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A REVIEW OF THE DIETETIC FACTORS IN LIVER DISEASE

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II.—THE APPLICATION OF NUTRITIONAL PRINCIPLES IN TREATMENT*

Acute Necrosis of the Liver

Acute necrosis of the liver is an anatomical diagnosis which cannot be made with certainty without biopsy or necropsy. Usually, however, we must rely on the indirect evidence of acute hepatic insufficiency. Jaundice is intense and the serum bilirubin rises to 20 mg. per 100 ml. or higher. The patient is critically ill with delirium, stupor, coma, and up-going toes. There are ascites, oedema, purpura, and occult blood in the stools. If we confine the terms "acute necrosis" and "acute hepatic insufficiency" to such cases—and I believe we shall make no therapeutic advance until we establish rigid criteria—we shall find ourselves dealing with a hepatic disorder which is uncommon and which has a mortality of 50 to 100%. From a sample analysis of death certificates carried out for the Jaundice Committee of the Medical Research Council by Dr. W. H. Bradley and Dr. Percy Stocks in 1944 (unpublished report), it appeared that there were approximately 400 deaths a year from acute hepatic insufficiency, of which only about 8% were toxic jaundice, whereas the greater part were probably due to the viruses of infective hepatitis, homologous serum jaundice, and post-arsphenamine jaundice. The average number of deaths from notifiable toxic jaundice during the years 1940–4 was fewer than six a year. I stress the rarity of fatal toxic jaundice in man in view of the fact that so much of our present information has been derived from toxic jaundice in animals.

The difficulties of carrying out therapeutic trials on a disease which is uncommon and hard to diagnose are great. Much of the literature on the subject is worthless, recording isolated successes, changes of fashion, and the surprising capacity of the organism, even in sickness, to withstand onslaughts on its integrity. This state of things should improve as a result of the careful collection and study of morbidity and mortality statistics which is occurring in several parts of this country. More is to be hoped from animal experiments, which are still curiously incomplete in the matter of treatment. The drawbacks to animal experiment are the dissimilarity of animals and man, and the failure to transmit infective hepatitis to animals. Another possibility, which it is to be hoped we shall be spared, is the occurrence of epidemics of infective hepatitis with a mortality of the order of 15%, such as have lately appeared in Denmark and Switzerland.

It will be simplest to begin by discussing orthodox therapy with glucose. The untreated hepatectomized animal always dies of hypoglycaemia, and life may be prolonged for many hours by the administration of glucose. Dextrose therapy in diseases of the liver in man has been reviewed by Althausen (1933), but perhaps the most convincing data are those of Chester Jones (1936). He collected 56 cases of acute hepatic insufficiency from the records of the Massachusetts General Hospital and showed that the mortality had fallen from 95 to 63% over a period during which glucose therapy had been made more intensive. In the final period an attempt had been made to give the patient 450 to 500 g. of carbohydrate by mouth, usually combined with intravenous therapy, with solutions of glucose ranging from 5 to 25%.

There is no magic in glucose, whether it is given by mouth or intravenously, but there are, nevertheless, circumstances in which the intravenous injection of glucose may be of special value. There is normally a careful adjustment between the level of blood sugar and the release of sugar into the circulation by the liver. When the liver is damaged it may require a much higher concentration of blood sugar than normal to inhibit the formation of hepatic sugar. Such levels may not be attainable by oral feeding, and the intravenous infusion of dextrose may be essential. The fact that the hyperglycaemia so produced may lead to glycosuria is of no moment, and insulin should not be used as a rule or it will defeat the very purpose for which the glucose was given (Soskin and Hyman, 1939). A small number of human cases of acute hepatitis was treated by Minot and Cutler (1929) on a meat-free diet rich in carbohydrate, accompanied by oral administration of calcium lactate, but the work does not seem to have gone very far. Nevertheless, it has become standard practice in acute hepatic insufficiency to administer calcium intravenously, usually in the form of 10 ml. of 10% calcium gluconate, though few who carry out this procedure have read Lamson's (1930) advice on the need for extreme care and slowness.

