Reports

Incidence of Familial Hyperlipemia

Abstract. Familial hyperlipemia is an inherited disease associated with early onset of coronary atherosclerosis. In a survey of a student population in Sweden, an estimated case incidence of 2 to 3 percent was discovered. This study also demonstrates that there is probably a heterogeneity of causes for the primary elevation of blood triglycerides in man.

Familial hyperlipemia is an inherited disease thought to be due to a single gene difference causing a defect in the lipemia clearing system. The disease was first described by Bürger and Grütz in 1932 (*1*), and since that time over 100 cases have been studied; it is generally agreed that the heterozygous condition manifests itself by a delay in the clearing of ingested fat from the plasma, milky serum with elevation of all lipids but mainly of the neutral fats, the appearance of severe atherosclerosis in early adulthood, and occasionally xanthomatosis. The homozygous condition is characterized by hepatosplenomegaly, abdominal crisis, milky serum, childhood atherosclerosis, and xanthomatosis (*2*).

While it is known that the elevated lipid levels are due to an abnormal prolongation of the clearing of ingested fat from the plasma, there is no general agreement about the exact biochemical lesion responsible for the phenomenon. The three leading explanations are absence or diminution of tissue lipoprotein lipase (clearing factor) (*3*), an abnormality of the chylomicrons (*4*), or an inhibition of the lipoprotein lipase system (*5*).

Although there have been a number of individual case reports, until this time no study of the incidence of this disease in an apparently normal population has appeared. During the routine screening examination of entering students, blood samples were obtained from 998 consecutive students at Uppsala University in Sweden (*6*). The students ranged in age from 18 to 60, 95 percent being 19 to 29, and 80 percent being 19 to 23. There were 496 males and 502 females.

The samples were examined for optical density both visually and by the use of a Beckman DU spectrophotometer at a wavelength of 640 mμ, with the red-sensitive photocell. All those students whose plasma showed a density above the lowest photometric level associated with faint visual turbidity were recalled for fasting specimens. Of the 274 students recalled, 269 returned. Their serum was analyzed for optical density as described above, as well as for "total lipids" by the phenol turbidity method of Kunkel, Ahrens, and Eisenmenger (*7*). The latter method was utilized only as a rough screening test and was not interpreted as an indication of true lipid level.

Thirty-six of these students showed an optical density of over 0.080, a phenol turbidity level equivalent to over 800 mg percent of lipid, or both, or borderline elevations in both these tests. These 36 students were recalled again for a complete medical history, physical examination, urinalysis for sugar and albumin, a fat-tolerance test, and a total determination of serum cholesterol. Five other students were chosen at random, and they, as well as two healthy staff members, were exposed to the same series of examinations. For the fat-tolerance tests a meal of 90 g of fat consisting of normal breakfast foods was given, and blood samples were drawn at the fasting level and at 3 and 9 hours after the meal; there was no food intake between the time of the meal and 9 hours later.

Of the 36 students recalled, 16 demonstrated a marked delay in clearing of neutral fat from the serum, and four showed borderline delay in such clearing. These 20 students ranged in age from 19 to 47, 80 percent being 19 to 27; thus they were somewhat older than the original group. Fifteen of these, including the four borderline cases, were male, perhaps indicating that the disease may be more easily discovered in the male, at least in the younger age group.

Five other students were found to have primary hypercholesterolemia, while three students demonstrated elevated serum optical density both before and 9 hours after the meal, but without delayed return to the fasting levels. Eight of the 36 students were found to be completely normal, showing normal fasting levels at this time. It was strongly suspected that they had eaten before the initial (fasting) samples were obtained.

Some of the students showing hyperlipemia, who had been recalled for fat-tolerance tests because of elevated optical density in their initial samples, showed a serum optical density of below 0.080 in the fasting samples of the fat-tolerance tests despite marked prolongation of clearing time. This indicates that the previously chosen borderline for normal had been too high, and that several cases must have been missed. A statistical analysis leads us to suspect that at least 10 more cases of essential hyperlipemia were missed in the original sample because of fasting optical density values below 0.080, but above the true upper limit of normal.

