Rep.*, 103, 161.

Medical Memoranda

Agranulocytosis with Recovery During Promazine Therapy

Promazine, one of the newer ataractic drugs, has recently been introduced for the treatment of certain types of mental illness. Like chlorpromazine it is a phenothiazine derivative, but differs from chlorpromazine in that the chlorine atom is absent from its structure. Agranulocytosis has been recorded during the course of chlorpromazine treatment (Goldman, 1955), and we record below details of a case under our care in which this complication occurred during promazine therapy.

CASE REPORT

The patient, a woman aged 60, was admitted to hospital on March 26, 1957. A severe depressive illness had been present for five months and there were features of considerable anxiety, with restlessness. Physical examination revealed nothing of importance with the exception of moderate hypertension (B.P. 190/110 mm. Hg). There was no anaemia. The W.B.C. count was 6,000 per c.mm. Sedation with amylorbarbitone sodium was not effective and was discontinued. On April 2 promazine treatment was begun with 100 mg. thrice daily, and the dose was increased on April 4 to 200 mg. thrice daily. Thereafter the excitement and agitation were observed to diminish. In the ensuing weeks regular white-cell counts fluctuated from 5,000 to 8,000 per c.mm. A representative differential white cell count was: neutrophil polymorphs 62%, neutrophil stab cells 2%, eosinophils 2%, lymphocytes 27%, monocytes 7%.

On April 27 the patient complained of sore throat. There was no fever, and on inspection the throat appeared healthy. On April 29 the temperature rose to 100.6° F. (38.1° C.), the fauces were noted to be inflamed and oedematous, and cervical adenitis appeared. Blood examination revealed a complete neutropenia: W.B.C., 1,900 per c.mm. (lymphocytes 48%, monocytes 52%); Hb, 11 g./100 ml.; platelets, 316,000 per c.mm. Sternal marrow examination yielded only a few islets of fatty tissue with no cellular areas.

Promazine administration was discontinued and 1 mega unit of crystalline penicillin was given twelve-hourly. Daily differential white-cell counts were performed. Corticotrophin gel was given intramuscularly in dosage of 50 mg. twelve-hourly from May 3, and on May 4, for the first time for six days, a differential count done on a buffy film showed

2% of neutrophil stab cells: segmented polymorphs remained absent. On May 5 1 pint (570 ml.) of fresh blood was transfused. Each ensuing day thereafter was associated with a gradual increase in the proportion of neutrophil polymorphs in the peripheral blood, and by May 13 the white-cell count was 11,850 per c.mm. (neutrophil polymorphs 86%; neutrophil stab cells 6%, lymphocytes 5%, monocytes 3%). Clinical recovery from the agranulocytic episode was then complete, and corticotrophin and penicillin were withdrawn.

COMMENT

Agranulocytosis complicating promazine therapy has been reported on one previous occasion (Woodward and Solomon, 1956), and in that case proved fatal. This patient also was a middle-aged woman, and dosage had been instituted at 100 mg. a day, increasing to 1,000 mg. a day over a 42-day period. In contrast to our patient, lymphocytes rather than monocytes had predominated in the peripheral blood during the agranulocytic period, and this is said to indicate a worse prognosis (Whitby and Britton, 1953). It is clear that serious depression of the red bone marrow can occur following both promazine and chlorpromazine administration, and vigilance during their use remains essential.

We wish to thank Professor T. Ferguson Rodger for permission to publish this case.

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REFERENCES

- Goldman, D. (1955). *J. Amer. med. Ass.*, 157, 1274.
Whitby, L. E. H., and Britton, C. J. C. (1953). *Disorders of the Blood*, 7th ed. Churchill, London.
Woodward, D. J., and Solomon, J. D. (1956). *J. Amer. med. Ass.*, 162, 1308.

A Case of Carcinoid Tumour

The general features of carcinoid tumour, with the effects of the substance hydroxytryptamine (5-H.T.) which is secreted by the tumour cells, were described in the *British Medical Journal* (1956). A clinical report of such a case exhibiting many of the classical signs and symptoms of the syndrome is given below. The patient is still alive despite a history dating back for at least eight years.

CASE REPORT

A woman now aged 71 first came under observation in 1949. She was married and had borne four children. The previous medical history was irrelevant until 1948, when she had attacks of abdominal discomfort and flatulence for which her gall-bladder was removed without more than temporary relief.

In 1949 she suffered from definite abdominal pains which were periumbilical, colicky, and intermittent, occurring in attacks at irregular intervals and lasting between 6 and 24 hours. Many such attacks were witnessed during the succeeding four years. They were often associated with a low fever, loose stools, and occasional vomiting, and were succeeded by a few days' anorexia and malaise. During the colicky phases abdominal examination was negative, but during the ensuing days tenderness which slowly disappeared was present in the right iliac fossa. In all other respects clinical examination was negative and her general health and nutrition remained good. Barium meal, barium enema, and stool tests were carried out with negative results. A tentative diagnosis of recurring mild appendicitis was expressed, but in view of the diarrhoea and the absence of maintained pain during the attacks this was not made with great conviction.

