"even in cases of cardiac decompensation with hypertension in the portal area considerable quantities of fat may occasionally be found in the stools."

A recent paper includes a comparison between the plasma levels of radioactivity obtained after an oral dose of I-131 triolein in patients while in congestive cardiac failure with those obtained after recovery (Berkowitz *et al.*, 1959). Few details were given, but low levels of plasma activity were said to revert to normal after recovery from cardiac failure.

It is known that disturbed liver function is often found in patients with chronic cardiac failure. This is especially so in those with constrictive pericarditis and rheumatic valvular disease, in particular mitral stenosis with tricuspid incompetence (Koletsky and Barnebee, 1944; Sherlock, 1951; White *et al.*, 1955). Analogy with infective hepatitis and cirrhosis suggests that the findings of Gross *et al.* (1950) in these diseases may be relevant. Fat-malabsorption, which they assumed to be due to lack of bile salts, correlated moderately well with the serum bilirubin concentration and roughly inversely with faecal sterobilinogen output.

Other possible explanations for fat-malabsorption in cardiac failure are pancreatic and intestinal malfunction. Masoni and Pellegrini (1953) have demonstrated impaired pancreatic function in patients with severe chronic cardiac failure, and Meakins (1940) thought that such patients had an intestinal absorption defect for glucose; de Langen (1953) suggested that intestinal congestion or ischaemia in cardiac failure might explain fat-malabsorption. It is possible that one of these two explanations may apply in the cases described, but the point was not investigated further.

Summary

Fat-malabsorption has been demonstrated in 3 out of 17 patients with congestive cardiac failure and may have been present in two more. No correlation with cause or chronicity of cardiac failure, loss of weight, or digitalis therapy was observed. The possible significance of the raised serum bilirubin in three of the cases of fat-malabsorption is discussed.

I am grateful to Dr. R. R. McSwiney, Dr. J. L. Pinniger, and Professor F. T. G. Prunty for help, and to the physicians of St. Thomas's Hospital who have allowed me to study their cases.

REFERENCES

- Annegers, J. H., Boutwell, J. H., and Ivy, A. C. (1948). *Gastroenterology*, **10**, 486.
 Berkowitz, D., Sklaroff, D., Woldow, A., Jacobs, A. G., and Likoff, W. (1959). *Ann. intern. Med.*, **50**, 247.
 Crowe, P. J., Blackburn, C. R. B., Mashford, M. L., and Reed, C. S. H. (1956). *Aust. Ann. Med.*, **5**, 36.
 Frazer, A. C. (1949). *Brit. med. J.*, **2**, 769.
 Gross, J. B., Comfort, M. W., Wollaeger, E. E., and Power, M. H. (1950). *Gastroenterology*, **16**, 140.
 Jones, R. Vaughan (1960). *Brit. med. J.*, **2**, 1236.
 Koletsky, S., and Barnebee, J. H. (1944). *Amer. J. med. Sci.*, **207**, 421.
 Langen, C. D. de (1953). *Acta med. scand.*, **146**, 7.
 Masoni, A., and Pellegrini, P. (1953). *Cuore e Circol.*, **37**, 171.
 Meakins, J. C. (1940). *J. Mich. med. Sci.*, **39**, 474.
 Pimparkar, B. D., Tulskey, E. G., Kalsner, M. H., and Bockus, H. L. (1960). *Brit. med. J.*, **2**, 894.
 Prunty, F. T. G., McSwiney, R. R., and Hawkins, J. B. (1959). *A Laboratory Manual of Chemical Pathology*. Pergamon Press, London.
 Sherlock, S. (1951). *Brit. Heart J.*, **13**, 273.
 Van Handel, E., and Zilversmitt, D. B. (1958). *J. Lab. clin. Med.*, **52**, 831.
 Weijers, H. A., and Kamer, J. H. van de (1953). *Acta paediat. (Uppsala)*, **42**, 24, 97.
 White, T. J., Leevy, C. M., Brusca, A. M., and Gnossi, A. M. (1955). *Amer. Heart J.*, **49**, 250.
 Wollaeger, E. E., Comfort, M. W., and Osterberg, A. E. (1947). *Gastroenterology*, **9**, 272.

