of lung cancer. That these relations could arise fortuitously is hardly credible, nor is any other explanation of them.

When the large towns and rural districts are included the correlation with density in the area itself is larger (0.573) and the partial coefficient with the average density in surrounding districts is smaller (0.233) than when only the small towns are considered, but there is a higher coefficient with population density in the area itself plus half that in surrounding districts (0.603). Differentiation of the adjacent districts into those abutting on four sectors of the boundary shows highest correlation with density of population to the north-east, and lowest with density to the south-west. It has to be remembered that the geography of Lancashire is peculiar, with the Pennine chain along its eastern side and the sea as its western boundary, whilst population and heavy industry tend to be concentrated eastwards in the county. It is a matter of common observation that air pollution in south-west Lancashire is worst when the wind is easterly, and this could more than counteract the greater prevalence of westerly winds.

In males, mortality from cancer of the stomach shows an insignificant correlation with the average population density in the districts surrounding the area, and it becomes zero when the density in the area itself is held constant, indicating no appreciable effect of smoke from adjacent districts on this form of cancer.

Conclusions and Summary

When standardized mortality ratios for bronchitis and cancers in the county boroughs of England and Wales are related to the average amounts of undissolved deposit and smoke from the air in those towns, highly significant statistical correlations are found for bronchitis and lung cancer with both types of pollution after eliminating the effects of population density on the correlations. In all administrative areas in Lancashire and the West Riding of Yorkshire having the necessary pollution data bronchitis is significantly correlated with deposit but not with smoke, whilst for lung cancer the reverse is the case. In Lancashire areas lung cancer is strongly correlated with population density in adjacent districts even when that of the area itself is held constant, and this appears to confirm the effect of wind-borne smoke on the incidence of the disease.

Stomach-cancer mortality is related significantly with both deposit and smoke in the county boroughs, and among females in the Lancashire and Yorkshire districts also, whereas breast cancer shows negative correlations in the county boroughs and no relation with air pollution in the counties. The most likely explanation of this is the exposure of food to dirty air, and this hypothesis is supported by the fact that in the U.S.A., where wrapping of food was the rule long before it began to be practised in Britain, death rates from stomach cancer have fallen steadily in contrast to their lack of improvement in this country. Intestinal cancer also shows small correlations with deposit and smoke in the county boroughs, but they are below the conventional level of significance.

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ASSOCIATION OF GASTRO-DUODENAL LESIONS WITH MÉNIÈRE'S SYNDROME

BY

ROGER WYBURN-MASON, M.A., M.D., M.R.C.P.

That an association exists between the function of the inner ears and that of the stomach and duodenum is shown in various ways. Wolf (1946) recorded the activity of the duodenum both by introducing a balloon into it and by barium-meal investigation, and showed that irrigation of the external ear with cold water caused both nausea and narrowing of the lumen of the first part of the duodenum and replacement of its normal pattern of motor activity by slower and larger contractions. These changes were never seen in the absence of nausea, and vice versa. Clinically, irritative lesions of the labyrinth may result in Ménière's syndrome, which consists of attacks of vertigo, tinnitus, nausea, and vomiting, often accompanied by sweating, faintness, and vasomotor changes, and sometimes by actual syncope. They are often associated with progressive deafness and persistent tinnitus on one or both sides. It must be assumed that a nervous connexion exists by which disturbed function of the stomach and duodenum follows stimulation of afferents in the labyrinth.

Conversely, irritation of the stomach and duodenum by poisonous substances or other agents or by gross distension often leads to nausea, vomiting, sweating, tinnitus, and vertigo, symptoms suggestive of labyrinthine disturbance. That an undoubted labyrinthine disturbance may result from a gastro-duodenal lesion does not seem to have been observed previously. Below is given an account of a number of cases in which such a relationship was present. Furthermore, it has often been denied that diverticula of the second or third part of the duodenum ever produce symptoms (Hahn, 1929), but Ogilvie (1941) and others (see Aird, 1949; Elstner and Waugh, 1957) showed that they certainly can do so. In one of the cases described below a diverticulum appeared to give rise to the symptoms of labyrinthine disturbance. An account of five of the cases follows. Six other cases of Ménière's syndrome in association with long-standing duodenal ulcer have been observed.

