invalidism if treated firmly at an early stage, but when weekly payments have been made for periods extending over months it will be considered an "injustice" to withdraw it; it will, therefore, be necessary at a very early stage to have these cases visited and reported upon, preferably by independent medical men. For this purpose a medical referee visiting staff would be particularly useful.

The practical experience of the working of the Asylum Officers' Superannuation Act, 1909, is of assistance in this connexion. It will be remembered that Clause 3 (subsection 1) of this Act provides for the re-examination of pensioners at intervals of a year. As medical officer appointed under the Act for the County of London, I can well appreciate the difficulty a medical man is in when asked to revise at intervals the advisability or otherwise of continuing a pension in which the pensioner considers he has a vested interest, merely because so many antecedent weekly or monthly payments have been made.

For these and other reasons which the exigencies of time and space prevent my setting out in further detail I have formed the opinion that medical referees should be appointed. Their coming is inevitable. Their advent will be welcomed. The sooner they are arranged for the better for those members of the profession who are about to wrestle with difficulties which I know well, for the special nature of my work compels me to encounter them daily.

STUDIES ON BERI-BERI.

FURTHER FACTS CONCERNING THE CHEMISTRY OF THE VITAMINE-FRACTION FROM YEAST.

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[WITH SPECIAL PLATE.]

At the end of 1911¹ I described a method for the isolation of the vitamine-fraction from rice polishings. At this time only a single substance was detected, which was studied to some extent in its chemical properties and curative power. Early in 1912² I was able to show that the same method might be successfully used for the isolation of the vitamine-fraction from other foodstuffs, namely, milk, yeast, brain, and lime juice. Even at this time it was noticed that the isolated pure substance of the melting point 233° had a slightly diminished curative power as compared with the crude product. As a second substance at that time could not be isolated, there was no explanation of this fact available. Since then I have been able to show³ that a number of purin and pyrimidin derivatives possess a slight curative effect—a very interesting fact, which, however, did not simplify the problem.

It was therefore conceivable that besides the substance of the melting point 233°, small quantities of other substances might be present in this fraction, the physiological effect of which therefore would be the resultant of the individual actions of these constituents.

A fractionation of the yeast extract was therefore carried out on a large scale and the results of this are shortly summarized in this preliminary communication.

The alcoholic extract of 100 kg. dried yeast was prepared, following the method already described in my earlier papers. The fractionation itself was carried out without any change of methods and only the silver and baryta fraction which represents the vitamine-fraction was carefully investigated. The total amount of substances obtained in this fraction from 100 kg. of dried yeast was 2.5 grams. This initial product was crystalline and melted at 210° (uncorrected).

A number of pigeons were treated with this product. Polyneuritis was induced in them by artificial feeding with an exclusive diet of polished rice. After a time, varying from ten to twenty-one days, they developed the characteristic symptoms of avian polyneuritis, as they are represented in the figures 1, 3, and 5. By a series of controls it was found⁴ that the animals in this condition

live rarely longer than six to twelve hours, twenty-four hours being perhaps the utmost limit. The product mentioned above was injected into the pectoral muscle in quantities varying from 4 to 8 mg. and in each case a complete recovery was obtained (Figs. 2, 4, 6). Before and after treatment the animals were kept on an unchanged diet of polished rice. In spite of that they lived after the recovery for four to six days without any symptoms of neuritis. As the food did not secure a new supply of vitamine, the birds developed neuritis again after the injected substance was apparently used up for metabolic processes. In one of these cases after a new supply of substance a second cure was effected.

CASE I.—Severe symptoms of polyneuritis; 4 mg. of the above-mentioned product were injected into the pectoral muscle. Three hours later a great improvement; next day a complete recovery; four days later shows again symptoms, and dies.

CASE II.—Severe symptoms (Fig. 1);* 8 mg. injected. Two hours later a complete recovery (Fig. 2); was able to fly away, and had to be photographed, therefore, in a cage; relapsed after six days, and was again cured by a new injection of the product.

CASE III.—Severe symptoms (Fig. 3); injected 4 mg. Recovery after three hours (Fig. 4); lived for four days.

CASE IV.—Polyneuritis (Fig. 5); injected 8 mg. After three hours a complete recovery (Fig. 6), which lasted for four days.

We see from these experiments that the initial vitamine-fraction possesses the undiminished curative power of the original yeast extract. As in some cases the change of diet alone (an addition of maize, for instance) is capable of improving very markedly the condition of the sick birds, the fact that an unchanged diet of polished rice was kept throughout the experiment cannot be too much emphasized.

By a further fractionation I was able to separate the crude fraction into at least three substances, each of which has been carefully purified (recrystallization till constant melting point) and analysed. The original product (2.5 grams) yielded the following substances:

Substance I.—1.6 grams, melting at 229° (corrected); needles and prisms nearly insoluble in cold water. When mixed with the substance previously obtained from yeast² it does not show any depression of melting point; the substances might therefore be regarded as identical.

Substance II.—0.4 gram, very soluble in cold water, and gives a difficultly soluble picrate. The substance melts at 235° (uncorrected).

Substance III.—0.3 gram, more soluble in water than the first substance; melts at 222° (uncorrected).

These observations have an interesting parallel with the case of pituitary extract, as recently recorded by Fühner,⁴ where also in the first instance a crystalline fraction was isolated, which showed the whole physiological action of the gland, but on further fractionation was found to consist of not less than four different substances. Each of these had a specific action, but the effect of the original product could only be obtained by the collective action of all the four substances. It will be interesting to see whether the same is the case with the vitamine-fraction, or whether a single substance plays a preponderating part in the process of cure.

For therapeutic purposes, therefore, the best results may at present be expected by a paraenteral administration of the whole vitamine-fraction, especially in acute cases which have proceeded too far to be influenced by a change of diet—in such cases, for example, as have been described by Strong and Crowell⁵ and Schüffner.⁶ This fraction which is suggested to be employed contains the active constituents unimpaired of the original starting material, and is free from any harmful substances.

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* The photographs have been kindly made for me by Dr. A. B. Macallum, jun., to whom I would like here to express my thanks.

CASIMIR FUNK: BERI-BERI (POLYNEURITIS) IN PIGEONS.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.