is significant, as the saturated fatty acids—palmitic and stearic acids—do not stain with osmic acid, whereas unsaturated fatty acids such as oleic acid do. I would therefore suggest that these fat compounds secreted or excreted by the tubular glands may under abnormal conditions block the lumen of the gland, and so render them liable to be more easily infected by micro-organisms than they would be if carrying out their normal functions.

The close relationship between appendicitis and colitis has been frequently suggested. Harley and Goodbody,¹⁰ in discussing the etiology of mucous colitis, do not admit that it is generally consequent on appendicitis. A great number of cases undoubtedly follow appendicitis, but this fact does not necessarily imply that the appendicitis is responsible for the condition. The underlying pathological condition which caused the appendicitis is probably the same as that which caused the colitis.

Intestinal lithiasis is, according to Nothnagel, usually associated with mucous colitis, and may be prolonged over many years.

In relation to the above views, Case 1, mentioned above, is of interest.

The appendix was removed in November, 1905, on account of repeated attacks of abdominal pain. The patient stated that one month afterwards the same pain recurred, and continued intermittently until December, 1906, when she was admitted to Sir James Barr's wards. Colic was present at this period, with attacks of nausea and vomiting. The vomiting was unrelated to food. The patient was of a neurotic temperament. In the stools were found much mucus and quantities of intestinal sand. The sand was not immediately obvious, and was gathered by the methods mentioned above. It was analysed and shown to be true intestinal sand. After some weeks' treatment the symptoms and stools were much the same as on admission. With the view of relieving the symptoms the patient was placed on a diet containing much unsaturated fat (olive and sardine oils, both of which have very high iodine values). After a week on this diet the amount of sand and mucus in the stools was very much diminished. On the patient resuming a diet containing butter fat and meat fats (saturated), the sand and mucus increased very definitely in quantity. The stools were carefully collected under these conditions, and are being subjected to special examination for separation and determination of the different saturated and unsaturated fatty acids. After three months' treatment with olive oil, the pain is much less, and there is very little sand or mucus in the stools. The fact that unsaturated fats might be of value was suggested by obvious theoretical considerations, the formation of more soluble and more easily split-up soaps. This is borne out in a case related to me by Dr. Thomas Clarke who, many years ago, had a patient suffering from abdominal symptoms, with which was associated intestinal lithiasis. Treatment for a very considerable time failed to relieve the patient until she was placed on a diet containing olive and salad oils, when the symptoms and sand both disappeared in a few weeks.

French authors (Dieulafoy, Matthieu, Talamon, Reclus, and others) attach special importance to a peculiar form of catarrh as being the cause of the formation of intestinal sand, a catarrh which they consider to stand in close relationship to enteritis membranacea or also to gout, and which, according to some, is also the cause of appendicitis. Dieulafoy¹¹ has called attention to the number of patients suffering from muco-membranous typhlo-colitis who are operated on for an appendicitis which they have not got. He described thirteen cases, all suffering from abdominal pain. It has frequently occurred that patients have been operated on for appendicitis when they have had enterocolitis, and Dieulafoy has observed the painful crises to recur at the same spot and with the same intensity after the operation. Bottentuit¹² has similarly collected 22 cases who have suffered from muco-membranous typhlo-colitis, or intestinal lithiasis, who have been operated on for a non-existent appendicitis.

It is therefore possible that the observations recorded above may afford a solution to the suggestions which have been made as to the relations between appendicitis and mucous colitis on the one hand, and mucous colitis and intestinal lithiasis on the other, and go still further to suggest a possible relation between the three diseases, they having in common some abnormality in the conduction of the processes associated with the digestion and absorption of fat, and the production of calcium salts of saturated fatty acids.

FAT CONCRETIONS IN THE INTESTINE.

That these are not the only conditions in which pathological fat processes are associated with disease is seen from the following cases:

From a patient suffering from acute intestinal obstruction Mr. Paul removed a mass which was causing the obstruction. It was situated in the small intestine in the upper part of the jejunum. Recognizing the unusual character of the mass, Mr. Paul kindly sent it to me to examine. It was about the size of a small tangerine orange. In the centre was a raisin, around which was a bright yellow pultaceous mass held together by stroma of vegetable material. The exterior was stained by faecal material. It was found to contain 34.1 per cent. of fat (of this 74 per cent. was present as combined fat having the low iodine value of 18 per cent.). The unsaponifiable material was isolated, and proved to be cholesterine. That this was not a concretion such as is sometimes formed by the administration of large quantities of olive oil was proved by the nature of the fat.

In another case of Mr. Paul's, a male, the symptoms suggested the presence of gall stones. Intestinal sand was found in the stools. When operated upon there were found in the bile passages and neighbouring portions of the intestines numerous very small brownish-red granules, but no stones. An analysis of these granules showed that they contained fat in quantity. This specimen is of interest in relation to the work of Duckworth and Garrod, who, from the nature of the pigments in their specimen of intestinal sand, suggested that it had been formed in the region of the duodenum.

