EXPERIMENTAL STUDIES RELATING TO "SHIP-BERI-BERI" AND SCURVY.

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I. INTRODUCTION.

On polyneuritis of poultry (polyneuritis gallinarum Eijkman).

Among the diseases which have of late attracted the attention of the official medical authorities of Norway, so-called ship-beri-beri takes a prominent place. The symptoms of this disease consist, in the great majority of cases, in weakness and a prominent dropsy of the lower limbs, extending often to other parts of the body. There also exists shortness of breath and other symptoms of a weak heart, causing often sudden deaths from acute paralysis of the heart. But as Nocht in Hamburg and the Norwegian Ship-beri-beri Committee have shown, symptoms of neuritis of the limbs are comparatively rare. For instance, Nocht was only able to ascertain neuritis in cases from four of his thirty-four beri-beri-ships; and though the investigations of the Committee extended to fifty-seven affected ships, the neuritis was only found in men from four of them. Considering that neuritis is the essential symptom of the beri-beri of tropical countries and Japan, and that dropsy, though present, as a rule is not prominent in cases of this disease, it seems, therefore, rather doubtful whether ship-beri-beri is identical with tropical beri-beri. This doubt, first emphasized by Bullmore and Nocht, is strengthened by the fact that the great majority of patients suffering from the ordinary, i.e. dropsical ship-

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1 Read before the Epidemiological Society of London.
2 Hansa, No. 29, 1900, and Festschrift zum sechzigsten Geburtstage von Robert Koch, Jena 1903.
4 Lancet, 22. ix. 1900.

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disease, recover as soon as they are able to change their food, which is not the case with the disease of the tropics and Japan.

The subject of this and the following articles will be limited to experiments relating to the dependence of the ship-disease on food, the etiology of tropical beri-beri being outside the field of these investigations.

The recovery of patients suffering from ship-beri-beri is due to fresh food. This fact has chiefly been emphasized by Nocht, while the report of the Norwegian Committee contains many corresponding observations. No doubt, some cases do not appear to agree with this observation, which fact, perhaps, favours the idea that “ship-beri-beri” occasionally comprehends more than one disease. This idea may possibly also be supported by the occurrence of cases of neuritis. But in the great majority of cases the effect of fresh animal food, such as eggs or meat, but above all of fresh green vegetables or potatoes, is very marked. For instance, Nocht (l.c.) has pointed out that the symptoms regularly disappear within 8—14 days after the patients get fresh food: even after 4—5 days many patients feel able to resume their work.

That ship-beri-beri is very closely connected with food, is further evident from the fact, that the disease appears almost solely on board sailing-ships on long voyages. On account of this fact, first observed by Dr Stian Erichsen in Norway, Nocht has introduced the name “beri-beri of sailing-vessels.” Cases very seldom appear on board steamers on the same waters. It seems natural to explain this difference by the fact that on long voyages sailing-ships take considerable time before they reach a port where they are able to get fresh provisions, whereas this is not the case with steamers.

Apart from the sore gums and haemorrhages in the skin and muscles, which Nocht observed in cases from twelve of his thirty-four ships, but which the Norwegian Committee could not find, it therefore seems probable, that ship-beri-beri is, in accordance with the opinion of Nocht, a food disease, showing a marked congruence with scurvy.

That the malady is a form of scurvy (Nocht) or related to it (Nocht and the Norwegian Committee), is also supported by the fact, quoted by Nocht, that cases of dropsy without haemorrhages or sore gums often occur during epidemics of manifest scurvy. For instance, Nocht quotes authors relating a considerable number of cases of this kind in