Case 1

A woman aged 66 was admitted to hospital giving a 20-years history of periods of severe high epigastric pain about half an hour after meals. Four years prior to examination this was replaced by the sensation of food sticking behind the lower sternum coming on immediately after meals and followed by water-brash and heartburn, and sometimes by vomiting. These symptoms lasted for about 15 minutes. They were worse if she lay flat, so she slept almost erect. Stooping caused oral regurgitation. Two years prior to examination, during a period of exacerbation of symptoms, she suddenly vomited for an hour and next day was violently vertiginous, being unable to rise from her bed or move her head, attempts at which caused violent vomiting. These symptoms lasted for three days and then gradually subsided. After a further three days they returned severely, and after 10 days she noticed marked tinnitus and some deafness in the right ear. During the next two years attacks of vertigo and vomiting of varying duration recurred and there was an increase in the right-sided tinnitus and deafness with a constant feeling of unsteadiness on her feet. She was treated by her doctor with phenobarbitone and "avomine" without any appreciable change in her condition. She was admitted to hospital in an acute exacerbation.

Examination.—She was obese, with lax abdominal musculature, otherwise nothing abnormal was found in the abdomen. B.P. 145/85 mm. Cardiovascular and respiratory systems normal. Hb, 92%. Barium meal and swallow: para-oesophageal hernia of stomach of moderate size, apparently incarcerated, but with no observable regurgitation into the oesophagus and only slight obstruction to emptying of the latter. Duodenum normal. A solitary gall-stone present. Aurist's report (Mr. C. P. Malley): "External auditory meatuses normal. Partial right-sided nerve deafness. Audiogram shows well-marked high-tone deafness on right. Left ear normal. Caloric responses greatly diminished on right, normal on left. The changes are typical of Ménière's disease."

She was kept in bed propped up, treated with a convalescent gastric diet, magnesium trisilicate, 1 dr. (4 g.) t.d.s., p.c., and a mixture containing tincture of belladonna, 10 min. (0.6 ml.) t.d.s., a.c. Both the gastric and vertiginous symptoms rapidly improved and the tinnitus considerably lessened. The deafness persisted, however. After six weeks in hospital she stated that she felt better than she had for 10 years. During the next two years she continued the above regime. She had only occasional recurrences of epigastric discomfort, especially after bending, and slight vertigo, but no severe attacks. Repetition of the audiogram and caloric tests at the end of this time showed no change.

Case 2

A man aged 65 attended hospital giving a 35-years history of periods of gnawing epigastric pain, with intervals of freedom. The pain occurred about two hours after meals and sometimes woke him at 1–2 a.m. It was unrelieved by taking a meal. He also suffered from flatulence, and breaking wind relieved the pain. His appetite was poor and he was afraid to eat because of pain, which was often accompanied by nausea, occasional vomiting, and cold sweats. One year prior to his attendance at hospital the pain became much worse, and a month later, during a particularly severe attack of pain, he became violently vertiginous and thought he was going to fall to the right side. He felt alternately hot and cold, and faint; he sweated profusely, and had difficulty in focusing. He was unable to stand for nearly a week and was confined to bed for three weeks. He was treated with "vasano" and phenobarbitone and a dehydration regime, but his symptoms persisted in moderate degree. During the next 10 months the onset of epigastric pain was often followed by recurrent attacks of violent vertigo. The severe symptoms usually persisted for three days, then gradually improved, but after that he constantly

felt he was falling. If he looked upwards or downwards or moved his head suddenly, he felt giddy, and external objects seemed to be going round. These symptoms were accompanied by much flatulence.

Examination.—He was well-built but edentulous; there was no evidence of anaemia. Cardiovascular system normal. B.P. 110/70 mm. Respiratory system normal. C.N.S. normal. Abdomen very tender on palpation in mid-epigastrium. Aurist's report (Mr. C. P. Malley): "Bilateral nerve deafness, more marked on right side and especially for high tones. Caloric tests show considerable diminution in responses in right ear. The left appears normal. The condition is typical of Ménière's disease." Hb, 109%. Barium meal; rapid evacuation of barium. A large gastric ulcer present in the pyloric antrum.