ULCERATIVE COLITIS AND PARATHYROID DYSFUNCTION

BY

I. J. GREK, M.D.

AND

B. SENIOR, M.R.C.P.

*From the University of the Witwatersrand Medical School
and the Johannesburg General Hospital*

A significant proportion of patients with hyperparathyroidism have concomitant peptic ulceration (Rogers, 1946), and a recent survey of a group of 300 consecutive peptic-ulcer patients (Frame and Haubrich, 1960) resulted in the discovery of hyperparathyroidism in 4. The hyperparathyroidism precedes and in some as yet undefined way provokes the ulceration. The association of pancreatitis and hyperparathyroidism is also recognized, but this relationship is more obscure. It has been suggested that the hypercalcaemia causes intraductal calcium precipitation with blockage, but such deposition is not always present, and in one patient the pancreatitis appeared to precede the hyperparathyroidism (*British Medical Journal*, 1959).

Steatorrhoea has been observed in combination with hypoparathyroidism (Jackson, 1957; Williams and Wood, 1959) and more rarely hyperparathyroidism (Davies *et al.*, 1956). Again the link is perceived but the mechanism of association remains to be elucidated.

These examples of the coexistence of gastro-intestinal and parathyroid disorders lend interest to the presence of hypoparathyroidism and hyperparathyroidism, respectively, in two patients with long-standing ulcerative colitis, who were treated with steroids.

Case 1

A 40-year-old white physician was seen in January, 1957, because of cramps in the extremities. His relevant history went back approximately 20 years, when he first experienced attacks of mild diarrhoea which recurred every few months. In 1947 the diarrhoea became more severe and was accompanied by a blood-stained rectal discharge. In 1951 he again had severe diarrhoea and in addition frank rectal bleeding. He was admitted to a London hospital, and after investigation, which included a barium enema and a sigmoidoscopy, the diagnosis of ulcerative colitis was made. He returned to South Africa and a year later developed severe pain and some swelling of the joints of the fingers, wrists, ankles, and knees, for which hydrocortisone was prescribed in a dosage of approximately 60 mg./day. Both the diarrhoea and the arthritis lessened, and this treatment was continued for two years, until 1955, when severe diarrhoea recurred, with marked loss of weight. It was thought that the steroid dosage was inadequate, and prednisone 40 mg./day was substituted. The diarrhoea subsided and the prednisone was slowly reduced to 20 mg./day. He gained weight and felt stronger, but experienced carpal spasms which were ascribed to hyperventilation. He later attended a hospital in San Francisco, where the diarrhoea became worse and was accompanied by severe carpal spasms, paraesthesias of the extremities, and tingling around the mouth.

Laboratory tests at the time revealed: serum calcium, 5.5 mg./100 ml.; serum phosphorus 5.7 mg./100 ml.; serum protein, 6.1 g./100 ml. (albumin 3.6 g., globulin 2.5 g.), and alkaline phosphatase 4.4 King-Armstrong units.

He was told that his symptoms resulted from the steroid therapy, but attempts to reduce the dose provoked such severe diarrhoea that intravenous-fluid therapy was necessary. He was given parenteral calcium and calciferol, 200,000 units/day. Thyroid function was reported as normal. He then visited another clinic, where reduction of

the dose of prednisone again caused incapacitating diarrhoea. Because of continued deterioration an ileostomy and a subtotal colectomy were eventually done at a London hospital. He was extremely ill during the post-operative period, losing large amounts of fluid from the ileostomy. Eight months after the first operation the rectum was removed and the prednisone discontinued. Some weeks later he again had severe generalized spasms almost amounting to opisthotonos, but after intravenous calcium therapy these subsided. Approximately two weeks later he felt tremulous, his neck was enlarged, and his pulse rate became rapid with runs of ectopic beats. There were no spasms at this time. A diagnosis of thyrotoxicosis was made, being confirmed by a radioactive iodine uptake test. Methylthiouracil was prescribed, the symptoms abated, and he gained weight. He returned to South Africa, but shortly after arrival the cramps returned, affecting the feet, calves, and hands.