1 *Tidsskrift for den norske lægeforening (Journal of the Norwegian Medical Association).* 1899 and 1901.
the epidemic of scurvy, during the siege of Paris in 1870-71. He has further stated, that such cases often occur during epidemics of scurvy in Russia. I may add that many dropsical cases without sore gums and hemorrhages were also observed during the Crimean war where scurvy was very prevalent1. (Some of these Crimean cases were connected with anaesthesia of the feet and looked like "acrodynie" or beri-beri; but as they were sometimes associated with a local gangrene of the feet or with distinct symptoms of scurvy, the opinion prevailed that they were due to the cold of the winter in addition to latent or manifest scurvy2.) It may further be mentioned, that many cases of dropsy without sore gums, &c. occur every year besides manifest scurvy on board the French vessels fishing for 5—6 months on the banks of Newfoundland3. Finally I may add, that during the first part of the 19th century not only scurvy, but also dropsy without sore gums and haemorrhages was very common in European and American prisons. For instance, besides typhoid fever and consumption, this "prison-dropsy" (Wassersucht der Gefängnisse) is stated, in 1847, to have been the most prevalent cause of death in 41 prisons in England, France and North America4. In 1857 it caused one half of the deaths in a prison in Breslau5; and if it were not that nothing is said about the occurrence of neuritis, some reports from those days recall the descriptions of the Asiatic beri-beri-prisons of our own time6.

Proceeding to the question as to which faults in diet may be the essential causes of ship-beri-beri, Nocht limits himself to expressing the opinion, that it must be left to the future to decide whether the disease is due to some special sort of starvation or to an intoxication by fermenting food or another poison, or to an autointoxication. The question is more positively answered by Bullmore (l.c.), who, basing his opinion on the fact that the disease mostly appears on board ships in the tropics, has started the idea, that the malady is due to an intoxication through all sorts of food, including tinned foods, becoming tainted in

1 Grellois, Recueil de mémoires de médecine, de chirurgie et de pharmacie militaire, vol. xvii. p. 269 a. f.
3 Bonnin, Arch. de médecine navale, 1907.
5 Baer, Weyls Handbuch der Hygiene, "Hygiene des Gefängniswesens," pp. 42, 43.
6 Kersandt, quoted by Baer, Vierteljahrschr. f. öffentl. Gesundheitspflege, 1876.

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consequence of the hot climate. This idea has also been adopted by the Norwegian Committee, which also founds its opinion on the corresponding theory as to the etiology of scurvy. According to the Committee, the principal cause of the disease is tainted tinned meat and fish, since Stian Erichsen (l.c.) has shown, that the disease did not become prevalent on board Norwegian ships, before tinned meat and fish were largely introduced in their dietary. As for scurvy, this theory will be discussed in the following paper. As for ship-beri-beri Bullmore does not base his opinion on direct observations of food on board beri-beri-vessels. And though the Committee mentions seven crews who got bad provisions and were attacked by the malady, in none of these cases was it evident that the cause was damaged tinned articles of food. In some of these cases, indeed, the tainted aliment consisted in potatoes; but they were thrown overboard, and the disease did not break out before from 4—6 weeks afterwards. On the other side, the report of the Committee contains evidences of six crews being attacked in spite of the food being proved to be of good or even excellent quality. Finally it may be added, that the medical inspector of the Medical Government Board of Norway, Dr Geirsvold, Christiania, has examined a great number of boxes of tinned meat and fish from six beri-beri-ships. He examined them microscopically and made aerobic as well as anaerobic cultures of their contents; but none of the boxes showed any sign of being tainted. On the contrary, all boxes were sterile except one containing a small number of an aerobic bacillus, which had not been able to develop under the anaerobic conditions inside the tin.

It seems a more probable theory that the disease is due to some special form of underfeeding, i.e. that it is due to a food containing some, but not all necessary nutritive elements. Starting from the above-mentioned observation of Stian Erichsen concerning the connection between the disease and tinned food, it is, in the first place, a question whether the high temperature or steam-pressure used in the manufacture of such food, may not destroy some nutritive elements of the meat and fish. Many observations tend to show that strongly heated milk may cause another form of scurvy, i.e. Barlow’s disease. And experiments in Java, described below, have proved that chickens get polyneuritis when fed on meat boiled for a long time at 120° C.