The remarkable success of a high intake of certain proteins and protein derivatives in the prevention of acute necrosis in animals and in the treatment of cirrhosis in man has naturally given rise to the hope that these substances might be of value in acute hepatic insufficiency. Many theoretical objections can be raised against this new heterodoxy. The metabolism of proteins and amino-acids demands work from the liver, and it is a cardinal principle of therapeutics to rest a damaged organ. There is abundant evidence that meat and meat extracts may be positively harmful to animals with acute or repeated damage to the liver from carbon tetrachloride. The patient with acute hepatic insufficiency is liable to extrarenal azotaemia and uraemia, though opinion is divided whether this should indicate or contraindicate the administration of protein (Leitis, 1946; Zondek, 1946). In some cases of severe damage to the liver a state of acute renal failure develops which is known as the hepato-renal syndrome and which has been attributed to toxic derivatives of protein (Helwig and Schutz, 1932; Reich, 1941; Trueta *et al.*, 1946).

In this atmosphere of dubiety the ordinary clinician will do well, in the treatment of acute hepatic insufficiency, to concentrate on the relief of shock and the restoration of the normal internal milieu of the organism by fluids and glucose. Milk protein appears to be harmless, and milk should therefore form part of the fluid intake, though it is unlikely that more than 30 to 40 g. of protein will be supplied in this way. The therapeutic value and application of nitrogenous materials such as choline, amino-acids, protein hydrolysates, and plasma still await demonstration in

* The second of two University of London Lectures in Medicine given at the Westminster Hospital Medical School on Oct. 29, 1946. The first lecture appeared in last week's issue.

animal experiments and in controlled trials in man, and are the province of the research worker. No one knows yet whether they are helpful or harmful.

It would nevertheless be cowardly to leave the subject here without reviewing such data as are available. It is true that there is no evidence, even in animals, that proteins or amino-acids influence hepatic necrosis favourably once it has been established, though there is good evidence that choline accelerates recovery from fatty change. On the other side of the slate the research worker would note that 90% of deaths from infective hepatitis occur relatively late, when the disease has lasted more than 20 days (Lucké, 1944). The necrosis of experimental carbon tetrachloride poisoning may be repeatedly repaired, perhaps up to 40 times, but in the end there is a final phase of exhaustion when the rat is no longer able to restore the liver to normal (Cameron and Karunaratne, 1936). This suggests that patients with necrosis may run out of critical materials for regeneration of liver tissue. Regenerative ability doubtless varies from individual to individual owing to differences in hereditary and acquired characteristics, of which the previous state of nutrition is the most obvious. Death in acute necrosis may therefore be due either to temporary hepatic insufficiency or to exhaustion of the recuperative power. In our orthodox treatment we concentrate on tiding the patient over the period of hepatic insufficiency. In the future we may learn to fortify the recuperative power.

Acute Infective Hepatitis

Far and away the commonest disease of the liver in this country is infective hepatitis, or catarrhal jaundice. During the war acute hepatitis was made notifiable in Region IV, which had a population of over two and a half millions. Notification has been in force over two complete years, 1944 and 1945. The number of cases decreased from 3,559 in 1944 to 1,626 in 1945, and the incidence rate fell from 1.3 per 1,000 to 0.6 per 1,000. Voluntary notifications showed that the incidence had been higher in 1943 than in 1944. Practically all the cases notified were acute infective hepatitis. From these and other data we can assume that there were somewhere between 25,000 and 50,000 cases of infective hepatitis a year in Great Britain during the war. The mortality of infective hepatitis is about 0.2 to 0.4%, that of homologous serum jaundice and post-arsphenamine jaundice is probably higher. Owing to its low mortality and its prevalence in children, infective hepatitis is not usually regarded very seriously. During the war, however, epidemics occurred amongst our troops overseas which came near to disabling whole armies and air forces. Moreover, there was a high incidence of homologous serum jaundice and post-arsenical jaundice. These last two forms of jaundice are due to a virus which is similar to but probably not identical with the virus of infective hepatitis, and I shall consider the treatment of all three without discriminating between them.