Physical examination in January, 1957, showed him to be tall and thin—height 6 ft. (183 cm.), weight 120 lb. (54.4 kg.)—and mentally alert. Slight exophthalmos was present and the thyroid gland was moderately enlarged and smooth. The heart and lungs were normal, and the blood-pressure was 120/76 mm./Hg. The ileostomy appeared healthy. Both the Chvostek and the Trousseau signs were positive. The reflexes were brisk and the plantar responses flexor. There were numerous fine excoriations of the skin and he complained of generalized pruritus. Slight swelling with restriction of movement of the proximal joints of the fingers was present.

Laboratory Investigations.—The relevant biochemical tests, which were repeated several times over a period of a few days, gave the following results: calcium, 4–6.4 mg./100 ml.; phosphorus, 5.6–6.8 mg./100 ml.; alkaline phosphatase 8.2–8.8 K–A units; total protein, 6.9–8 g./100 ml. (albumin 2.2–4.1 g., globulin 3.8–4.7 g.); urea, 24 mg./100 ml.; Sulkowitch reaction in urine, 0–14. The serum electrolytes were normal, the haemoglobin 13.4 g./100 ml., and the leucocyte count 5,600, with a normal differential count. The urea clearance was 102%. An electrocardiogram showed Q–T prolongation compatible with hypocalcaemia. Skeletal x-ray films revealed generalized decalcification. A four-day fat balance showed over 95% absorption.

A diagnosis of hypoparathyroidism with hypocalcaemic dermatitis (Dent and Garretts, 1960) was made and therapy with dihydrotachysterol instituted. He was given initially 3 ml. daily, and this was decreased gradually to a maintenance dose of between 0.4 and 0.8 ml. daily. The cramps were alleviated and the serum concentration of calcium rose and that of phosphorus fell. However, when taking sufficient dihydrotachysterol to cause complete disappearance of tetany the Sulkowitch reaction in the urine would become strongly positive. As he had had urinary calculi in the past, fear of calcium precipitation in the urinary tract prompted him to reduce his dose of dihydrotachysterol. He found that with a smaller dose of dihydrotachysterol tetany could be averted by a concomitant reduction in the dose of methylthiouracil. Since then he has controlled his own treatment, remaining relatively well by balancing mild hypocalcaemia with mild thyrotoxicosis. His main disability at present is periodic pains in the joints which, fortunately, respond to salicylates. He has gained approximately 15 lb. (6.9 kg.) in weight, carries out his normal professional activities, and feels stronger than he has done for years.

Case 2

A 29-year-old white male clerk was seen in April, 1960, because of generalized weakness and a painful swelling of the right calf.

Diarrhoea first occurred soon after an automobile accident some 10 years earlier. He felt very depressed at that time, ate little, and lost approximately 40 lb. (18.1 kg.) in weight. He had three or four loose dark stools daily. After six months of illness he first consulted his doctor. A presumptive diagnosis of amoebiasis was made and various drugs

were prescribed, without benefit. The diarrhoea persisted, and in 1954, after approximately four years of illness, he was admitted to the Johannesburg General Hospital, where, on radiological examination of the colon and sigmoidoscopy, a diagnosis of ulcerative colitis was made.

A year later the diarrhoea became worse and he developed severe pain and swelling of the joints of the fingers, wrists, elbows, feet, and knees. He was readmitted to hospital and steroid therapy begun. Initially cortisone was prescribed, but this was later changed to methylprednisolone and again to dexamethasone. Maintenance therapy with dexamethasone was continued up to the present episode. Both the arthritis and the diarrhoea improved on steroids and he was able to resume work. The stools continued to be loose, but he was not incapacitated.

His general state of health was fairly satisfactory until January, 1960, when he first experienced renal colic and passed gravel in the urine. More or less simultaneously he developed polydipsia and polyuria and severe nocturia. His appetite diminished and he again lost weight.

In April he was readmitted to hospital because of generalized weakness and a tender swelling of the right calf. After admission the diarrhoea became severe and a few days later nausea and vomiting occurred and he complained of an unpleasant metallic taste. He had not taken excessive quantities of milk or alkalis nor any vitamin D.

Physical examination revealed an extremely ill, apathetic, dehydrated man. Blood-pressure 100/50 mm. Hg. His mouth and tongue were so dry that speech was difficult. Apart from the dehydration, he appeared to have lost much weight. The presence of band keratopathy was questioned but could not be confirmed. Apart from a tender, warm, swollen right leg, the remainder of the examination was negative.