He was treated as an in-patient with rest in bed, gastric ulcer regime with "bellergal" tablets, 1 t.d.s., a.c., and pulv. "aludrox," 1 dr. (4 g.) t.d.s., p.c. and at night. After six weeks both abdominal and labyrinthine symptoms were completely relieved, apart from some right-sided tinnitus. At the end of this time a barium-meal examination showed that the gastric ulcer had healed. Repetition of the audiogram and caloric tests showed no change. He was observed for two years, during which time he complained only of an occasional slight feeling of epigastric distension and slight giddiness on rising in the morning, but he had had no severe attacks of vertigo.

Case 3

A man aged 55 was admitted to hospital giving a seven-years history of attacks of vertigo and retching occurring about three times a year, but in the last six months much more frequently. During the vertigo objects appeared to move from right to left. He also suffered from anorexia and water-brash after meals, and felt bloated. The latter symptoms were relieved by alkaline powders. He had no abdominal pain. For six years he had complained of slight bilateral deafness and distortion of hearing, especially on the right. The symptoms came on at any time, sometimes woke him at night, and were unrelated to meals. He gained relief by lying on the left side. He constantly felt giddy with the eyes closed.

Examination.—Cardiovascular system normal. B.P. 145/90 mm. Respiratory system normal. Abdomen: some tenderness on palpation in the mid-epigastrium. C.N.S.: no spontaneous nystagmus; positional nystagmus present with vertigo on inversion of the head. Aurist's report (Mr. W. A. Mill): "External auditory meatuses normal. Bilateral nerve deafness, more marked on right, with loss of hearing for high notes. Caloric responses diminished in right ear. History and findings typical of Ménière's disease, but with some positional element." Haemoglobin 114%. Blood urea 21 mg. per 100 ml. Serum protein, 6.1 g. per 100 ml. W.R. and Kahn negative. E.C.G. normal. Histamine test meal, hypochlorhydria. Barium meal: constant stricture about 3 cm. in length in immediate prepyloric region, not dilating after antispasmodics (Fig. 1). Gastroscopy: No lesion observed.

Laparotomy revealed an adult pyloric stenosis. Partial gastrectomy was performed. The removed specimen showed a narrow pylorus with a circumference of about 3 cm., the pyloric musculature being up to 0.7 cm. thick. Section showed a subacute inflammatory cell infiltration of the mucosa and thickening of the submucosa by fibrous tissue. No ulcer was found. During the next two and a half years he had almost complete relief of all symptoms, except for a slight deafness and occasional mild postural vertigo. Two years after operation repetition of the audiogram and caloric tests showed no change.

Case 4

This man, aged 33, developed nine years previously epigastric pain occurring about two hours after meals. A barium-meal examination showed the presence of a duodenal ulcer, for which he received medical treatment; he

remained symptomless for about five years, after which time pain recurred at intervals of several weeks and lasted three to six weeks. Three years before being seen, at the height of one of these attacks of pain, he was seized with severe right-sided tinnitus and violent vertigo, in which he felt he was falling to the right, and the right ear felt blocked. Over the next month the symptoms gradually improved. After this they had repeatedly recurred, usually at the height of an attack of epigastric pain. The tinnitus varied in severity with the vertigo, and the deafness had gradually increased. He had become nervous of going out by himself.

Examination.—General condition good. No evidence of anaemia. Cardiovascular system normal. B.P. 130/80 mm. Respiratory system normal. C.N.S. normal. Slight tenderness on palpation in mid-epigastrium. Aurist's report (Mr. C. P. Malley): "Auditory meatuses normal. Right-sided

and tender on palpation. There was acute tenderness on palpation over the gall-bladder. The stools were pale and contained excess of fat, chiefly unsplit, and bile was present in the urine. There was no pyrexia. A cholecystogram showed that the gall-bladder failed to give any concentration of the radio-opaque material. For this cholecystectomy was carried out and a large tense gall-bladder was found and removed. Many faceted "mixed" gall-stones were present, but none were found in the cystic or bile ducts. The jaundice died down only slowly after operation, in spite of which the attacks of epigastric pain continued during the next three years. She also suffered from flatulence and had become dyspnoeic, tired, and lethargic. Ten weeks before her last hospital admission she developed an attack of pain and swelling of the left leg, which had persisted, and three weeks later the right leg was similarly affected.

