obtained only by keeping down consumption in the more fortunate countries.

According to a recent report in the *Journal*[3] Dutch children, aged 7 to 15 years, brought over to England in February had been living for a long time mainly on bread, potatoes, and cabbage. They did not appear seriously wasted, but were generally undersized; they must have been much under weight for their size, as they gained up to 6 lb. 6 oz. in three weeks after arrival. Feeding these children presented no serious difficulty; the only precaution taken was to limit the amount of fat and the total calories during the first week. When the initial difficulties are over nutrition will improve on almost any diet that will provide calories. The typical dinners supplied to children in canteens run by relief organizations for malnourished children in 1919–21 provided daily an average of only 5 grammes of animal protein, the vitamins A and D of 70 ml. of milk, and almost no vitamin C. The children probably got some carotene and C from vegetables at home, but precious little animal protein; yet their condition improved steadily. Children from the areas of Holland where rations have fallen to 300 calories a day will be in a far worse condition. Experience among the International Brigade and Spaniards in concentration camps in Southern France showed that no state of starvation, except the final coma, is beyond hope.[4] In the Bengal famine the more severe cases were divided into (1) collapsed cases, likely to die without parenteral feeding; (2) the less collapsed cases, who were capable of recovery when fed by mouth; and (3) those capable of taking a simple milk diet.[5] For the first group intravenous injections of protein hydrolysates, containing glucose, riboflavin, niacine, and thiamin, were recommended. It was claimed that this treatment saved patients who otherwise would certainly have died. The second group needed to be fed with small amounts at short intervals; it might be necessary to feed by nasal tube. This group and the third group were given liquid mixtures supplying 800 to 1,200 calories per day; about half the calories were provided by sugar (4 oz.); the remainder were made up with flour or milk. Recent studies on the efficacy of various nutrients in maintaining life have shown the special importance of aneurine; it would therefore be advisable to give one international unit of aneurine for every gramme of sugar.

TREATMENT OF SEVERE STARVATION

In 1939 Elman and Weiner[6] reported the use of an acid hydrolysate of casein fortified by the addition of tryptophan and by supplementation with cystine or methionine for intravenous alimentation of human subjects; evidence was obtained of satisfactory utilization of the amino-acids, and favourable therapeutic effects were observed. The work of Elman and Weiner constituted a practical application of the observation of Henriques and Andersen[7] in 1913 that nitrogen equilibrium could be maintained in the goat when the sole source of nitrogen was provided by the intravenous administration of amino-acids. During the last few years numerous papers have appeared dealing with the clinical use of hydrolysates of protein for alimentation either by the intravenous or oral routes (for reviews see Gaunt[8] and Cuthbertson[9] and this *Journal*[10]); most of these referred to the use of the American product "amigen," a pancreatic hydrolysate of casein, and it has been stated by Allbright[11] that complete maintenance can be effected with "amigen" and glucose alone for as long as forty days. Some attention has also been paid to acid hydrolysates and to digests of meat prepared with papain. The ideal preparation is yet to be found; pancreatic digests are highly susceptible to bacterial contamination during their production and are therefore liable to be pyrogenic; papain digests, while relatively free from this disadvantage, may contain partial breakdown products of protein which are harmful, and the acid hydrolysates require fortification with tryptophan, which is not a very easily accessible substance. The only report so far published on the use of protein hydrolysates in the treatment of starvation has come from India (Narayanan and Krishnan[12] and Krishnan, Narayanan, and Sankaran[13]); a considerable measure of success was claimed as the result of intravenous administration of papain digests of meat together with glucose to patients who were so far weakened by starvation that they were unable to take anything by mouth. The Indian work was undertaken in conditions of such difficulty that a carefully controlled investigation was not possible, and the evidence for the favourable effect of intravenous alimentation rests on clinical observation only.

