The problem of the parenteral administration of nitrogen derived from protein sources is of importance particularly in circumstances in which hypoproteinemia may develop. It then becomes necessary to supply protein, or protein precursors, to an individual who, because of either his clinical condition, the loss of voluntary action, or other reasons, is unable to obtain or utilize orally administered protein. It has been established that experimental animals and humans utilize parenterally administered nitrogen for maintenance of positive nitrogen balance and for plasma protein regeneration. The sources of nitrogen commonly employed have generally been products prepared from proteins by acid hydrolysis or by enzymatic digestion.

The acid hydrolysis procedure is ideal except for the decisive difficulty that under the usual conditions employed extensive destruction of tryptophane results. Since this amino acid is essential for production of nitrogen retention and plasma protein synthesis, tryptophane must be added to acid hydrolysates. The cost of tryptophane makes this approach to the clinical problem impractical. Enzymatic digests of casein have proved quite satisfactory for parenteral administration; however, the enzymatic process, while preserving tryptophane, has undesirable features: (1) the time required for protein digestion, and (2) the use of crude enzyme sources for large scale preparations. The first point is not completely objectionable; the second is minimized by employing purified enzymes. However, when large quantities of digests are needed, the cost of better enzyme preparations becomes of importance. Ground, fresh pancreas has been employed for the commercial preparation of enzymatic digests. While satisfactory products have been obtained, there always exists the possible contamination of the enzyme source with a variety of tissue substances which might appear in the final preparation.

A more satisfactory solution of the problem appeared to be the development of conditions of acid protein hydrolysis which would (1) hydrolyze the protein to smaller fragments that produce no undesirable reactions when rapidly injected intravenously, and (2) cause minimal destruction

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of the amino acids of the protein, with particular reference to tryptophane. These conditions have now been established.

Hydrolysis of casein or of pumpkin seed globulin with 2.6 N sulfuric acid for 6 hours liberates 60 per cent (for casein) and 55 per cent (for pumpkin seed globulin) of the total amino nitrogen liberated by the usual conditions of protein hydrolysis (8 N sulfuric acid, 24 hours boiling). Tryptophane analyses of these hydrolysates indicate that 85 per cent of the tryptophane present in casein is not destroyed. 65 per cent of the total tryptophane of pumpkin seed globulin is found in similarly prepared hydrolysates. Sulfuric acid is removed with baryta, the barium sulfate filtered and washed, and the filtrates and washings decolorized with norit and concentrated to dryness in vacuo. The final products are light colored powders, very soluble in water, and produce no undesirable reactions in dogs when administered rapidly in solution by vein. The similarity of the amino acid composition of these preparations to that of the starting proteins is indicated from two types of comparative investigations, (1) rat growth experiments and (2) nitrogen balance studies in dogs. Plasma protein regeneration studies are in progress.

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