Examination.—Pale conjunctivae and mucosae. Teeth carious. Tongue clean. No lymphadenopathy. Cardiovascular system normal. B.P. 170/95 mm. Lungs normal. Abdomen: well-healed Kocher's gall-bladder incision; acutely tender on palpation in the right hypochondrium; no mass felt. C.N.S. normal. Gross pitting oedema of both legs reaching to the knees. Acutely tender over calves.

She was observed in an attack of epigastric pain and vertigo. She complained that objects were moving round in clockwise direction and to the right. Examination showed a nystagmus with rapid component to the left and slow to the right. There was marked past-pointing to the right. She tended to lean and fall to the left when standing. Marked tenderness and guarding were present in the mid-epigastrium. The symptoms lasted 72 hours, after which all signs had disappeared. Aurist's report (Mr. W. A. Mill): "Marked right-sided nerve deafness. Caloric responses in left ear normal, in right minimal. The findings

suggest Ménière's disease." Blood urea, 36 mg. per 100 ml. Fractional test meal; complete achlorhydria. A barium-meal examination showed a large diverticulum present in the second part of the duodenum arising close to the ampulla of Vater (Fig. 2). Supine films showed a filling defect within the diverticulum, possibly due to food residue. Another diverticulum was present in the third part of the duodenum. Intravenous cholecystogram showed the common bile duct a little dilated but not obstructed, as the opaque medium passed very readily into the small intestine. X-ray examination of the chest revealed nothing abnormal.

She was given anticoagulant treatment for 20 days, and during this the oedema of the lower limbs disappeared completely. Avomine tablets had no effect on the symptoms. It was therefore decided to resect the diverticulum. Laparotomy revealed numerous adhesions of the omentum in the right hypochondrium. A diverticulum in the concavity of the second part of the duodenum presented into the wound. A dissection of the lateral side of the duodenum was extended round to the pancreas. The diverticulum was dissected down to its neck and excised. Troublesome bleeding occurred from a large vein in the region of the superior pancreaticoduodenal vessels.

The excised duodenal diverticulum consisted of a strip of tissue 5.5 cm. long, 1.8 cm. wide, and 0.5 cm. thick. Microscopically the wall of the diverticulum consisted of mucous membrane, muscularis mucosae penetrated by small Brunner's glands, and, outside this, loose fibro-fatty tissue containing lobules of pancreatic tissue.

Post-operatively the attacks of pain and vertigo ceased, but she vomited small amounts occasionally. During this period she felt lethargic and tired, and ran a slight temperature, which was found to be due to cystitis. Between the eleventh and the twenty-second day after operation the

FIG. 1.—Radiograph taken after a barium meal, showing constant stricture in immediate prepyloric region, found at operation to be due to adult pyloric stenosis in association with Ménière's syndrome (Case 3). FIG. 2.—Barium meal showing presence of duodenal diverticula in association with Ménière's syndrome (Case 5).

nerve deafness. Audiogram: well-marked high-tone deafness on right side. Caloric responses markedly depressed on right." Barium meal: large duodenal ulcer with evidence of old scarring. Hb, 96%.

He was admitted to hospital and treated medically with peptic ulcer regime and a mixture containing 10 mm. (0.6 ml.) of tincture of belladonna t.d.s., a.c., and pulv. aludrox, 1 dr. (4 g.) q.d.s., p.c. After 10 days all the symptoms, apart from the deafness and right-sided tinnitus, had disappeared, and during the next six weeks the tinnitus also diminished considerably. On discharge the vertigo had ceased. During the next three years he adhered to a convalescent peptic ulcer regime and had no return of pain and only occasional mild vertigo on rising.

