often found to increase the serum cholesterol levels (Hatch and Kendall, 1952)? We are inclined to doubt that the serum lipid differences observed in the present studies are caused by low fat intakes.

We have proposed in another study (Mann, Teel, Hayes, McNally, and Bruno, submitted for publication) that muscular exercise may exert an effect in reducing or controlling the serum lipid levels in a manner analogous to the favourable effect of exercise on carbohydrate tolerance in diabetic subjects. This hypothesis would attribute the low cholesterol levels found in Guatemalans and Africans not to the limited diet but to the muscular activity and energy expenditure required in those cultures. This proposes that a large muscle mass or a large muscular expenditure is the effective agent, and that this, not the diet, is the important element in preventing hyperlipaemia and perhaps atherosclerosis. Reflection will show that such an explanation is at least as compatible with the available observations as is the dietary fat explanation which has been so widely advocated. When this effect of exercise was examined experimentally in human subjects it was found that doubling the calorie intake of young men who were consuming a very high fat diet did not increase the serum cholesterol or lipoprotein levels so long as the excess energy was expended in physical activity. There was some evidence that physical training actually diminished the serum lipid levels in the presence of large food intakes, and that a large muscle mass tended to delay the hyperlipaemia which results from periods of positive calorie balance (Walker *et al.*, 1953). The same experiment did not confirm the hypothesis that the level of serum beta-lipoprotein is directly correlated with the magnitude of the energy exchange.

There is no evidence in human subjects that the protein intake influences the regulation of the serum lipid levels. We have shown in cebus monkeys (Mann *et al.*, 1953) that a mild deficiency of cysteine and its precursors is necessary for the production of hyperlipaemia and atherosclerosis in that species by cholesterol feeding. The association of low dietary protein intakes with low serum lipid levels, and the dissociation of cholesterol and beta-lipoprotein levels in the human subjects studied here, all detract from the possibility that these dietary situations produce the same results in the two species.

Summary

It has been shown that the serum cholesterol levels of 46 Nigerian men were significantly lower than the levels of an age- and weight-matched group of United States citizens. The serum lipoprotein levels of the Nigerians were only slightly lower than those of the North Americans, and these differences were of doubtful significance.

The Nigerian subjects were found to consume diets of low protein and fat content.

The relation of these dietary characteristics to the serum lipid findings has been discussed.

The data are interpreted as supporting a hypothesis which relates muscle mass and the magnitude of energy expenditure to the control of the serum lipid levels.

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TRUE ENTEROLITHS OF THE SMALL INTESTINE

WITH REPORTS OF THREE CASES

BY

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True enteroliths of the small intestine are of three main types: (1) those consisting mainly of bile acids; (2) those consisting mainly of calcium oxalate; and (3) those consisting mainly of phosphate. Bile acid enteroliths are formed mainly of choleic acid; a small proportion of cholic acid may also be present. Two such stones, formed in duodenal diverticula, were analysed by me a few years ago (Fowweather, 1949), and the clinical features of the case were also described (Armitage, Fowweather, and Johnstone, 1950). Three cases involving the other types of stone have since come to my notice.

Case 1

The first case was that of a woman of 65 who was first seen by Dr. A. Leese, who diagnosed the presence of enteroliths and referred her to Mr. George Armitage for operation. It was then found that a portion of small intestine just proximal to the ileo-caecal valve was the seat of considerable changes. These consisted mainly of a series of constrictions, eight in all, with stones lying in pouches above some of the dilatations. To indicate the position of the stones the constrictions were numbered 1 to 8, from the ileo-caecal valve upwards.

Stones Marked "Above 8."—Two stones were present, both dark brown in colour and oval in shape. (1) Weight 10 g.; length 30 mm. In the centre was a plum stone weighing 0.6 g. The material surrounding it was dark in colour and laminated. There was evidence of loss of part of the outer layer. When broken, the fractured surface was lighter in colour than the unbroken surface, and when powdered was bright orange. (2) Weight 7 g.; length 28 mm. In the centre was a plum stone weighing 0.5 g. The surrounding material was very similar to that of (1) and also showed some loss from the outer layer.