The fact that the fatty acids present in all the above conditions are saturated—such as palmitic and stearic—is of high interest, for it is well known that these fats, when given alone, are only absorbed in very small quantities, from 86 to 91 per cent. remaining as residue in the faeces, whereas, when given mixed with unsaturated fatty acids, such as oleic, they are absorbed to a higher degree. Olive oil, when given alone, is almost all absorbed, only 2 per cent. remaining in the faeces.

Equally interesting, from the point of view of the value of the various fats in human food, is the fact that human milk contains a very high proportion of unsaturated fatty acids compared with the milk of the cow. The fact that unsaturated fatty acids aid the absorption of the saturated suggests that in the above conditions, where insoluble compounds of saturated fatty acids occur, the administration of olive oil might be of value in aiding the absorption of these deleterious products.

Observations which are being made tend to show that the nature of the fats in the diet have some effect in producing the conditions mentioned in this paper.

My thanks are due to Professor Vaughan Harley, in whose laboratory the work was commenced, and to Mr. Thelwall Thomas for many valuable specimens. To the surgeons and physicians of the Royal Infirmary, Liverpool, I am indebted for the use of their cases, for specimens, and for the time to conduct these researches. The work was conducted in the Bio-chemical Laboratory of the University, under the direction of Professor Benjamin Moore. My thanks are due to him for his valuable advice, and to my colleagues in the laboratory for much kind assistance.

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ON THE ETIOLOGY AND PATHOLOGICAL HISTOLOGY OF BERI-BERI.*

BY

R. TANNER HEWLETT, and W. E. DE KORTÉ,
M.D., F.R.C.P., M.B.

PROFESSOR OF GENERAL PATHOLOGY
AND BACTERIOLOGY IN KING'S
COLLEGE, LONDON.

A NUMBER of hypotheses have been advanced respecting the etiology of beri-beri. It has been ascribed to a microbial infection by a staphylococcus (Pekelharing and Winkler), by a bacillus (Rost), by a micrococcus found in the urine (Okata and Kokubo), to arsenical poisoning, to nitrogen starvation, to an intoxication from emanations

* Abstract of a paper read at the British Medical Association Meeting at Toronto, 1906. The publication of this paper has been delayed owing to the loss of the manuscript in transmission.

from the soil (Manson), or from bad rice, etc. Hamilton Wright believes it to be an intoxication due to products formed by a large bacillus living in the duodenum; Daniels suggests that it is due to a protozoan, the parasite being conveyed probably by lice.

We have recently obtained several monkeys suffering from a disease which in some respects bears a considerable resemblance to beri-beri. The animals were evidently very ill, in most of them there was considerable oedema of the face and genitals, much like renal dropsy, but the urine never contained any albumen, and the knee-jerks were either increased, or diminished, or absent. They all died, and the only constant lesion found was congestion of the kidneys, which showed cloudy swelling of the renal epithelium, and in scattered areas haemorrhages into the convoluted tubes with denudation of their lining epithelium, and congestion of the glomerular vessels. Hyaline casts were constantly found in the urine, which in some of the animals contained highly refractile cells of an unknown nature (? protozoa). Attempts to infect healthy monkeys from the sick were not very successful, the condition of marked oedema was never obtained, but in two animals the eyelids became puffy, they became weak and ill, and the knee-jerks were exaggerated. These results suggested that possibly in beri-beri an infective organism exists, protozoan in nature, and eliminated in the urine, by which the infection may be conveyed.

We therefore fed monkeys with the urine of cases of beri-beri occurring at the Seamen's Hospital, Royal Albert Dock. These experiments unfortunately were vitiated by the presence of tuberculosis in some of the animals, but in two which were free from tubercle a condition of illness, emaciation, puffiness, cyanosis, weakness of hind legs, and alteration of the knee-jerks seemed to result from the feeding with urine.

We also examined the urine of cases of beri-beri at the Seamen's Hospital. The urine in the acute stage is generally concentrated and high-coloured, and deposits urates. Centrifugalized, the deposit constantly shows hyaline and granular casts more or less abundantly. Small refractile spherical bodies are also present, measuring 2 to 3 μ in diameter, apparently having a thick capsule, enclosing hyaline contents. These do not give the reactions for fat with osmic acid and Sudan III, but may be products of degeneration (? "myelin bodies"). Other cells also occur; these measure 20 μ in diameter, are globular, and contain a cytoplasm studded with very refractile granules and having a single nucleus. A third form of cell may be met with, 30 μ in diameter, enclosed within a thick capsule, and containing a finely granular oval nucleus with rounded nucleolus. Both the last two varieties of cells stain faintly with neutral red, methylene blue, and methyl green in physiological salt solution in wet specimens, but if smears be made and dried they seem to disintegrate and cannot be found. These cells either are peculiar degenerate cells or possibly are protozoa.

We have also examined a number of kidneys obtained from cases of acute beri-beri, kindly forwarded to us by Dr. McDougall of Singapore, to whom we would tender our best thanks. Sections of these kidneys show changes similar to those met with in the monkeys' kidneys, but in a more intense form—namely, congestion of the glomerular vessels and haemorrhages into the glomeruli, scattered patches of haemorrhages into the tubuli recti and convoluted tubules, with denudation of epithelium in these areas, and much widespread cloudy swelling of the renal epithelium. We believe that these changes have not been described before.