Case 5

For 10 years a woman aged 63 had been subject to irregular attacks consisting of a sudden onset of vertigo, malaise, right-sided tinnitus, and nausea followed within half an hour by epigastric pain, constant and severe in nature, radiating to the midline of the back below the shoulder-blades. This was followed by retching and vomiting, which had no effect on the pain. The pain would last two to three hours, but the vertigo, nausea, and vomiting might continue for three days or more. She was unable to stand during the attacks. She noted that fried food and milk tended to aggravate the condition, but otherwise the attacks had no relation to food. Since the onset of the attacks she had become progressively deaf on the right side.

Seven years after the onset she developed a thrombophlebitis of the left leg, and some months later, during an attack of pain, she became jaundiced and was admitted to hospital. The liver was found to be enlarged three finger-breadths below the costal margin. Its surface was smooth

blood haemoglobin level fell from 100 to 59%. A blood transfusion of 3 pints (1.7 litres) restored the level to 91%, and it remained normal thereafter. Six weeks after operation she developed a superficial thrombophlebitis of the long saphenous vein of the left leg. A repeat barium-meal examination at this time showed the diverticula still present in the second and third parts of the duodenum. The outline of the former was still irregular. It seemed that the diverticulum which had been removed lay anteriorly and did not fill with barium at the previous examination. Six months post-operatively she had put on 28 lb. (12.7 kg.) in weight, and, apart from right-sided deafness and some oedema of the legs following the thrombophlebitis, she was completely symptomless. During the next four years she had no further attacks of vertigo or epigastric pain, and right nerve deafness of moderate severity persisted. Caloric tests showed the right labyrinthine hypoactivity still present. The blood count remained normal. The barium-meal findings were unchanged at the end of this time.

Discussion

In the above cases symptoms of a para-oesophageal hernia, gastric and duodenal ulcers, adult pyloric stenosis, and diverticula of the duodenum, usually of long standing, preceded or coincided with those of Ménière's syndrome. The onset or an exacerbation of the symptoms of the latter usually corresponded with an increase in those of the gastro-intestinal disturbance. In the six other cases of duodenal ulcer associated with Ménière's syndrome mentioned the same time relationships were observed. Surgical or medical treatment of the gastro-duodenal lesion appeared to cure or stop the progress of the labyrinthine disturbance.

Another patient observed, a man aged 33, was seized with intense vertigo and vomiting lasting five days some nine years previously, and ever since had been subject to vertigo, especially on rising in the morning or on movement of his head in space. Caloric responses were absent in the right ear. No complaint was made of tinnitus or deafness, and the audiogram was normal. The condition corresponds to the vestibular neuritis of Dix and Hallpike (1952). This patient found that taking a meal almost invariably precipitated an attack of vertigo within 15 minutes. The larger the meal the more severe the vertigo. Such observations seem to suggest that the labyrinthine disturbance in the cases described is secondary to the gastro-duodenal lesion and not the mere coincidence of two common conditions. Search of the literature on gastric and duodenal lesions and Ménière's syndrome has failed to reveal any mention of the association of these conditions.

In all the cases described in full the tests for vestibular and cochlear function were abnormal, and in three of the five this was confined to the right side, while in the other two the right ear was more severely affected than the left. In all six cases of duodenal ulcer associated with Ménière's syndrome mentioned, but not described, the labyrinthine disturbance was confined to the right side. This suggests that the most likely connexion between the disturbance of the stomach and duodenum and of the labyrinth is through a nervous reflex and that the labyrinthine disturbance in these cases is neurogenically produced.

In one case (No. 3) symptoms pointing to the gastro-duodenal lesion were absent or minimal, and the latter was only discovered radiologically. It seems possible that such a silent lesion may be present in other cases of Ménière's syndrome. Moreover, hyoscine or atropine

often relieves the symptoms of the syndrome. This could be produced indirectly by action on the gut rather than directly on the labyrinth.