The food situation in the Netherlands is exceedingly grave. This applies particularly to the large towns of North-West Holland, where there is good reason to believe that few people have been getting more than 800 calories and where they may now be getting only about 400 calories daily. After considering the data available the Netherlands authorities and the military authorities concerned agreed that the food situation in N.W. Holland was so serious that special measures would be required if a large proportion of the population were to be resuscitated; being impressed by the evidence in favour of the use of protein hydrolysates, they invited the Medical Research Council to advise on the provision of suitable preparations in adequate quantity. At the same time a scheme for the application of the emergency treatment was agreed upon with the Netherlands authorities; this scheme included not only the formation of relief teams but also full provision for clinical and laboratory study of the cases of extreme starvation, so that the best method of treatment might be determined without delay. As the result of work carried out during the last eighteen months the Medical Research Council was in a position to give the necessary technical advice, and in view of the urgency of the need the Ministry of Food and the Ministry of Supply took immediate steps to increase production; with the whole-hearted co-operation of the firms concerned the amount of material which was

[3] Tauber, J., *British Medical Journal*, 1945, **2**, 488.
[4] Zimmer, R., Weill, J., and Dubois, M., *New Engl. J. Med.*, 1944, **230**, 303.
[5] Committee of Inquiry into Effects of Starvation, India Research Fund Association, *Treatment and Management of Starving Sick Destitutes*, All India Institute of Hygiene and Public Health, Calcutta, 1943.
[6] *J. Amer. med. Ass.*, 1939, **112**, 796.
[7] *Hoppe-Seyl. Z.*, 1913, **88**, 357.
[8] *Nutr. Abstr. Rev.*, 1944, **13**, 501.
[9] *Brit. med. Bull.*, 1944, **2**, 207.
[10] Leading article on "Intravenous Alimentation," *British Medical Journal*, 1943, **1**, 416.
[11] Bi-monthly Progress Report No. 10, Dec. 31, 1944, to Committee on Medical Research of the Office of Scientific Research and Development.
[12] *Indian med. Gaz.*, 1944, **79**, 158.
[13] Ibid., 1944, **79**, 160.

asked for was produced in less than the specified time. Since it also seemed desirable to test the efficacy of plasma and serum in the treatment of extreme starvation, large supplies of these materials were requested and were furnished by the Lister Institute. The work in Holland is now in progress. Representatives of the Medical Research Council and of the Ministry of Food, together with American experts, are acting, at the invitation of the Netherlands Government, as scientific advisers.

It is now depressingly apparent that the problem of treatment for extreme starvation is of wide extent; it concerns a proportion of British prisoners of war and large numbers of occupants of enemy concentration and labour camps. Quite recently the Medical Research Council, at the request of the military authorities, has nominated a further team of three experts to proceed to the Continent to study the value of protein hydrolysates in treatment of starvation; this team is already at work with full equipment for the investigation required. Provision has also been made, at the request of the Ministry of Health, for material to be available for repatriated prisoners of war who may reach E.M.S. hospitals in urgent need of treatment. All these demands have increased the need for medical personnel, and use has been made of Belgian and English medical students who were enrolled, trained, and organized in anticipation of such a need. Two methods of treatment were considered. In the first a solution of protein hydrolysate, which may be prepared by complete enzymic digestion ("amigen") or by acid hydrolysis and subsequent fortification with tryptophan, is given by intravenous infusion. The second method consists in administration of the hydrolysate by slow intragastric drip, and in this case the material is an enzymic digest of casein or meat in which the digestion has not been carried so far. In both cases glucose is given in large amount to provide energy and thus to spare the amino-acids for purposes of repair. Vitamins are also given to enable the glucose to be utilized and to prevent the development of acute deficiency states. It is anticipated that successful treatment should lead within three days to resuscitation to the point at which ordinary food may be taken.