The therapeutic problem in infective hepatitis is not mortality but the long period of disability, which averages 40 days. Various experiments have been carried out with diets and dietary principles, but no specific effect on the disease has been discovered. There is a general impression that strict rest is more important than strict diet. All that has been done—and this is undoubtedly gain—is to prevent patients being made miserable or unwell by unnecessary dietetic restrictions. Two observations can be offered in partial explanation of the failure of dietetic therapy in infective hepatitis. The main onslaught of the disease has usually occurred by the time the patient comes under treatment, and it is unusual to encounter the metabolic disturbances which arise in severe injuries and infections.

Pollock (1945) has shown that bromsulphthalein retention, biliuria, and a qualitative change in serum bilirubin may be present in the pre-icteric stage of infective hepatitis several days before the onset of jaundice. There is also a pre-icteric rise in phosphatase (Higgins and O'Brien, 1946). The earliest biopsies show gross changes in the liver, and Dible, McMichael, and Sherlock (1943), in their account of aspiration biopsy studies, say that the liver inflammation probably begins with the prodromal symptoms which are so often regarded as gastro-intestinal in origin. With the onset of clinical jaundice all the functions of the liver are found to be disturbed—carbohydrate metabolism, biliary excretion, hippuric acid and protein synthesis. Recovery usually occurs in the sequence of falling bilirubin, recovery of carbohydrate metabolism, normal hippuric acid excretion, normal level of albumin and globulin. I have already described carbohydrate as the great source of energy for the metabolic activities of the liver; and the impairment of carbohydrate metabolism, coupled with the restricted food intake, may be the cardinal event in the general depression of liver function.

Interest has recently been revived in the great loss of nitrogen which sometimes occurs in acute illnesses and after operations, accidents, and burns (Cuthbertson, 1944). The reason for this nitrogen loss, which reaches its maximum about the middle of the second week after the incident, is not known. It is not mere shortage of calories, and there is a suggestion that body protein is broken down to supply scarce substances for repair. Not only is weight lost during this phase but the healing of wounds, burns, and fractures may be retarded. Peters and his group (Peters, 1945) have made a particularly interesting study of the biochemical lesion in experimental burns. They found that there were heavy losses of nitrogen on the basal diet which could be largely prevented by a high-protein diet. They suggested that the losses were due to the raiding of tissue stores of nitrogen for one or more essential amino-acids, and showed that these could be prevented by the addition of 1% methionine to the basal diet, but not by cystine. The administration of high-protein, high-calorie diets has been recommended for general use for human convalescents (Stevenson, Whittaker, and Kark, 1946), and it is natural that similar diets should have been specifically recommended for infective hepatitis, where there is considerable cellular damage to the liver.

We have found no evidence of toxic destruction of protein in infective hepatitis. My colleagues Higgins and O'Brien (1946) found a negative nitrogen balance in three out of six of our patients, but in only one was it serious; the other three patients were in positive balance. The patients were studied as early as practicable, and it is unlikely that a negative phase was missed. Creatinuria, though frequent, was variable in degree and capricious in appearance. The evidence suggests that only occasionally is there a serious nitrogen imbalance in infective hepatitis, and in the majority of cases the negative balance which is apparent in the early stages is a reflection of the duration of the nausea rather than the severity of the hepatitis as judged by the bilirubinaemia. Similar rather negative conclusions were drawn by Higgins and O'Brien from a study of the plasma proteins in our patients. All the patients with serum bilirubin over 5 mg. per 100 ml. showed a slight to moderate fall in serum albumin and a slight rise in globulin. In cases followed from the pre-icteric stage the first event was the fall in plasma albumin. Albumin quickly returns to normal when the bilirubinaemia declines, but globulin may be much slower. The fall in serum albumin is certainly not entirely due to nausea, for it continued in patients who ate well and had a high protein intake, and in others who

had additional amino-acid therapy. It is probably related to a failure of manufacture of plasma proteins due to impairment of the liver and not to a shortage of raw materials.