Stones Marked "7 and 8"—Two stones were found between constrictions 7 and 8. (1) This was a plum stone weighing 1 g. and 22 mm. in length. The surface was shiny and smooth as if worn. (2) This was also a plum stone, covered with a thin, hard, yellow-brown coating. Total weight 1.4 g.; length 24 mm. The plum stone itself weighed 1 g.

Stone Marked "5 and 6."—This was of irregular shape (about 12 mm. in diameter) and weighed 0.8 g. It had the same brownish colour as those already mentioned, but no foreign body could be recognized within it. It is conceivable that a portion of the outer layer lost from the first or second stone referred to may have acted as the nucleus for deposition in this case.

Stone Marked "4 and 5."—This was a small plum stone, weight 0.5 g. and length 17 mm., covered with a thin shell of deposit which weighed 0.1 g.

Stone Marked "3 and 4."—This was 18 mm. in length and weighed 1 g. It was a small fruit stone, in shape and size more like a cherry stone than a plum stone, covered by a layer of deposit, from which portions had been lost. The fruit stone weighed 0.4 g.

Stone Marked "2 and 3."—This was 16 mm. long and weighed 1.1 g. It had a smooth, unbroken surface and was a small fruit stone weighing 0.3 g. and 15 mm. long, with a thin black-and-brown covering. It resembled a damson stone.

Analysis

"Above 8."—These stones were much the largest and provided the most suitable material. The coverings of the two fruit stones were identical in appearance, and were ground up together to a fine powder and used for the analysis. The results were :

Moisture (loss at 100° C.)	..	..	5.16%
Free fatty acids	..	..	0.27%
Neutral fat and cholesterol	..	..	0.15%
Bile acid (mainly choleic acid)	..	..	5.45%
Calcium oxalate	..	..	85.11%
Calcium sulphate	..	..	0.78%
Bile pigment, food residues, etc.	..	..	3.08%
			100.00%

Examination of the other materials showed a substantial amount of calcium oxalate—that is, they were qualitatively similar to the above, but there was evidence of some quantitative differences; there seemed little point in making detailed analyses of all of them even if the quantity of material available had made it possible. Some of the differences noted were :

"7 and 8."—The covering of (2) when ground was not so bright as "above 8."

"5 and 6."—This also differed in colour, being of a dark buff shade. This material contained less calcium oxalate and more bile acid than "above 8."

"4 and 5."—Similar in colour to "5 and 6" but harder, and contained more oxalate.

"3 and 4."—Darker in colour than any of the above, and harder; probably contained still more oxalate.

"2 and 3."—Very similar to "3 and 4"; if anything, a little darker in colour.

Case 2

The second case was that of a woman of 63, who was operated on by Mr. Digby Chamberlain. He found a loop of small intestine a short distance above the ileo-caecal valve. This loop had been formed many years earlier by a short-circuit operation which had been carried out to relieve an intestinal obstruction. Mr. Chamberlain removed the loop, and in it were four stones. All were similar in shape, size, and colour, being disk-like and roughly circular in outline, and almost black. I obtained two stones for analysis, the other two being retained with the excised loop of intestine for a museum specimen.

The first stone was about 25 mm. in diameter and weighed 3.2 g. It had a hard shell with a faecal core. The second was slightly larger and weighed 3.7 g.; its core was a plum stone 20 mm. in length. Both were laminated. A portion of the shell of the first stone was used for qualitative analysis, and the residue was later added to the shell of the second for quantitative analysis; moisture was first removed by drying in the steam oven. The analysis showed :

Free fatty acids	..	..	0.15%
Neutral fat and cholesterol	..	..	0.44%
Bile acid (mainly choleic acid)	..	..	11.48%
Calcium oxalate	..	..	83.45%
Bile pigment, food residue, etc.	..	..	4.48%
			100.00%

Case 3

This patient was a woman of 47 from whom Mr. Michael Oldfield removed a stone which he found impacted in the ileo-caecal valve. The stone was almost black in colour, of somewhat irregular shape, and weighed 2.5 g. Besides oxalate and phosphate it contained a considerable amount of organic matter. The analysis showed :

Neutral fat and cholesterol	..	..	2.47%
Bile acid (mainly choleic acid)	..	..	3.78%
Calcium phosphate	..	..	44.25%
Calcium oxalate	..	..	23.00%
Organic matter	..	..	24.30%
Undetermined	..	..	2.20%
			100.00%

It is hoped that more complete clinical details of these cases will be published later.