It would appear, therefore, that the incidence of familial hyperlipemia in an apparently normal northern European population is between 2 and 3 percent, probably closer to 3 percent. In view of the increased predisposition to atherosclerosis in this illness, as partly demonstrated by an increased incidence of atherosclerosis at relatively young age in the families of these students, it is felt that this group makes up a fairly sizable proportion of the increasing number of patients with atherosclerosis. This opinion seems to be confirmed by the findings of delayed lipemia clearing in the plasma of atherosclerotic individuals (*8*).

It is strongly suspected that thrombosis and fibrin deposition may be vital factors in the pathogenesis of atherosclerosis. It is of significance in this connection that increased blood coagulation (*9*) as well as inhibition of fibrinolysis (*10*) have been found in hyperlipemia.

It is of special interest that three individuals were found during this study who maintained an elevated optical density of the serum despite the ability to clear ingested fat normally. A study of the cloudy material in the serum of one of these patients has shown it to be a form of lipid, and it may well represent the abnormal chylemicra held responsible for this disease by some investigators. Although we would hesitate to call

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

these three subjects familial hyperlipemics, since they clear ingested fat in a normal period of time, it is fairly certain that they would have been included in such a group on the basis of fasting specimens only. This not only points out the importance of the fat-tolerance test in the diagnosis of familial hyperlipemia but also accentuates the importance of recognizing the possible heterogeneity of biochemical causes for the primary elevation of neutral fat in the blood (*11*).

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References and Notes

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6. This study was aided by a grant from the Population Council, Inc., New York.
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9. J. C. F. Poole, *Brit. J. Haematol.* 1, 229 (1955).
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11. A detailed description of our results is in preparation. We wish to express deep gratitude to Dr. Gunnar Wallenius of the clinical chemistry department of Uppsala University for invaluable advice and for the cholesterol determinations.
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18 November 1958

Predaceous Feeding in Two Common Gooseneck Barnacles

Abstract. *Lepas anatifera* and *Mitella polymerus*, while relatively unselective omnivores, behave at times like predatory macrophagous carnivores. Observations suggest a greater range of food size for gooseneck barnacles than is generally suspected and clearly indicate that large organisms, when available, are effectively captured and handled.

Thoracican barnacles are generally considered to feed on *small* organisms and particles of detritus caught by combing the water with highly setose thoracic appendages. Very few observers have described barnacles feeding on larger forms: Darwin (*1*) notes prehensile behavior of the cirri in capturing crustaceans and other prey; Batham (*2*) notes the curling motions of the cirri in *Mitella* (= *Pollicipes*) *spinosus*, which deposit crustaceans "often of no mean size" in the mouth; Brown (*3*) states that in the laboratory *Lepas* will feed on animals even larger than itself; but Gruvel (*4*) is apparently the only worker who has described the coordinated behavior of the cirri and mouth parts of *Lepas* in seizing and ingesting food of various sizes, and his observations have gone largely unheeded. It is the purpose of this report to present evidence that at least two common gooseneck barnacles not only capture and feed upon large prey but, on occasion, show the feeding habits and food-capturing mechanisms, and have the diets, of macrophagous predators, exhibiting a behavior more reminiscent of the lion than of the anteater.

