LETTERS TO THE EDITORS

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Liver Ribonucleic Acid

IT has previously been shown[1] that mammalian tissues contain, in addition to nuclear desoxyribonucleic acid (thymonucleic acid), appreciable amounts of pentose nucleic acid, which appears to be mainly a cytoplasmic constituent[2]. Liver tissue, for example, is known to contain both a desoxyribonucleic acid similar to the thymus nucleic acid[3] and a pentose nucleic acid[1]. The latter has now been isolated from the liver tissue of the sheep. The finely minced liver is dehydrated with ethanol and the nucleic acids extracted with 10 per cent sodium chloride. They are precipitated with ethanol, and the barium salts fractionated by the method used by Jorpes[4] for the pentose nucleic acid of the pancreas. The pentose nucleic acid is finally purified by precipitation from glacial acetic acid. The material so obtained is free from protein and from desoxyribonucleic acid. It is similar to yeast ribonucleic acid in its pentose content and in its absorption spectrum. Its contents of purine and easily hydrolysable phosphorus are consistent with a tetranucleotide structure with equimolecular amounts of purine and pyrimidine. It appears to differ, therefore, from the pentose nucleic acid of the pancreas, for which a pentanucleotide structure has been suggested[4].

From the hydrolysis products obtained by the method of Bredereck and Richter[5], we have prepared the pentose and identified it as ribose by the *p*-bromophenylhydrazone, which melted at 168–169°. This melting point showed no depression when the derivative was mixed with a sample of the *p*-bromophenylhydrazone prepared from pure *d*-ribose. The nucleic acid can therefore be correctly designated 'liver ribonucleic acid'. Gulland and Barker[6] have recently proved conclusively that the pentose of yeast ribonucleic acid is *d*-ribose, and have shown that small amounts of *l*-lyxose are also present. The amounts of liver ribonucleic acid so far available have been too small to enable tests for lyxose to be made.

Liver ribonucleic acid acts as a substrate for crystalline ribonuclease. When sections of liver tissue, fixed, embedded and mounted, are stained with toluidine blue, both nuclei and cytoplasm take up the stain. If the sections are treated with ribonuclease in the manner employed with other tissues[7], and then with toluidine blue, the nuclei alone stain. The liver ribonucleic acid, therefore, probably occurs in the cytoplasm, in which it may be present in the form of phospholipin-ribonucleoprotein complexes in the particulate components (mitochondria[8], secretory granules[9], microsomes[10]). These complexes are known to contain a nucleic acid of the pentose type which is presumably identical with the ribonucleic acid which we have isolated.

In confirmation of the work of others[11], we have found that the total nucleic acid concentration in the liver of the rat rises on fasting, although the liver weight relative to the body weight falls. Dry powders of rat livers from which acid-soluble and lipoid phosphorus had been removed, contained 554 ± 10·7 mgm. residual phosphorus per 100 gm. in the case of fed animals and 583 ± 20·5 mgm. in the case of fasted animals. Of this residual phosphorus, 75·3 ± 2·33 per cent in the fed animals and 66·0 ± 2·86 per cent in the fasted animals was accounted for as ribonucleic acid phosphorus; 17·6 ± 0·59 per cent in the fed animals and 20·2 ± 0·84 per cent in the fasted animals was accounted for as desoxyribonucleic acid phosphorus. The fall in ribonucleic acid and the rise in desoxyribonucleic acid on fasting were both statistically significant. These results would be consistent with the disappearance from the cytoplasm of particulates containing ribonucleic acid, and with the loss in phospholipin and in nucleoprotein observed in the livers of rats fasted or placed on a protein-poor diet[12].

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Effect of Dietary Protein on Liver Cytoplasm

IT is well known that the protein content of the liver can be lowered by fasting or by feeding a low-protein diet and raised by feeding a high-protein diet. The question arises: Is the protein stored in the liver as is glycogen, or is it built into the structure of the cytoplasm? Since the evidence so far available on this point is equivocal, it was decided to correlate, under various nutritional conditions, the protein content of the liver with other cytoplasmic constituents, namely, phospholipin and nucleic acid.

In a previous communication[1] it was shown that fasting caused a loss in the protein as well as the phospholipin and nucleic acid contents of the livers of rats. Similar changes are obtained if the animals are placed either on a protein-free diet or given protein deficient in one or more essential amino-acids. On the other hand, a high protein diet causes an increase in the protein, phospholipin and nucleic acid contents of the liver. There is no change in the number of liver cell nuclei (Table 1).

If the protein content of the diet is varied, the relative concentrations of protein and phospholipin remain remarkably constant, while that of nucleic acid rises gradually with falling protein intake (Table 2). This latter fact is probably due to there being no, or only little, loss in nuclear material which, although in mass much smaller than cytoplasm, has a much higher concentration of nucleic acid than cytoplasm. This interpretation is supported by the recent findings[2] that the ratio of ribonucleic to desoxyribonucleic acid is lower in livers of fasted rats than in those of fed rats. The relative