In advanced cases of Ménière's syndrome the commonest pathological findings are oedema of the labyrinth, gross dilatation of the endolymph system, albuminoid coagula in the semicircular canals, and degenerative changes in the organ of Corti and hair cells (Hallpike and Cairns, 1938; Hallpike and Wright, 1939; Dix and Hallpike, 1952). Hallpike believed the attacks to be due to a rapid rise in the fluid pressure within the endolymph system owing to an increase in its volume. There are various theories concerning the aetiology of the changes. These include disturbances in water, sodium, or potassium metabolism and allergy. In favour of the latter are reports of Ménière's syndrome in patients with other allergic manifestations. The cases described above, however, suggest a nervous mechanism as the basis of the lesions.

The association of Ménière's syndrome with angio-neurotic oedema and the role of vasomotor nervous changes and abnormal capillary permeability in producing the lesions in the labyrinth have been stressed by Kobrak (1928), Vogel (1929), Dean (1939), Dohleman (1939), Atkinson (1940), and Meyer (1940). Brunner (1939) ascribed the changes to a "vasomotor internal otitis." Others have attributed them to disturbances of sympathetic vasomotor control of the labyrinth (see Fischer and Wolfson, 1943), but experimental observations do not suggest that the dorsal sympathetic has any effect on the vessels of the labyrinth (Strong, 1957). Moreover, there is no evidence to suggest that changes in sympathetic activity lead to oedema of tissues. Furthermore, while claims for benefit in 60% of cases of Ménière's syndrome were made by Passe (1951), dorsal sympathectomy has given disappointing results in most cases (see Johnson, 1954; Strong, 1957). Thus, while disturbed vasomotor innervation of the labyrinthine vessels may play a part in causing Ménière's attacks, the mechanism by which this is brought about is unknown.

The endolymph is produced in the stria vascularis, and its formation is probably through capillary filtration. Ultimately the hydrops of the labyrinth would seem to be due to increased filtration from blood capillaries in the stria. The permeability of the capillaries is largely dependent on the functional state of the local capillary pericytes or macrophages (Volterra, 1925; Volterra and Schupfer, 1934), and I have shown (Wyburn-Mason, 1958) that this is again controlled by activity in the neighbouring naked nerve endings of unmyelinated fibres of the posterior nerve roots and corresponding fibres in the cranial nerves. The afferent and efferent pathways by which labyrinthine irritation affects gastro-intestinal activity are respectively the vestibular and the vagus nerves. It might be expected that these were also the pathways for the reverse reflex. Unmyelinated nerve fibres with naked nerve endings and conducting *centrifugal* impulses of unknown nature are present in the eighth cranial nerve and pass to the cochlear and labyrinth (Lorente de Nó, 1938; Portmann and Portmann, 1954), and afferents are found in the vagus, so that it is possible that these are the reflex pathways by which gastro-intestinal lesions affect the labyrinthine capillary permeability. It may be that abnormal discharges in the unmyelinated efferent fibres in the eighth nerve increase the normal endolymph formation

and that pressure in this way is responsible for the sudden distension of the endolymph system in cases of Ménière's syndrome.

Summary

Reports are given of a number of cases in which a lesion of the stomach or duodenum was associated with Ménière's syndrome. The latter usually followed the symptoms of the gastro-intestinal lesions, and onset or exacerbation of the labyrinthine disturbance was associated with increase in those of the gastro-intestinal lesion. Medical or surgical treatment of the latter relieved the symptoms of the former, suggesting the labyrinthine disturbance was secondary. The significance of the observations in relation to the aetiology of Ménière's syndrome is discussed.

I thank Mr. R. C. B. Ledlie for permission to publish the details of Case 3, Miss A. H. Baker and Mr. R. W. Raven, who operated on Case 5, and Mr. W. A. Mill and Mr. C. P. Malley, who carried out the aural investigations.