Tinned food may also be of importance in other respects. Such food in the long run is not palatable. The sailors, therefore, as a rule, eat little of it. The result is that their diet becomes comparatively
one-sided, consisting chiefly of farinaceous constituents; and these aliments are, to a large extent, not so good as the corresponding articles of food on shore. I may, in the first place, draw attention to the fact that the sailors on long voyages are very often reduced to preserved, i.e. dried, instead of fresh potatoes. That the dried potatoes often have something to do with the disease seems probable, because the disease often breaks out from 4—6 weeks after the fresh potatoes have been finished; and vice versa the patients often recover as soon as they get fresh potatoes on shore or from a passing vessel. This may be due to different causes. For instance the nutritive value of the potato may already be diminished by drying; neither dried potatoes nor dried green vegetables were found to protect against ordinary scurvy during the North American war of rebellion. But perhaps also the special methods of preparing the preserved potatoes may have an influence. They are not simply dried; if this is done they get an ill-coloured, greyish appearance. They are therefore first boiled in water containing hydrochloric acid or, sometimes, sulphate of lime, before being dried at 90° C.

It must further be mentioned that the Norwegian sailors on long voyages are, to a large extent, reduced to eating a poor bread. The government has, since 1895, ordered the sailors to use as much soft bread as possible. On long voyages they are, however, to a large extent compelled to use old flour, which does not bake well. At the same time ordinary bakers' yeast does not easily keep on long voyages in the tropics. Instead of yeast, which has been shown, in Germany, to be a remedy against scurvy, the sailors therefore very often use a farrago of fermenting squashed potatoes, groats, molasses, hop and other stuffs. The stewards are, in addition, not always good bakers, the result being, according to the papers of Nocht and Kjennerud, that the bread is to a large extent raw and not easily digested.

Finally, it may be mentioned that beri-beri has often appeared on Norwegian ships in spite of a daily use of lime-juice. But, it is true, this point has not been quite cleared up; the juice may, for instance, have been adulterated.

Considering these possibilities of an explanation of the disease, I have made a considerable number of experiments on animals. My starting point has been the excellent researches of the Dutch authors Eijkman and Grijns on the so-called polyneuritis gallinarum. Dr Grijns most obligingly showed me his experiments during my stay in
Batavia in 1902. About 10 years ago Eijkman\textsuperscript{1} found that chickens get polyneuritis and die when fed only on peeled rice, i.e. rice-groats; the same happened when they were fed on sago or tapioca; in one case the same applied also to barley-groats\textsuperscript{2}. On the contrary, the animals did not get ill after unpeeled rice, barley, oats or rye\textsuperscript{3}, or after meat, boiled at 100°C.; nor did they get ill when Grijns\textsuperscript{4} added small quantities of a special sort of beans (\textit{Phaseolus radiatus}—in Malay, Katjang-Idjo) to the peeled rice. But if these beans were boiled for two hours at 120°C., Grijns stated that they lost their preventive power; the same applied, also, to meat and—to some extent—to unpeeled rice. Finally meat also produced the disease when boiled for some days at 100°C.

These experiments of Grijns have recently been continued by Eijkman, who found that unpeeled rye, oats, millet and barley produce the malady when boiled for two hours at 115, 125, and 135°C. respectively. As far as oats are concerned, this effect did not, however, appear after a boiling for two hours at 110°C. Nor did three chickens get any neuritis when fed on horse-flesh, boiled for two hours at 120°C.

There has been, in the Dutch medical press, a discussion, still going on, regarding the bearing of these experiments on the causes of tropical beri-beri. The more, because Vorderman found, in prisons of Java, a marked congruence between the frequency of the latter disease and the extent to which the prisoners were fed on peeled or “half-peeled” rice. One of the latest phases of this discussion has been the book of Hulshoff Pool\textsuperscript{4} who believes that he has proved, by means of many observations on men, that \textit{Phaseolus radiatus} protects also against tropical beri-beri. I do not propose to enter into this discussion; but it seemed to me that a continuation of the experiments of Eijkman and Grijns might, perhaps, throw some light upon the possible unwholesomeness of the articles of food which I have mentioned in connection with ship-beri-beri.

