AMAUROTIC IDIOCY AND THE LIPOIDOSSES

From the frequency of reports and observations on many diseases it is often assumed that their nature may be taken for granted, though a more careful consideration of their manifestations may suggest a more cautious inquiry.

The present-day knowledge, for instance, of the nature of the Tay-Sachs form of cereboretinal degeneration might reasonably be assumed to be comprehensive. For some fifty years this degeneration has obtruded itself as a clear-cut entity on the attention of the clinician and the neuropathologist. Yet the fact remains that until quite recently the theories and hypotheses employed in the elucidation of its pathogenesis have failed to establish exhaustively the processes involved; and it has now been shown that amaurotic family idiocy bears a hitherto unsuspected relationship to certain infantile forms of hepatosplenomegaly, in which lipoid substances are deposited in the reticuloendothelial cells of the body.

It may be recalled that in addition to their functions of hæmatopoiesis, antibody formation, and phagocytosis, this far-flung system of reticular Aschoff cells, distributed in the bone-marrow, lymph nodes, liver and spleen, plays a leading part in the intermediate metabolism of lipoids, and, under certain pathological conditions, may acquire the capacity of acting as a storage system for lipoids and other substances present in excess in the body fluids. For all these clinical conditions in which lipoid substances are deposited in the reticular and endothelial cells of certain tissue systems of the body it has become customary to employ the term 'lipoidoses.'

Apart from secondary forms, which are merely symptomatic manifestations of disturbances of lipoid metabolism associated with other diseases, such as diabetes, there exist
a number of primary or essential forms which, having as their basis a constitutional anomaly of lipoid metabolism, can be readily differentiated by the morphological, optical, and microchemical properties of the lipoid cell contents. Two of the best known of them are Gaucher's disease and Niemann-Pick's disease. Though differing widely from one another in their clinical course and symptomatology, both are of extraordinary interest from the neurological aspect, since it is possible to discern in both certain features which were thought until lately to be confined to the infantile, juvenile, and adult types of cerebroretinal degeneration.

In all of these types, as is well known, a ubiquitous swelling of the neurones is the most distinctive histological feature. Within the nerve-cells there is an accumulation of lipoid substance which, taken in conjunction with the balloon-like swelling of cell-bodies, and often of the cell-processes as well, is definitely recognizable and characteristic.

As to the significance of these changes there has been much controversy. On the one side the view of Schaffer may be cited. He claims that the deposit found with such remarkable constancy in the nerve-cells of every part of the nervous system represents a constitutional weakness confined to the ectodermal elements, the whole process being a primary degeneration of the hyaloplasm—the structureless cytoplasmic element of the cell-body. On the other side Bielschowsky, Pick, and others maintain that the loading of nerve-cells with lipoid material is nothing more than the localization in one organ of the body of a general disturbance of lipoid metabolism. From the fact, however, that nerve-cells, being of ectodermal origin, have no claim to be regarded as part of the reticuloendothelial system, it follows that the presence within them of lipoid infiltrations provides no evidence for the inclusion of amaurotic idiocy in the lipoidoses group.

Acceptance of Bielschowsky's view demands that evidence shall be forthcoming of lipoid storage in true mesodermal elements known to be part and parcel of the reticuloendothelial system. Whether it is permissible to place in this category the third element of the nervous system, the microglia, has not been finally settled. Those who favour its inclusion point to its
essentially phagocytic function, and to its special affinity for iron pigment, as points of resemblance. The constancy with which ‘gitter’ cells, derivatives of the microglia, take a prominent part in lipoid storage in the more acute forms of amaurotic idiocy is certainly suggestive of a microglial function analogous to that of the reticuloendothelial cells. There is no need, however, to settle the exact status of microglia. Recent research has provided ample evidence of widespread lipoid storage in amaurotic idiocy. In a few cases of this disease Bielschowsky and Pick have been able to demonstrate in the tissue of the spleen the peculiar large foam-cells which occur in the accepted types of lipoidoses. That these should have escaped discovery so long may seem surprising, but it must be remembered that enlargement of the spleen is not a usual feature of this disease, nor even, indeed, of cases in which these cells have been detected. Moreover, it has to be admitted that until 1912, when Kinnier Wilson introduced the concept of hepatolenticular or hepatocerebral degeneration, the visceral organs were seldom subjected to close scrutiny in neurological studies.

But perhaps the most convincing support for the inclusion of Tay-Sachs’ disease among the lipoidoses is to be found in a comparison of its histological features with those of Gaucher’s disease and Niemann-Pick’s disease, which are, both of them, examples par excellence of general lipoid degeneration.

Clinically, Gaucher’s disease is characterized by its benign and chronic course, and by the enormous enlargement of the spleen, accompanied by cirrhosis of the liver without ascites. Histologically, it is characterized by the invasion of the reticuloendothelial system by masses of large clear cells containing a lipoid substance which chemical analysis has shown to be composed of cerebrosides. In these features it bears little resemblance to amaurotic idiocy, but when the nervous system, and especially that of the juvenile type in which spastic paralysis occurs, is examined, changes in the ganglion-cells may be revealed which have a morphological identity with those found in the former condition.

Such a finding is indeed unexpected; but even more impressive is the clinical and pathological similarity of
Niemann-Pick’s disease. Here we are dealing with a condition which, like the infantile form of amaurotic idiocy, has the peculiarities of being racial rather than familial, and of terminating fatally in the second year of life. Nor does the similarity end here. In some cases an ophthalmological link of the greatest importance is furnished by the presence in the retina of the cherry-red spot which every student has learnt to associate with Tay-Sachs’ disease. From the pathological standpoint the unnatural hardness of the brain, the gaping of the Sylvian fissure, and the marked frontal atrophy are sufficiently characteristic to justify a macroscopic diagnosis of amaurotic idiocy; and when lipoid stains are employed the expanded ganglion-cells filled with dark-staining granules are equally suggestive.

It has indeed been submitted that the two diseases are in reality one affection. Differences, however, do exist. The enormously enlarged liver and spleen packed with foam-cells, and the presence of similar cells in the entire connective and vascular tissues of the brain, are peculiar to Niemann-Pick’s disease; and it has yet to be shown that the cellular changes of Tay-Sachs’ disease occur in all cases of Niemann-Pick’s lipoid storage. Nevertheless, the fundamental similarity of the pathological changes in both these conditions, as well as in Gaucher’s disease, inhibits the idea of any merely accidental combination. It affords, on the contrary, the strongest evidence for the view that the cellular changes of Tay-Sachs’ disease are primarily conditioned by a metabolic disturbance which leads to lipoid deposition in ganglia and glia-cells.

It would appear then that different localizations of disordered lipoid metabolism may determine different clinical types of lipoidosis. When the disturbance exercises its greatest effects on the nervous system the clinical feature is that of Tay-Sachs’ disease; when its greatest effects are on the visceral organs, Gaucher’s splenomegaly is depicted; and, when the entire body is involved, the syndrome is that of Niemann-Pick’s disease.

Thus, by a broad and indirect approach, some light has at last been thrown on the pathogenesis of a cerebral disease which has too long remained a mystery. Whatever the ulti-
mate conclusions may be, it seems imperative to abandon the old concept of amaurotic idiocy as a singularly interesting but isolated disease-entity. All natural phenomena show transitions, and it may be anticipated that further investigation may reveal other intermediate types, and so provide additional evidence for the nosological linkage of amaurotic idiocy with the lipoidoses.
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