It was suggested by Todd *et al.*[4] that the antimalarial activity of pyrimidine derivatives may be due to interference with nucleoside synthesis. This view finds support in the recently published observations of Madinaveitia and Raventós[6], and the results obtained by Hellerman, Bovarnick and Potter[7]. The present data suggest that both purines and pteroylglutamic acid may be involved in the systems affected by the antimalarials, but in neither case is the antagonism clearly of a competitive nature.

A series of 2 : 4-diamino-5-aryloxypyrimidines has been prepared. These compounds, which are all powerful pteroylglutamic acid antagonists, are being examined for antimalarial activity.

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Lipids of Peripheral Nerve during Wallerian Degeneration

The histological changes that follow section of a peripheral nerve have been described in great detail[1–5]. Hitherto, most of what we know concerning the nature of nerve lipids during degeneration has come from the use of histochemical, rather than chemical, methods.

The sciatic nerve of thirty cats was sectioned at the level of the greater trochanter, the nerve of the other side serving as a control. At intervals of time from 4 to 96 days after the operation, the animals were sacrificed and the lipids of the nerve estimated by the micro-methods previously described[6]. Since there were great changes in both water and lipid content of the degenerating nerve, all results have been referred to unit fresh weight of the same length of nerve from the control side. The following changes were observed.

Water Content : increased rapidly after section, reaching a maximum in four days. Thereafter the water content decreased steadily, and after eighty days it had reached the same value as that of the control nerve.

Total Lipid Content : decreased steadily throughout the course of the degeneration.

Neutral Fat : decreased rapidly at first, reaching a minimum between four and eight days after section. The concentration of neutral fat then slowly increased, and by the end of thirty-two days it was the same as that of the control nerve. Even after ninety-six days there was no significant difference between the neutral fat content of control and degenerated nerves.

Myelin Lipids (cerebroside, free cholesterol and sphingomyelin, substances which we have previously suggested are the chief lipid components of the myelin sheath[6–9]) : changed little in the first eight days and thereafter decreased steadily, and to the same extent. After the initial fall there was little change in the concentration of neutral fat, so that, as degeneration progressed, the myelin lipids accounted for less, and the neutral fat for more, of the total lipid.

Total Cholesterol : changed little during the first week and then decreased, but at a slower rate than the myelin lipids.

Ester Cholesterol : absent from all control nerves and did not appear in degenerating nerves until at least eight days after nerve section. The concentration of ester cholesterol then increased, reaching a maximum by sixteen days. Thereafter the concentration of ester cholesterol decreased, but more slowly than the concentration of the myelin lipids including free cholesterol, so that after eighty days more cholesterol was in the ester form than in the free.

Total Phospholipid : decreased more slowly than the myelin lipids because kephalin, like sphingomyelin, decreased at the same rate as the myelin lipids, but lecithin decreased more slowly.

From these observations it is possible to piece together the changes in the distribution of lipids in a nerve when it undergoes Wallerian degeneration. There is an early increase in water content and a reduction in the absolute amount of neutral fat. After eight days, corresponding in time to the appearance of macrophages along the course of the degenerating nerve[4,5], there is a steady decrease in the myelin lipids, that is, cerebroside, free cholesterol and sphingomyelin. These substances are presumably slowly hydrolysed, and the products of hydrolysis, for example, glycerol, fatty acid, choline, galactose, sphingosine and phosphate, are removed. There is, in addition, a hydrolysis of kephalin and a slower hydrolysis of lecithin. Some of the fatty acids liberated during hydrolysis presumably combine with free cholesterol to form ester cholesterol, while others may be converted into neutral fat. Such a process would explain many of the histochemical observations made on degenerating nerve tissue. It should be stressed that analyses were performed on the whole nerve and therefore represent not only the lipids of myelin, but also the lipids of the axon, Schwann cells and connective tissue incorporated in the nerve trunk.

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