\textsuperscript{1} Virchow’s \textit{Arch.} vol. cxlvi. 1897.
\textsuperscript{2} \textit{Archiv für Hygiene}, vol. lvi. 1906.
\textsuperscript{3} \textit{Geneeskundig Tijdschrift voor Nederlandsch Indië}, vol. xli. 1901.
\textsuperscript{4} Beri-Beri. \textit{Voorkoming en Genezing door Toediening van Katjang-Idjo} (\textit{Phaseolus radiatus}, L. Amsterdam 1904).
Experiments on pigeons.

My first experiments were on pigeons. These animals are cheaper than chickens and do not take so much room; at the same time it has been shown, by Grijs, that pigeons, also, are susceptible to the polyneuritis.

The experiments gave the following results:—When fed exclusively on ordinary rice-groats and water, pigeons die without any exception after 3—7 weeks. This occurs whether the rice is raw or boiled for half-an-hour at 100 or 110—120° C. In some cases immediately, in others 8—14 days after the commencement of feeding, the animals begin to emaciate; and they die with a loss of weight of 25—50%, on an average 40%. Before death many of the animals seem paralytic; their gait is unsteady and stumbling, and they are not able to fly. But in other cases these symptoms are less prominent.

I have made 30 experiments with rice-groats. Post mortem there is as a rule a distinct but moderate oedema under the skin of the legs and feet, extending in few cases to a universal anasarca. Sometimes the oedema is only to be found on the upper limbs or on the throat and head; or there is no oedema at all. Sometimes there is also some hydropericardium and very seldom ascites.

When examined microscopically, the nerves show, to a varying extent, typical Wallerian degeneration, but without any other proliferation of cells than the multiplication of the nuclei of the sheaths of Schwann, which occurs in all cases of Wallerian degenerations; i.e. the process is no inflammation in the common sense of this word.

The number of degenerated fibres was usually greatest in the nerves of the lower limbs, where it was, in 15 of the 30 cases, very great. In the other 15 cases the corresponding number was moderate or small. Still, in these last cases I very often found some greatly degenerated fine twigs or single fibres between the muscles.

On the whole, the process is most pronounced in the smaller ramifications of the nerves, though this is not always distinct. The degeneration affects also the nerves of the skin; on the other hand, I have only exceptionally been able to prove its presence in the vagus nerve.—As to the spinal cord, there are usually some, but rarely many affected fibres in the white substance: in the grey substance I have, in accordance with Eijkman, not been able to prove any alteration of importance.—The muscles of the limbs and the heart often show fatty degeneration, but without any proliferation of cells.—It may be added,
that there sometimes appear small haemorrhages in the heart: haemorrhages rarely appear in other organs.

Proceeding to the question whether the disease may not be produced by other than tropical cereals, I made experiments with barley. In accordance with the corresponding experiments on chickens made by Eijkman, I found that unpeeled barley is an excellent food for pigeons. But when fed on barley-groats the animals die as constantly and after the same time as when fed on peeled rice. I have made 16 experiments with barley-groats. Seven of the animals showed a very great, nine but a moderate or small number of degenerated fibres in the nerves of the lower limbs. I further have tried with barley flour. Two animals died after being fed for 24 to 39 days on flour mixed with water and dried. Both of them had a very great number of degenerated fibres. Three animals received flour mixed with salt and water and baked as the so-called "flat-bread"—a hard, paper-like sort of bread, which is used in country places in Norway. The animals ate this food with avidity, but died after 35, 48 and 55 days, the first one with a great, the last ones with a moderate number of degenerated fibres in the nerves of the lower limbs.