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A review of how colour prejudice has developed over the centuries, and some suggestions on how it may be counteracted, are given in a pamphlet entitled *Colour and Commonsense*, by Kenneth Little (Fabian Society and Commonwealth Bureau, 2s. 6d.). In a foreword Mr. Norman Manley, Chief Minister of Jamaica, draws attention to the fact that in his country "a wide variety of races and their admixtures" live together in mutual respect, "in spite of 300 years of colonialism and the legacy of slavery." Mr. Little, who is reader in anthropology at Edinburgh University, traces the growth of the colour bar through the institution of slavery and its rationalization by the racialist myths of the nineteenth century, into which Darwin's ideas on the origin of species were dragged and misinterpreted. In suggesting ways to prevent individuals from forming an antipathy to coloured people the author stresses the need to present children with natural and objective information. As he says: "Younger children are rarely colour-prejudiced." If they are, they have learnt it from their parents, and here he advises on how the press and B.B.C. could help more.

TWO CASES OF AUTO-IMMUNE HAEMOLYSIS AND APLASIA

BY

J. BURSTON, M.B., B.Sc.

O. A. N. HUSAIN, M.D.

M. S. R. HUTT, M.D., M.R.C.P.

AND

E. I. TANNER, M.B., B.Chir.

From the Louis Jenner Laboratory, St. Thomas's Hospital, and the Group Laboratory, Lambeth Hospital, London

It has been recognized for several years that marrow aplasia is the basis of some of the haemolytic crises in congenital spherocytosis (Owren, 1948; Dameshek and Bloom, 1948; Gasser, 1950) and also in sickle-cell anaemia (Singer, Motulsky, and Wile, 1950; Chernoff and Josephson, 1951). More recently, reports have appeared of aplastic episodes in idiopathic immune haemolytic anaemia (Davis *et al.*, 1952; Linke, 1952; Eisemann and Dameshek, 1954; Seip, 1955; Henneman and Falck, 1957). This report records two further cases in which hypoplasia of the marrow was associated with an auto-immune type of haemolytic anaemia. Radioactive ^{59}Fe and ^{51}Cr studies were carried out, using the techniques described by Wetherley-Mein *et al.* (1956, 1958).

Case 1

A man aged 76 was first seen on November 9, 1955, with symptoms of anaemia which had been increasing for two to three months. Examination at this time showed him to be anaemic but with no other abnormal physical signs. Blood examination revealed: Hb, 5.92 g./100 ml.; R.B.C., 1,300,000/c.mm.; P.C.V., 16%; M.C.V., 123 cubic microns; M.C.H.C., 37%; W.B.C., 2,700/c.mm. (polymorphs 45%, lymphocytes 54%, monocytes 1%). The red blood cells showed macrocytosis and anisocytosis, and there were two normoblasts per 200 white blood cells. Platelets appeared to be plentiful. A diagnosis of pernicious anaemia was made on these results, and on November 10 100 μg . of cyanocobalamin (vitamin B_{12}) was given intramuscularly as a therapeutic trial.

He was seen again on November 25, when his symptoms and pallor were more severe and he was a little jaundiced. Blood examination showed: Hb, 3.85 g./100 ml.; R.B.C., 740,000/c.mm.; P.C.V., 10.5%; M.C.V., 142 cubic microns; M.C.H.C., 36.5%; reticulocytes 2%; W.B.C., 2,000/c.mm. (polymorphs 48%, lymphocytes 50%, monocytes 1%). The film appearances had not changed.

Because of this marked deterioration he was admitted to hospital immediately. Further investigations were performed. Aspiration of sternal marrow on two consecutive days revealed a very poorly cellular specimen on each occasion. Only 6% of the cells were erythroblasts, and one-third of these showed transitional megaloblastic changes. Of the remaining cells, 65% were lymphocytes, 5% neutrophil polymorphs, 13% band neutrophils, 6% neutrophil metamyelocytes, 3% neutrophil myelocytes, 1% monocytes, and 1% plasma cells. A histamine test meal revealed no free acid. Serum bilirubin was 1.1 mg./100 ml. and platelets were 47,000/c.mm.

In view of the hypoplastic marrow picture he was treated with repeated small blood transfusions, and because of the transitional megaloblastic appearance of the remaining erythroblasts he was given folic acid, 15 mg. twice daily. ^{59}Fe studies showed the picture of complete functional aplasia of the marrow with a red-cell utilization of only 2%