The technique of therapeutic trials in infective hepatitis is now more or less standardized. We cannot use the death rate, and must rely on the duration of illness, the occurrence of relapses, and the frequency of permanent damage. The disease varies greatly in severity, but satisfactory criteria can be established for duration of biliuria, anorexia, hepatic enlargement, etc., comparability of cases, and the requisite number of cases and controls. Using such a technique Darmady (1945) found no difference between a high-calorie, high-protein, high-vitamin diet and a classical low-fat diet. Hardwick (1945) found no difference in patients allowed 180 and 50 g. of protein a day. Wilson, Pollock, and Harris (1946) found no difference in groups of patients on 202 and 68 g. of fat a day.

Results with dietary supplements are likewise disappointing. Higgins *et al.* (1945) and Wilson, Pollock, and Harris (1945) observed no effect from methionine, 5 g. a day by mouth, and Hoagland and Shank (1946) were equally unsuccessful with methionine, 5 g. a day intravenously. Rennie (personal communication, 1945) had no success with cystine, 15 g. a day by mouth. On the other hand Peters and his co-workers (Peters, Thompson, *et al.*, 1945) observed significant improvement of results with cysteine, 2 g. daily by mouth, and with methionine, 2.5 to 5 g. daily by mouth, and Wilson, Pollock, and Harris (1946) observed significant improvement with cysteine, 5 g. daily by mouth. The latter group of workers noted that the improved figures were largely explained by a smaller number of exacerbations or relapses in the treated series, and in both series the difference between the treated cases and the controls was not great. Viswanathan (1945) claimed improvement from intravenous injections of protein hydrolysate. Richardson and Suffern (1945) and Hoagland and Shank (1946) had no success with choline, 1.5 to 5.0 g. daily by mouth. Lenz (1944) had no success with insulin and glucose, and Gordon (1944) none with insulin, glucose, and vitamin C. Hoagland and Shank (1946) also had no success with intravenous liver extract.

These therapeutic trials have not escaped criticism. The diets which were being compared were not always isocaloric, but that is chiefly because a low-fat diet is unappetizing. It is objected that the intake of protein was so low that the methionine or cysteine could do little more than compensate for this. Protein intakes in our patients varied at different times from 34 to 120 g. a day, with an average of 80 to 90 g. The high-protein diets used in jaundice are not very high in comparison with the 300 g. a day forced in by Taylor (1944), but anything more than 150 g. a day is a *tour de force*. Finally it is calculated that the curative dose in man would be 20 g. of choline a day for two or three weeks, or 20 to 60 g. of methionine (Barclay *et al.*, 1945). Such large amounts are impracticable of ingestion and would require intravenous administration. This technique would be justifiable as part of a planned research on the treatment of acute necrosis of the liver, but surely not for so benign and common a disease as infective hepatitis.

My practical advice (Witts, 1945) on the treatment of infective hepatitis is that neither the fat nor the protein should be too low. A low-fat diet is unappetizing and commonly implies undernutrition. A very low protein diet is undesirable in a patient who has to regenerate shattered columns of liver cells. "Clinical experience has confirmed Bollmann's (1943) conclusions from the treatment of animals whose livers had been damaged by carbon tetrachloride,