As, however, Norwegian sailors do not eat much barley, I tried rye-flour, the effect of which has not hitherto been examined. I fed four animals on bread baked with yeast, while four got bread baked with "Royal baking powder." This last bread is not very porous, has a viscous crumb, is often badly baked, i.e. to some extent raw, and so far corresponds with the bread which the Norwegian sailors commonly receive, as mentioned above, on long voyages.

For the rest, each sort of bread contained 8 grms. NaCl pr. kilo of fine-sifted flour. The result of these experiments was negative. Some of the animals lost weight at first; but after four months with one exception all of them were alive and apparently quite healthy. This animal had been fed on yeast-bread and acquired a somewhat stumbling gait: it therefore was killed. But no degenerated fibres could be found in the nerves. The muscles of the lower limbs, it is true, showed a moderate fatty degeneration; but this alteration I have found several times in pigeons kept in cages for months even when fed on good food (peas).

Taking a similar result for granted I have made no experiments with unpeeled rye. The Norwegian sailors do not, however, use much rye on voyages in the tropics, since they can get, in tropical ports, hardly
anything but wheat-flour. Nor has the effect of this nutriment yet been examined. I therefore have fed pigeons on wheat bread, baked with 8 grms. NaCl pr. kilo of flour. Again I fed some of the animals on bread baked with yeast, and others on bread baked with Royal baking powder. Like the corresponding rye-bread the latter was not very porous, partly raw, and with a viscous crumb.

Two series of experiments were made with these two sorts of bread, each series comprehending eight animals. The results of the first series were as follows: three of the four pigeons fed on bread prepared with baking powder, died after 30, 32 and 42 days, the two latter with a great, the first with a small number of degenerated nerve-fibres. The fourth animal as well as the four pigeons fed on yeast-bread were alive after three months; but all of them had lost about 30% of their original weight. They were killed, and one of the animals, fed on yeast-bread, had a great, the others but a small number of degenerated fibres in the nerves of the lower limbs.

The results of the second series of experiments were about the same. The four animals fed on baking-powder-bread, died after 41, 43, 51 and 100 days, the others after 90, 103 and 116 days. Of both kinds two animals had a great, one a moderate and one but a small number of degenerated fibres in the nerves of the lower limbs.

These experiments show that bread of wheat-flour, i.e. the flour ordinarily used by Norwegian sailors on tropical waters, is much more injurious to pigeons than rye-bread. The experiments further show that the effect of wheat-bread similar to the poor quality bread used by Norwegian sailors on long voyages, was far more injurious than that of bread baked with yeast.

I may finally add that the latter difference cannot be ascribed to any poisonous effect of the baking-powder, because the rye-bread, prepared in the same way, did not give the same result.

As to unpeeled wheat, three pigeons were fed on this food for four months without any effect. The same applies to two animals fed for four months on peeled oats, the effect of which has not yet been examined either. The latter applies also to oat-flour, which was baked as the "flat-bread," mentioned above. This nutriment (mixed with water) produced, after three months, no effect on three pigeons. Taking the same result for granted, I have not made experiments with unpeeled oats.

Pigeons died constantly when fed on boiled potatoes, no matter whether fresh or the dried (preserved) potatoes mentioned above. The
effects of these two kinds of food were not wholly identical, since the fresh potatoes did not cause any marked polyneuritis except in one case out of 11. This pigeon did not die till the 153rd day. The others, however, showed very few degenerations of the nerves. One of these animals died after 80, the other nine after 18—39, or an average of 30 days. On the other hand, the dried potatoes produced an extensive degeneration of the nerves in three out of six cases: the other three pigeons showed a comparatively small number of degenerated fibres, though more than in the 10 fresh-potato-animals. These six pigeons lived for 45—60 days after the beginning of the experiment. It may, however, be objected, that the great majority of the fresh-potato-animals only lived a comparatively short time; had they lived longer, some of them might possibly have also got an extensive neuritis.