Stones in the Appendix.—In addition to the above, one case of stones in the appendix came to my notice. There were three stones—one about 13 mm. in diameter and two about 5 mm. in diameter, all dark brown. The stones contained a considerable amount of mineral matter, consisting mainly of calcium phosphate, together with organic matter in which protein and fat could be recognized. The composition seems similar to that of intestinal sand, but a more detailed analysis was not made.

Discussion

According to Blix (1935) a stricture or diverticulum of the small intestine is necessary for the formation of stones. Others have emphasized the importance which altered mechanical conditions must play in favouring the growth and retention of stones. Other factors are conditions favouring the deposition of some of the contents of the small intestine in insoluble form, and the presence of a suitable nucleus on which this material may be deposited and to which it adheres. It is possible that the body which forms the nucleus may sometimes play a major part in stone formation. The presence of plum stones in enteroliths has often been recorded in the literature, and it is tempting to regard them as more than a passive nucleus in some cases, for while smooth, rounded bodies may pass easily through the intestine, it seems likely that the sharp points of plum stones may well cause trauma, swelling, or spasm, which will result in slow passage of the stone or a definite arrest, giving ample opportunity for the deposition on them of insoluble material, so that they become true enteroliths.

The nature of the material forming the stones depends on conditions causing its precipitation, and this in many cases depends on the pH, which varies as one passes along the intestine. Hence each type of stone has a region where conditions are most favourable for its formation. But the locality in which a stone is found is not necessarily the place where it was formed; stones sometimes leave diverticula and pass further along the intestine, where they may gather other material before finally being removed. Also conditions where a stone is forming may favour the precipitation of more than one substance, so that, besides containing various proportions of food residues, they contain more than one substance that has been precipitated. Their rate of growth varies, owing to change in supply of the precipitated material or to change in pH where the stone is situated; these changes no doubt account for the fact that most stones consist of a number of layers.

Enteroliths consisting mainly of bile acid have been reported on about twelve previous occasions. All have been found in women, except in one case reported by Ward-McQuaid and Gordon (1950). In this case, that of a man of 80, multiple stones were found in a duodenal diverticulum. They were said to consist of cholic acid, but analytical figures are not given. It seems to me more probable that they consisted mainly of choleic acid. The conditions responsible for the formation of bile acid stones (of which an acid pH is one) have already been discussed by me in the report

already referred to. Their site of formation is usually the upper part of the small intestine.

According to McGee and Hastings (1942), the pH of the upper part of the small intestine is between 6.2 and 6.8 except in a few isolated instances. Information about the lower part appears to be less precise, but it seems to be accepted that the acidity decreases gradually as one passes further from the duodenum, so that the reaction in the lowest portion of the small intestine is frequently alkaline, and it is such a reaction which favours the precipitation of phosphate.

Stones of the small intestine consisting mainly of phosphate therefore have this part as their site of formation. Very few complete analyses of such stones have been recorded. More usually, the presence of phosphate is referred to in general terms. Thus Ho Dac Di (1935) removed from a woman of 40 a stone which he describes as the size of a mandarin orange, and which, on chemical analysis, revealed the presence of phosphate and oxalate of calcium; there were no calcium carbonate, cholesterol, bile pigments, or uric acid. More recently Richards (1951) removed three enteroliths from a woman of 44; he states that biochemical analysis indicated that they were composed mainly of organic debris, with some fat and lipid matter and a moderate amount of calcium and magnesium phosphates.

Calcium oxalate may be precipitated at a slightly acid as well as an alkaline reaction, and may therefore be deposited in any part of the small intestine. Barth (1928) made what appears to be the first report of a small intestine stone consisting mainly of this substance; it contained over 78% of calcium oxalate and 20% of organic matter, the latter mostly faecal material; no mention is made of bile acids. Blix (1935) described an enterolith containing about 58% of calcium oxalate and 11% of choleic acid. Grettve (1947) discussed enteroliths at some length and described a case of his own. He referred to the above-mentioned cases of Barth and Blix as the only published cases in which the stones consisted predominantly of calcium oxalate, and considered it most likely that the oxalic acid required for the formation of these stones comes from the food, which in the bowel is combined with calcium. The stone in his own case was analysed and reported on by Blix (1947). It contained approximately 79% of choleic acid and about 3% of calcium oxalate. Blix at the same time reported on a small-intestine stone sent by Dr. Waldenström. The interior of this contained 56% of calcium oxalate and about 19% of choleic acid, while the surface layer contained about 70% of calcium oxalate and only very little bile acid.