It is impossible at the present stage to predict the ultimate value of the protein hydrolysate treatment in extreme starvation, although there is already evidence that the intractable diarrhoea which is a prominent feature of the condition responds well to the intravenous method. It is much to be hoped that the intragastric drip will prove to be a satisfactory alternative form of administration; if so it will become the method of choice, not only because suitable material is so much more easily accessible but also because its use will be free from the risks which, at present at least, seem inseparable from the intravenous administration of hydrolysed proteins. Apart altogether from the prospect that the availability of protein hydrolysates may provide a valuable therapeutic measure in the present medical emergency, the studies which will be carried out offer the promise of useful information for the future; the observations which are made may be expected to have a bearing not only on the immediate problem but also on the treatment of all conditions of malnutrition associated with impaired absorption from the alimentary tract.

CONGENITAL DEFECTS AND RUBELLA

A curious association between maternal infection in pregnancy and congenital malformations in the infant seems to be a new manifestation of rubella. It is unlikely that such a dramatic sequence could have been overlooked in the past. In fact Gregg,[1] who first drew attention to it, traced examples back only until late 1939. Moreover, the defect which first attracted his attention was a congenital cataract which did not conform exactly to any of the clinical types previously encountered. This observation naturally aroused great interest. In a preliminary survey in South Australia Swan and his associates[2] examined 61 infants and found 36 with these congenital defects—cataract, deaf-mutism, heart disease, and mental retardation. The history of these 36 revealed that in 31 of the mothers there had been an illness during pregnancy (usually in the first three months) which was thought to be rubella. In 4 infants there was no maternal history of an exanthem. The mother of the remaining infant, who had a congenital corneal opacity, had had mumps during pregnancy. Viewed in another way, the survey showed that 49 mothers who suffered presumed rubella gave birth to 31 infants with congenital defects; 9 mothers who had had measles in pregnancy all produced normal infants; 1 of 2 mothers who had had mumps bore a child with a corneal opacity. Continuing their observations the same team later reported[3] 10 further examples of congenital defects in association with maternal rubella. Adding these to their 31 previous cases and to the 68 cases reported by Gregg, they find an impressive total of 109 such associations in Australia alone. Further examples have been recorded in America by Reese[4] (3 cases) and Erickson[5] (11 cases), and by Hope Simpson[6] (2 cases) in this country. The main points of agreement in the published data appear to be: (*a*) that the association is with rubella and not with other transmissible diseases (though not without exception); (*b*) that the risk of congenital defect is greatest if the rubella occurs in early pregnancy (i.e., within the first three months); and (*c*) that there are infants with congenital defects in which no link with a maternal transmissible disease can be traced.

Any explanation of the possible sequence of events is to some extent bound to be speculative. The general inference is that the unknown virus of rubella (with virulence possibly enhanced in the war years) is showing the preference of certain viruses for developing embryonic tissue. This it does by attacking the foetus via the placental circulation just at a time when important developmental changes are taking place in the foetal heart and eye. The high incidence of congenital heart disease suggests to these observers that the rubella virus has a primary affinity for vascular tissue, the lens damage being explained by possible indirect action through the hyaloid artery. Swan[7] later demonstrated in 3 infants who died of their defects a disproportionate vascular damage in the kidneys, the principal lesion being a glomerular sclerosis. While this view of pathogenesis is supported by recorded examples of intra-uterine transmission of other virus infections,[8] certain questions remain unanswered. Is the association between presumed rubella and congenital defects a significant one, or does it arise from pure chance? Swan and his associates[9] admit that a survey of the kind they undertook is likely to attract reports of the positive event; hence their material must necessarily be selective, perhaps highly so. Secondly, was the maternal disease rubella? Gregg was

1 *Trans. ophthal. Soc. Austral.*, 1941, **3**, 35.
2 *Med. J. Austral.*, 1943, **2**, 201.
3 Ibid., 1944, **1**, 409.
4 *Amer. J. Ophthal.*, 1944, **27**, 483.
5 *J. Pediat.*, 1944, **25**, 281.
6 *Lancet*, 1944, **1**, 483.
7 *J. Path. Bact.*, 1944, **56**, 289.
8 *Johns Hopk. Hosp. Bull.*, 1944, **64**, 240.
9 *Lancet*, 1944, **1**, 615.