that 'the caloric value of the diet should be as high as possible, and the ratio of carbohydrate and protein in the diet seems to be of less importance than the total caloric intake furnished by these substances.' The basic rule in the treatment of acute hepatitis is that the intake of fluid and food should be adequate to protect the patient from dehydration, acidosis, and tissue breakdown from malnutrition. The damaged liver is coping simultaneously with two tasks—the day-to-day needs of metabolism and the repair of its own substance—and it must be neither starved nor overburdened with material. A light diet with plenty of milk from which the top layer of cream has been removed fills the bill admirably. Self-selected diets also work out well, and it seems the patient will take no harm if he eats what he likes, whether he behaves like Jack Spratt or his wife. The real problem is when he does not want to eat at all. Turner *et al.* (1944) believe that if the patient were given an infusion of dextrose for every meal avoided or vomited some disasters might be obviated."

Treatment of Cirrhosis

Cirrhosis of the liver is not a common disease in Great Britain, for the number of deaths from this cause has fallen below 1,000 a year. The average duration of life of our Oxford patients is about two years after coming under treatment, so that the total number of cases being treated in the country at any one time is probably about 2,000. The small number of cases makes it difficult to carry out therapeutic trials, for in a chronic disease like cirrhosis the results are best assessed by the determination of survival rates, one year, two years, three years, etc., after the patients come under observation, and this technique necessitates a large number of cases. Moreover, we ought, if possible, to distinguish between alcoholic and non-alcoholic cases, between portal cirrhosis and postnecrotic fibrosis, and this is not always easy, even after post-mortem examination. British figures are not comparable with American figures owing to the much lower incidence of alcoholism in this country. Dr. A. R. Kelsall (personal communication, 1946) has reviewed the 48 cases of cirrhosis which have been admitted to the Radcliffe Infirmary in the last six years, and not more than two could be attributed to alcohol. The non-alcoholic cirrhotics have a closer affinity with postnecrotic fibrosis than with fatty infiltration or portal cirrhosis, and their course is more protracted and variable than that of alcoholic cirrhosis.

The changing character of cirrhosis of the liver must be borne in mind when we use past experience, such as the excellent data of Ratnoff and Patek (1942), to assess the value of new therapeutic procedures. These authors have also provided figures for the usual length of survival after the onset of ascites, jaundice, or haematemesis. There is great variability, and a small number of patients survive five years or more after these alarming symptoms. The chief desideratum, therefore, in any experiment on the treatment of cirrhosis is a large and unbiased sample of cases, which can be divided into treated and control groups and from which results of statistical significance can be deduced. In the study of individuals, chemical observations on the blood, in particular the level of serum proteins, afford objective evidence of the course of events.

Hurst (1946) has written of a precirrhotic condition of the liver, and on theoretical grounds we should expect fatty infiltration to do better than cirrhosis, but this can hardly be diagnosed clinically without biopsy. A fatty liver may be expected to be a large liver, but it is all too easy to confuse a large liver with a hard liver, and the determination of the size of the liver is a more difficult feat than many people have realized. Ravdin and co-workers (1943) proved by

biopsy that approximately 30% of patients with long-standing gall-stone disease had abnormally large amounts of lipid present in the liver, and they showed that this could be reduced by a diet of 74% carbohydrate, 20% protein, and 6% fat, in which bananas and casein figured prominently.

It has long been taught that milk is the ideal diet for cirrhosis (Rolleston and McNee, 1929). Beginning with this observation, we may omit description of the groping advance through regimens of low fat, high carbohydrate, adequate calories and vitamins, and high protein, and skip at one bound to the impressive studies of Morison (1946). Morison treated three groups of cases of cirrhosis. There were about 20 patients in each group, and about half of each group had ascites. The first group was given a high-carbohydrate diet and diuretics. The second group was given a high carbohydrate high protein diet, liver extract, and vitamins. The third group had a maximum intake of protein, liver extract, and vitamins, plus methionine and choline, of each 2 g. daily. In patients without ascites the intensive combined treatment in the third group resulted in the remission of all signs and symptoms in 7 out of 11, as compared with 1 out of 11 in the first (control) group. In patients with ascites complete remission occurred in 4 out of 9 of the third group, as compared with 0 out of 12 in the first. The death rate was very greatly reduced in the third group. The second group occupied an intermediate position. Morison's maximum protein regimen comprised a diet of 2,500 to 4,000 calories with 200 to 300 g. of protein, 300 to 500 g. of carbohydrate, and 50 to 100 g. of fat, and included 6 glasses of skim-milk a day.