The patient was admitted to hospital in March, 1953, as a case of subacute intestinal obstruction. Investigations failed to add light on the diagnosis, and it was decided to perform an exploratory laparotomy on March 17. The

operation report read as follows: "Three feet (91 cm.) above the ileo-caecal junction was a stricture of the ileum, the latter being dilated above this. The affected area of ileum felt hard and there were two small nodules in the wall of the small intestine below the stricture. No glands were seen in the mesentery. Twelve inches (30 cm.) of small intestine was resected, continuity being re-established by end-to-end anastomosis."

The pathological report on the specimen read: "There are three separate primary carcinoid tumours of the terminal region of the ileum. One of these growths is infiltrating through all layers of the gut and has caused much narrowing of its lumen. Metastases were demonstrated in regional lymph nodes." Figs. 1 and 2 show tumour sections.

FIG. 1.—Typical clumps of argentaffin neoplastic cells in carcinoid growth of lower ileum. (H. and E. $\times 110$.)

For some months after operation relief from symptoms was complete, and then there was a return of discomfort, indefinite colic, anorexia, and loose stools.

By April, 1954, an irregular liver edge became palpable and its consistency was noted at the time as one of rubbery firmness. About this date complaint was made of facial flushing in attacks associated with a feeling of bursting pressure in the head. These became more persistent and distressing, and the flushing involved the upper chest in addition to the face. At the time of writing these occurred between 6 and

FIG. 2.—Area of mucosa showing infiltrating clumps of argentaffin neoplastic cells. (H. and E. $\times 112$.)

12 times daily, were provoked by meals or defaecation, lasted about 10 minutes, and if severe were followed by a feeling of chilliness. On the chest the flushing assumed a blotchy distribution, but the face was diffusely involved, with much heightened colour on the malar area, where it could best be described as one of bright reddish blue. The flush was and has remained a striking objective sign as well as an unpleasant symptom. Its increasing frequency over the last two years has resulted in the face appearing permanently bloated and bright red, particularly over the cheeks.

The abdominal findings during this time have shown a very slow increase in size of the liver, which contained easily palpable firm nodules which distorted its surface and edge

and were moderately tender to palpation. An indefinite tender mass was palpable in the right iliac fossa, and another mass could be palpated in the pelvis by rectal examination. The patient was losing weight very gradually, and suffered from moderate abdominal discomfort and a diarrhoea which could be kept in check by simple medicinal measures. She continued to manage her household and was fully ambulant.

At no time has asthma or any element of bronchospasm been shown. A loud systolic murmur has appeared over the praecordium. Its site of maximum intensity was the mitral area, and all second sounds were closed. In particular the pulmonary second sound would not appear to be reduced. There was no hypertension. Neither an electrocardiogram nor an x-ray examination of the chest indicated any degree of right heart strain.

Recent examination of the urine for 5-hydroxyindole acetic acid (5-H.I.A.A.) showed this substance to be present in significant quantity.

COMMENT

A case of carcinoid tumour is described in which the patient is still alive. The following features are of interest. (1) A protracted history amounting to at least eight years. (2) Diagnostic difficulties which were solved only by laparotomy and histological examination of the intestinal tumour. (3) The development of secondary deposits in the liver, which has been felt to increase in size slowly over a period of more than two years and can be inferred from the demonstration of 5-H.I.A.A. in the urine. In addition there appear to be metastases in the pelvis which are most likely originating in the ovaries, a site which has been noted in other cases of this condition. (4) The retention of a remarkably good state of health in sharp contrast to that expected if the present condition was due to carcinoma. (5) The development of flushing and a bursting congestion of the head coinciding in onset with the palpable enlargement of the liver. This fact fits the accepted view that 5-H.T., which is secreted by the gut, is inactivated during its passage through the liver, whereas secondary deposits in the liver secrete the substance and deliver it direct into the venous circulation. An amount stated to be about one-third of the total 5-H.T. secreted in the liver finds its way through the pulmonary circulation and exerts its effect outwardly in the manner described.

The pulmonary manifestations included in the syndrome as originally described by Thorson, Biörck, Björkman, and Walderström (1954)—namely, asthma, right heart strain, and pulmonary stenosis—do not appear on clinical, electrocardiographic, or radiological grounds to have become manifest. It may be that the impact of 5-H.T. has not made itself felt on the pulmonary circulation for long enough to produce these changes. On the other hand, the review of 14 proved cases of argentaffinoma of the bowel with metastases by Thorson *et al.*, which included full clinical and electrocardiographic investigations, showed a striking lack of correlation between the cardiac findings in life and those at necropsy. Thus Case 2 of their series was described as exhibiting a systolic murmur over the whole praecordium and a left axis deviation in the electrocardiogram. At necropsy, sclerosis and retraction of the pulmonary cusps and narrowing of the pulmonary ostium were demonstrated, which suggests that a severe degree of stenosis of the pulmonary valve must exist, provided the septum is intact, before clinical evidence can prove its existence. Cardiac catheterization would possibly supply supporting evidence of pulmonary narrowing, but was not regarded as justified in an elderly patient.

For help and advice in the compilation of this note I am indebted to Mr. W. M. Beattie, surgeon, David Lewis Northern Hospital, Liverpool, who performed the operation, and to Dr. Winston Evans, pathologist, for the photomicrographs.

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REFERENCES

- British Medical Journal*, 1956, 1, 907.
Thorson, A., Biörck, G., Björkman, G., and Walderström, J. (1954). *Amer. Heart J.*, 47, 795.