In conclusion, as a working hypothesis, we would suggest that beri-beri is a protozoan infection, that the infecting agent is eliminated in the urine, and that the urine is the source of infection.

ARTHRITIS AND ERYTHEMA NODOSUM.

By J. ODERY SYMES, M.D., D.P.H. (Lond.),

PHYSICIAN TO THE BRISTOL GENERAL HOSPITAL.

THE generally-accepted view with regard to the arthritis which sometimes accompanies erythema nodosum is that it is a true acute articular rheumatism. This view is founded on the fact that endocarditis develops or is found to be present in a large proportion of the cases. Mackenzie collected records of 108 cases of erythema nodosum (90

females and 18 males), and 15.7 per cent. showed definite arthritis, and a further 15.7 per cent. complained of rheumatic pains; 21.3 per cent. of the total had or developed signs of endocarditis. Goodhart and Still found that of 29 cases of erythema nodosum, 19 were rheumatic, 5 were not rheumatic, and in 5 the history was not inquired into.

My own experience of six years in the medical outpatient department has been that the signs or a history of chorea, endocarditis, or arthritis are not found in more than 10 per cent. of all cases of erythema nodosum.

Other points in favour of erythema nodosum being a rheumatic manifestation are: The age-incidence of the two diseases (rheumatic fever and erythema nodosum) are practically identical, the majority of cases (63.2 per cent. of 125 cases of erythema nodosum, 55.8 per cent. of 193 cases of rheumatic fever) occurring in the second and third decades of life; the incidence of disease is, too, in both cases heaviest upon girls between the ages of 10 and 15 years. There is some evidence to show that both diseases occasionally occur in epidemic form, and may be infectious, and they have in common such symptoms as various forms of erythema, arthritis, tonsillitis, and endocarditis.

Erythema nodosum differs, however, from rheumatic fever in that it much more commonly attacks females than males (of 125 cases of erythema nodosum, 36 were males and 89 females). It is most prevalent in the last and the first two quarters of the year, whilst acute rheumatism in Bristol is most prevalent in the third quarter. A long prodromal period of malaise, comparative freedom from the risk of recurrence, slight constitutional disturbance during the pyrexial period, and the presence of phlyctenulae in the eyes, are characteristics of erythema nodosum. To these differences I wish to add another—namely, that the arthritis of erythema nodosum may differ entirely from that met with in rheumatic fever, and that this arthritis and the accompanying pyrexia and rash are little influenced by the administration of salicylates. In illustration of this last point I would quote the following three cases:

CASE I.

Mrs. W., aged 63, had suffered from erythema nodosum when 5 years old. With the exception of an attack of influenza when 50 years of age, which was followed by neuritis, and which had left her with an irregular action of the heart, her health had been good. On August 10th, 1906, she left for a holiday at the seaside, and for the first fortnight of her stay suffered from lassitude and pains about the limbs and trunk.

About August 24th there was fever, with dry, coated tongue, the joint pains became worse, and by August 28th the articulations were distinctly red and swollen, and a rash was noted on the arms and legs. She returned home, and was seen by me on September 2nd. The temperature when the patient was first seen was 101°, and, in spite of large doses of salicylate of soda and aspirin, pushed until tinnitus and delirium were produced, it remained between 100° and 102° for ten days. The joints affected were those of the wrists, ankles, fingers, and knees, and there was slight stiffness in the temporo-maxillary joints. Contrary to the condition generally seen in rheumatic fever there was much redness and puffiness of the joints, the overlying skin pitting as it does in gout. Although there was a sensation of stiffness the joints were not painful, even on movement. They did not resume their natural appearance for ten days. The rash of erythema nodosum was present on the arms and legs, and fresh crops of nodules appeared from time to time, lasting in all for five weeks. During the first week there was profuse sweating, and a sudaminal rash appeared on the trunk. There was oedema of the legs. There was no cardiac bruit or dilatation of the ventricles. The pulse-rate at no time reached a hundred beats per minute. Beyond some stiffness in the joints and slight pyrexia when aspirin was withdrawn, recovery was uninterrupted. In the early weeks of the illness there had been a pricking sensation in the conjunctivae, nose, and throat. This attack differed from acute rheumatic fever in that it did not yield readily to salicylates, also in the nature of the arthritis, which was painless, and accompanied by much reddening and oedema of the skin. There was never grave constitutional disturbance, but early in the illness there was slight bronchitis.

CASE II.

G. S., a married man, aged 36, attended the Bristol General Hospital on April 3rd, 1905, complaining of pains in both knees and in the left elbow. The pains were of five or six weeks' duration and were worse when in bed. The joints were swollen, painful and stiff, and suggestive of gonorrhoeal rheumatism, or of rheumatoid arthritis. Seven years previously he had a slight attack of rheumatism, but not of such a nature as to keep him home from work. Twelve months previously he had gonorrhoea, the discharge appeared again