Other workers have given much less protein than Morison, and they have not obtained such dramatic results, though their figures have shown an improvement on the past. Fleming and Snell (1942) found that among 150 patients treated with a high-carbohydrate and low-protein diet plus diuretics, they had good results in 30%, whereas among 50 patients treated with a diet including 350 to 500 g. of carbohydrate, 110 g. of protein, chiefly in the form of milk and vegetable protein, plus vitamin supplements, the results were good in 44%. Beams (1946) treated 20 patients on a regimen similar to Morison's second group, giving them in addition 30 to 45 g. of brewer's yeast, and choline and cystine, of each 1.5 to 3 g. a day. He found that 12 of the 20 patients whose livers were not enlarged gave no response, whereas 7 of the 8 who had large livers made a good recovery. Patek and Post (1941), in a statistical study which should be a model to later workers, gave a regimen similar to Morison's second group—i.e., 120 to 140 g. of protein, without thio-amino-acids or choline—and presented convincing evidence of improvement over previous treatment with high-carbohydrate and lower protein diet. Homburger (1946) studied carefully a patient who had been stabilized on a high-protein regimen. He produced evidence that substitution of the protein by an isocaloric amount of carbohydrate was attended by deterioration of the clinical and biochemical state.

In view of the many factors employed it has not been possible to isolate the effects of choline and methionine. Small series of cases treated with methionine with apparent benefit have been reported by Broun and Muether (1942), Herrmann and Rockwell (1945), and Russakoff and Blumberg (1944), the last giving up to 6 g. a day. On the other hand, Man and co-workers (1945) gave choline in large doses, 10 to 25 g. a day, to three patients with cirrhosis without demonstrable effect. Echaurren and Jorquera (1943) found the daily administration of 600 mg. of inositol helpful.

I will conclude with an account of our own efforts in the treatment of subacute and chronic hepatitis. Of the 48 cases admitted to the Radcliffe Infirmary in the last six years, 35 provided records suitable for analysis. Twenty-two of the patients were treated with high-protein diets, combined in most cases with a high carbohydrate and low fat intake and often supplemented by vitamin A and D concentrates, synthetic vitamin K, and food yeast. Protein intakes averaged 125 g. a day, but were supplemented by 30 to 60 g. of food yeast over long periods. No methionine was used, and a very small number received choline or protein hydrolysate, and then only for short periods. Thirteen patients received the classical treatment with relatively low protein diets and diuretics. The numbers are small, but there is no significant difference between the two groups, whether one compares the mortality, as in the following table, or the average duration of life in the various subdivisions. The results of dietary treatment in non-alcoholic cirrhosis are therefore discouraging.

	Alive	Dead	Total
Treated	15	7	22
Untreated	8	5	13
	23	12	35

Discussion

Disorders of the liver similar to those produced in experimental animals by dietary deficiency occur in man over wide territories of the world as a result of inadequate food supplies. The incidence of juvenile cirrhosis and primary carcinoma of the liver may well come to be regarded as indexes of nutrition. The problem must now be attacked by social engineering rather than medical science. It is merely one symptom of world pressure on food supplies, and it will not be solved by bread alone but by a completely different way of life among crowded people with high birth rates. The number of isolated dietary defects which are known to produce disease is already great, but we are still learning the simple arithmetic of nutrition and are not yet able to permute and combine the various factors so as to discover how they reinforce or neutralize one another. In the relatively simple problem of blood formation we are just beginning to realize how iron requirements may be affected by the protein and vitamin content of the diet. It therefore seems unlikely that fortification with individual principles will be as cheap or as effective as a general improvement of the diet in the prevention of hepatic diseases. Our knowledge is more likely to be useful in the selection of those natural foods which can be most expeditiously used to increase the biological value of the diet.