It will be seen that, judging from published reports, cases of stones in the small intestine are rare. No doubt cases are dealt with from time to time without any report being made. Of some in the literature the composition is described only in general terms. It would no doubt increase our understanding of the subject, and probably of lithiasis in general, if all such stones were reported and analysed as completely as possible.

Summary

Two cases of enteroliths consisting mainly of calcium oxalate, and one whose main constituent was calcium phosphate, have been described, and an analysis of the stones in each case has been given. In addition, a case in which stones were found in the appendix has been briefly referred to.

The conditions and sites of formation of enteroliths have been briefly discussed.

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Medical Memoranda

A Case of Human Parasitization by *Ixodes hexagonus*, Leach (Hedgehog Tick)

A welder aged 45 had noticed, a week before seeking advice, what he took to be a wart on his neck, and covered it with a strip of adhesive plaster. By the sixth day the "wart" had grown much larger, and on removing the plaster to inspect it he was concerned to discover something moving between the "wart" and the skin.

The "wart" was bluish grey in colour, spindle-shaped, and $\frac{3}{8}$ in. (1.6 cm.) long by $\frac{1}{8}$ in. (1 cm.) at its widest part. Black legs could be seen moving between the "wart" and the skin. Gentle traction revealed that the "wart" was the abdomen of a tick engorged with blood. The front end of the parasite was so firmly embedded in its host that further traction caused a part of its abdomen to come away with the forceps, spilling about 1 ml. of blue blood. The colour of the "wart" was due to the colour of the ingested blood showing through the integument of the parasite's abdomen. Firmer traction dislodged it completely, leaving a reddened vesiculated area, which completely healed in two or three days. The patient had not felt the bite, nor discomfort at any time.

At the British Museum (Natural History Section) the tick was identified as an adult female of *Ixodes hexagonus*, a blood-sucking parasite. This tick is most commonly found infesting the hedgehog. Its life-cycle consists of four stages—those of egg, larva, nymph, and adult—the active stages requiring a feed of blood from a host before passing to the next stage. As at each feeding stage it drops from the host when fully fed, the tick has to find a fresh host after each moult. Apart from hedgehogs, the tick is found on stoats, weasels, ferrets, dogs, cats, and other mammals; and, very infrequently, on man.

Records kept by the Natural History Section of the British Museum show that hedgehog ticks brought for identification after being found on human beings—mostly on the head and neck—numbered about 20 between 1940 and 1951. Other specimens were found in garden shelters, houses, and factories. Because of the protection afforded by the adhesive dressing in this case the tick had been allowed to feed for so long on a human host. The relatively large number of cases of human infestation in 1944 (13) were due to the greater recourse to Anderson shelters in that year. It is suggested by Arthur (1953) that the ticks are transferred by cats and dogs from the vicinity of hedgehogs' nests to houses and gardens. It was later discovered by my patient that three hedgehogs had recently been seen in his neighbour's garden.

When found on human hosts these ticks should not be removed by traction. The reason is that the anterior segments of the tick are modified into two laterally placed palpi and a central hypostome armed with recurved teeth like the barb on a fish-hook. The insect bites by first making an incision with the cutting organs, then inserting the hypostome. The host's blood is then taken up through a central canal in the hypostome in the same way as fluid is aspirated through a hypodermic needle. If the attempt is made to pull the tick off its host, the hypostome will be left in the skin. The best method of removal is to apply oil liberally to the tick and surrounding skin. This has the dual purpose of blocking up the two laterally placed spiracles through which *Ixodes hexagonus* respire, and of softening the skin of the host.

I am indebted to Mr. E. Browning, of the British Museum (Natural History), for his help in preparing this note.

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