Initial observations made on *Lepas anatifera* in 1951 at the Hopkins Marine Station of Stanford University by one of us (H.S.) have recently been confirmed and extended by further work on this species (by both of us) and on *Mitella polymerus* (by G.H.). In the laboratory, feeding was observed in both species. A large cluster of *Lepas* attached to driftwood was allowed to feed freely for 2 hours on the brine shrimp *Artemia salina* (5 to 11 mm in length) and on the small tide-pool copepod *Tigriopus californicus* (approximately 1 mm in length). A cluster of *Mitella* freshly removed from intertidal rocks was similarly fed these two animals. The gut contents of the barnacles were then examined. *Lepas*, ranging in size from 11.2/7.0 mm (shell length = ratio of total length of capitulum to gut length) to 7.7/4.8 mm, all ingested both *Artemia* and *Tigriopus*; smaller animals, ranging in size down to 3.6/2.3 mm, took copepods only. The largest individual *Lepas* took 56 *Tigriopus* and two *Artemia*. The second largest (10.8/6.8 mm) took four copepods and four brine shrimp. Individuals of *Mitella* greater in size than 5.8/7.2 mm ingested both *Artemia* and *Tigriopus*; smaller *Mitella*, down to 1.6/2.1 mm, took only copepods. Ingested organisms originally longer than the barnacle digestive tract (Fig. 1) were bitten in pieces, folded, or compacted to fit the gut.

How is the prey of these animals captured and handled? Activity of the cirri and mouth parts of these barnacles is most clearly demonstrated in *Lepas*, though the behavior of *Mitella* is similar. Individuals of *Lepas*, immersed in a suspension of *Artemia* and *Tigriopus*, consistently seized the animals with ravenous grabs, lassoing and caging the prey and holding it in their cirri. The six pairs of thoracic cirri may operate together or move quite independently of one another, a behavior not observed in balanoids but previously seen in *Lepas* (*4*), in *Scapellum* and *Verruca* (*5*), and in *Mitella* (*2*). If a brine shrimp contacts the cirri of *Lepas*, there is a total clutching motion of all the cirri; these then contract, forcing the food toward the mouth parts.

When the animals are feeding on smaller organisms, the functions of the individual cirri can be seen. Here the anterior three thoracic appendages. which are equipped basally with spinous pushing brushes, direct food to the mouth parts, where it is gripped and compacted. At the same time copepods may be trapped by individual rami of the last three cirri, which curl around them and hold them in reserve. We noted that one animal held seven copepods in separate coiled posterior rami while ingesting a brine shrimp. *Mitella* has cirri and mouth parts which are anatomically and functionally similar to those of *Lepas*. The cirri are thicker and shorter and, in general, less active than those of *Lepas*, but when cirri are presented with food, their response is quick. Food may be trapped separately by the last three pairs of rami and passed to the very heavily bristled pushing pads at the bases of the second two pairs of cirri and on the rami of the first cirri, which in turn cram it against the mouth parts for compacting and swallowing.

The differences in feeding behavior between *Lepas* and *Mitella* seem to be in accord with their respective ways of life. *Mitella* characteristically occurs in clusters on a fixed rocky substrate exposed to a great deal of wave action. Individuals are generally oriented in fixed positions to receive the down-wash

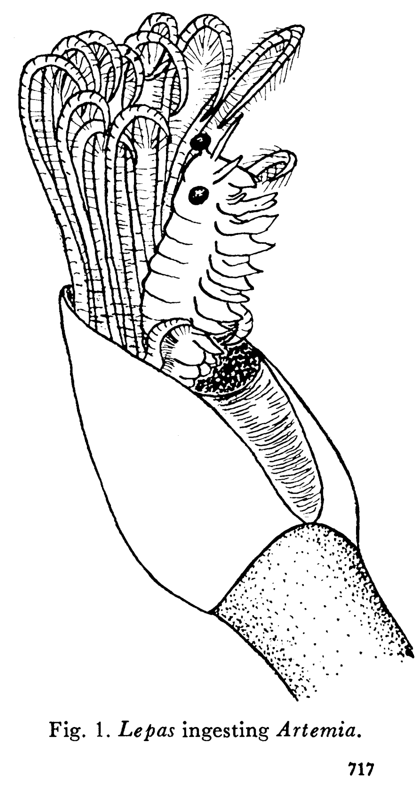

Fig. 1. *Lepas* ingesting *Artemia*.