It is too early to assess the value of the new knowledge in the treatment of hepatic disease in the better-nourished populations of the world. Among them infective hepatitis and allied virus infections vastly predominate over all other forms of disease of the liver, and advances are more likely to come from bacteriology than from the science of nutrition. Alcoholism is a symptom of prosperity rather than austerity, and can be overcome only by a general improvement in the art of living. Nevertheless, we can still hope that appreciation of the nutritional requirements of the hepatic cell, and of the body as a whole, will enable us to improve the chances of recovery in the acute phases of hepatitis and to accelerate regeneration and repair at a later stage.

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SURGICAL ASPECTS OF ROUNDWORM DISEASE

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During my last two years as surgeon to the native population of Cyrenaica I repeatedly came across roundworm infestation either simulating surgical conditions or indicating, and in my opinion justifying, surgical intervention. The following three case reports illustrate these points.

Case 1

A boy aged 13 was seized by spastic abdominal pains and violent vomiting while at school on Dec. 12, 1945. He was brought to hospital about an hour after the onset of symptoms. Inquiry revealed that he had been suffering from similar attacks of less intensity for the last ten months. They used to come on about twice weekly at odd times, his pain apparently being localized in the epigastric region. For the same period he had shown no appetite and had been constipated.

Examination showed a thin, very pale boy. The temperature was normal, pulse 100, weak. The tongue was coated and moist. Chest, N.A.D. The abdomen was not distended, its excursions on respiration were noticeably restricted, and it was very tender, with rigidity especially in the right iliac fossa. Per rectum the pouch of Douglas was slightly tender, but no effusion was palpable. An acute appendicular attack with peritoneal irritation was assumed. Following resuscitation, the patient's general condition improved, and operation, under open-ether anaesthesia, was performed about four hours after admission.

A right pararectal incision was made. The abdominal cavity contained much turbid fluid, but no pus. Coils of small intestine presented, thronged with roundworms. The caecum was found above the level of the umbilicus. The appendix was in the retro-caecal position, and not adherent. Its tip was swollen and covered with a pink serosa. After appendicectomy the presenting loop of ileum, which was crammed with worms, was opened, and the worms (*Ascaris lumbricoides*) were removed. Masses of worms contained in other parts of the small gut were "milked" towards the opening and taken out. The longitudinal opening of the bowel-wall was closed transversely, a rubber drain was inserted into the pouch of Douglas, and the abdominal wound was sutured. Altogether 91 worms were removed. The appendix contained a faecalith the size of a cherry stone. The mucous membrane underneath was blackened with ulceration, which, however, macroscopically did not involve the deeper coatings. The post-operative course was uneventful, but the patient now and again complained of abdominal spasms. Following a course of anthelmintic treatment two weeks after operation several more worms were passed. There has been no abdominal discomfort since, and he was discharged cured.

Case 2

A little girl aged 5 was admitted to hospital on May 2, 1946, having been sent by her physician, who diagnosed appendicitis. She had had abdominal pains and retching for the preceding two days. The bowels were normal. The mother stated that she had never noticed worms in the child's stools. The temperature was 99.5° F. (37.5° C.), pulse 90. The general condition was fair. Chest, N.A.D. The abdomen was moderately distended, with tenderness and slight rigidity in the right iliac fossa. On deeper palpation intestinal coils containing longitudinal masses, like bundles of pencils, and very suggestive of roundworms, could be felt through the thin abdominal wall. Santonin and castor oil were given on three subsequent days. Masses of ascarides were passed in several motions. Immediately after treatment the abdominal pains disappeared and the temperature fell to normal. The patient was discharged cured on May 10.