Laboratory investigations, made in May, resulted as follows: Calcium, 13.4–17.7 mg./100 ml.; phosphorus, 4.6–5 mg./100 ml.; alkaline phosphatase, 7.3–12.6 K–A units; total protein, 6.3 g./100 ml. (albumin 3.5 g., globulin 2.8 g.); urea, 57–130 mg./100 ml.; 24-hour urinary calcium, 375 mg. The serum electrolytes were normal, the haemoglobin 9.2 g./100 ml., and the leucocyte count 11,400, with an eosinophilia of 10%. Skeletal x-ray films revealed no abnormalities and dental films showed a normal lamina dura.

It was considered that the high concentration of calcium in the serum while he was on steroid therapy did not favour the diagnosis of sarcoidosis or inadvertent vitamin D overdosage, and a diagnosis of hyperparathyroidism and thrombosis of the calf veins was made. Intravenous fluid therapy was vigorously pursued and heparin administered. Despite a slight fall in the concentration of calcium in the serum, severe anorexia and nausea persisted to a degree that precluded oral maintenance, and he remained gravely ill. The left leg also became tender and swollen and he became disorientated, particularly at night. As his condition was deteriorating it was felt that the only possibility of improvement lay in the removal of the offending parathyroid. An emergency operation (Dr. M. Lautre) was done under local anaesthesia and a parathyroid adenoma (weight 3.4 g.—chief cell histology) was readily located and removed.

The patient suffered no ill effects from the operation itself, and the post-operative course was uneventful. The metallic taste, nausea, and anorexia disappeared and he was soon able to take fluids by mouth. The leg thrombosis subsided with no residual oedema. The serum calcium level returned to normal, as did the urea.

Discussion

Both patients had long-standing ulcerative colitis and had received steroids for some years. The first patient developed hypoparathyroidism, which was unrecognized for some time and which was then masked by the onset of thyrotoxicosis with its hypercalcaemic effect (Rothenberg and Redleaf, 1959). When the thyrotoxicosis was controlled the hypoparathyroidism again became

manifest. The problem of the appearance of hypercalciuria at relatively low serum-calcium levels while on treatment with dihydrotachysterol (Litvak *et al.*, 1958) has complicated his management. The second patient, critically ill with parathyroid poisoning, was cured by operation.

Possibly this association between parathyroid disorder and steroid-treated ulcerative colitis is purely fortuitous. Against this possibility is a previous report of the appearance of tetany in a patient with ulcerative colitis receiving steroid therapy (Moehlig and Steinbach, 1954). While the hypoparathyroidism might be explained by parathyroid involvement in a multisystem disease known to affect the skin, joints, eyes, liver, and kidneys as well as the bowel, the cause of the adenoma formation would remain obscure. Furthermore, one might expect that the steroid therapy which lessens the other manifestations of the disease might prevent parathyroid involvement, but in fact the opposite appeared to be the case.

A possible explanation for the association is that in severe long-standing ulcerative colitis calcium stores are reduced either through poor absorption or excessive excretion via the bowel. The use of steroids with their "anti-vitamin D" effect (Anderson *et al.*, 1954) might cause further embarrassment to the already depleted calcium stores. The effect of this might be a need for increased quantities of "para-thor-mone" resulting in either exhaustion, hypoparathyroidism, or adenoma formation.

Summary

Two patients with long-standing ulcerative colitis treated with steroids developed hypoparathyroidism and hyperparathyroidism respectively.

Both have fairly active arthritis, even though the first case has had a complete colectomy.

The tetany and cramps in the first case became more pronounced after colectomy and have persisted for four years. These symptoms respond to dihydrotachysterol, but he has a low renal threshold for calcium and a persistently positive Sulkowitch reaction in his urine. Furthermore, he has hyperthyroidism controlled by methylthiouracil.

The second case, one of hyperparathyroidism, presented with generalized weakness and a phlebotrombosis of his calf veins. He had had an episode of urolithiasis three months prior to admission. His condition deteriorated so rapidly after admission that he had to be subjected to an emergency operation for removal of a parathyroid adenoma, of chief-cell histology, with cure of his hyperparathyroidism.

The possible mechanism for this association of parathyroid dysfunction and ulcerative colitis is discussed.

We are grateful to Dr. B. M. Bloomberg and Dr. W. M. Politzer, who performed the biochemical investigations.

REFERENCES

- Anderson, J., Dent, C. E., Harper, C., and Philpot, G. R. (1954). *Lancet*, **2**, 720.
 Brit. med. J., 1959, **2**, 686.
 Davies, D. R., Dent, C. E., and Willcox, A. (1956). *Brit. med. J.*, **2**, 1133.
 Dent, C. E., and Garretts, M. (1960). *Lancet*, **1**, 142.
 Frame, B., and Haubrich, W. S. (1960). *Arch. intern. Med.*, **105**, 536.
 Jackson, W. P. U. (1957). *Lancet*, **1**, 1086.
 Litvak, J., Moldawer, M. P., Forbes, A. P., and Henneman, P. H. (1958). *J. clin. Endocr.*, **18**, 246.
 Moehlig, R. C., and Steinbach, A. L. (1954). *J. Amer. med. Ass.*, **154**, 42.
 Rogers, H. M. (1946). *Ibid.*, **130**, 22.
 Rothenberg, S., and Redleaf, P. D. (1959). *Arch. intern. Med.*, **104**, 783.
 Williams, E., and Wood, C. (1959). *Arch. Dis. Childh.*, **34**, 302.

PHENYLBUTAZONE SUPPOSITORIES IN TREATMENT OF NON-SPECIFIC PROCTITIS

BY

J. HANKISS, M.D.

Department of Internal Medicine, University School of
Medicine, Debrecen, Hungary

Recently the topical treatment of ulcerative colitis has come again into prominence. Truelove (1956, 1958). Schwartz *et al.* (1959), and others achieved a rapid clinical remission by local—that is, rectal—hydrocortisone. According to Truelove (1960) a better result is to be expected in moderate and mild cases from local treatment than from systemic prednisolone therapy. Local treatment has several advantages over systemic: (1) the active material acts directly on the diseased mucosa; (2) a greater local concentration can be attained; and (3) complicating side-effects are avoided.

We have successfully used local phenylbutazone treatment in ulcerative colitis (Hankiss and Keszthelyi, 1960; Hankiss, 1961). We tried this drug because of its excellent anti-inflammatory effect, and practical experience has supported our theoretical supposition. A rapid remission occurred in the responsive cases. This was similar to the results achieved by local hydrocortisone. The only essential difference was that, in contrast to Truelove's observations, the extent of involvement proved to be of decisive significance in the case of local phenylbutazone treatment. When the disease was limited to the distal part of the colon our results were good, whereas with diffuse colitis or with colitis involving mainly the right side of the colon local phenylbutazone was ineffective.

This treatment was given in the form of enemata which were excellently tolerated by the patients. It sometimes happened that the patients improved both subjectively and objectively but sigmoidoscopy still revealed a moderate hyperaemia above the anal ring. We thought that the enematas might maintain the inflammation here in a mechanical way and therefore we gave the phenylbutazone as suppositories. With this treatment the signs of inflammation soon disappeared.

At this time we began to be systematically engaged with the suppository treatment of non-specific proctitis.

Selection of Cases

The nature of non-specific proctitis is a debatable question. Some investigators (Thaysen, 1934; Brooke, 1953, 1954) consider it an independent unit, while others (Newell and Jones, 1958; Truelove, 1959) regard it as a concurrent phenomenon of ulcerative colitis. I hold to this second school of opinion, although in some cases of *primary proctitis* the process does not extend to the upper parts of the colon even after a long history. They show fewer general signs and are more benign *quoad sanationem*. We must bear in mind also the *secondary proctitis* which accompanies some other processes, as, for example, anal fissure, fistula-in-ano, haemorrhoids, perianal eczema, pruritus ani, helminthiasis, and post-radiation proctitis. These are usually mild forms of proctitis, without bleeding. Nevertheless they must be treated, because either they can exacerbate the underlying process—for example, perianal eczema or pruritus—or they may produce very unpleasant symptoms.