Considering that Norwegian sailors eat much fish, I also made experiments with so-called fish-balls, which food, when tinned, is much used on board ship. I added, however, much more flour to the fish than is generally used otherwise, preparing the balls of pounded codfish and wheat or potato-flour in equal proportions. The paste prepared in this way was boiled for 10 minutes and afterwards cut in small pieces and dried at 50° C. in order to preserve it. Before use the pieces were again soaked in water. I fed four animals on balls made of wheat-flour and four on balls made of potato-flour. The first ones died after 31—47, the last ones, which did not eat so well, after 9—43 days. Three of the first and two of the latter had a great many degenerated fibres in the peripheral nerves. In the remaining cases the number of degenerated fibres was but small. It may, it is true, be objected, that the fish, through being dried, may have lost in nutritive value.

The results of feeding with potatoes and potato-flour, mentioned above, differ from the experiments made by Eijkman with potato-flour without any addition of other food. His experiments (on chickens) gave a negative result, except when the flour was boiled for two hours at 125° C. Still, Grijns observed that chickens got polyneuritis, when exclusively fed on raw potato-flour. Personally I have not made corresponding investigations.

I further tried to ascertain what quantities of dried peas and unpeeled barley—both excellent food for pigeons—must be added to rice or barley-groats in order to prevent the development of polyneuritis. The result was, that a daily addition of 5 grams of peas or unpeeled barley was sufficient; while an addition of 1—2 grams in some cases had no preventive power, in other cases proved to be very advantageous. I have for instance fed one pigeon one year on 1 gram of peas a day in addition to barley-groats, the only result being that it lost somewhat in weight.

I also made experiments in order to ascertain whether neuritis may be produced by a simple starvation. The results will be mentioned below.

Finally I have studied the effects of strongly heated food. As to dried peas, this article of food seems to produce, when boiled for ½ hour at 120° C., a more pronounced moulting of feathers (four pigeons) than when eaten raw (four animals)
or boiled at 100° C. (four animals). But otherwise all these animals seemed after 4 months to be healthy and none of them had lost in weight, nor did the former, when killed, show any degeneration of the nerves. The same applies to four pigeons fed on unpeeled barley, boiled for \( \frac{1}{2} \) hour at 120° C. compared with four fed on the same barley in the raw state; all these animals, too, were after 4 months in splendid condition, though the former had moulted a good deal more feathers than the latter. Nor did some animals get ill, that were daily fed on 5 grams of dried peas or 5 grams of unpeeled barley, boiled for \( \frac{1}{2} \) hour at 120° C. in addition to peeled rice or barley.

**Experiments on chickens.**

Of quite another kind were the results of feeding on strongly heated ox-beef. Following Grijns I made experiments on chickens with this food.

As mentioned above Grijns\(^1\) found that chickens get polyneuritis when fed on beef, boiled for two hours at 120° C. His experiments comprehended eight animals. One chicken did not get sick in spite of being fed during 11 months. As to four of the other animals, the result was negative, not very distinct, or doubtful, one dying without degenerations after 9 days, two with few degenerations after 19 days and 5 months, and one after 19 days with paralysis, but without its nerves being examined. The remaining three chickens died after 14 and 15 days and 5 months, all of these animals having a great number of degenerated fibres in their peripheral nerves. In these experiments, however, the beef was more strongly heated than in the manufacture of tinned meat. For instance, according to the paper of Bischoff and Wintgen\(^2\), the meat is boiled in a German manufactory for from 1\(\frac{1}{2}\)—2 hours at 100° C. and afterwards only for 1 hour at 120° C. The same period of boiling at 120° C. is also indicated in the *Calender für Conservedindustrie*, 1905. It may also be objected that the experiments of Grijns were made with meat from the Java ox ("Karboëwen"); this meat does not taste quite as our beef does. Finally it may be added, that the corresponding experiments of Eijkman\(^3\) gave negative results. He fed three chickens on horse-flesh, boiled for 2 hours at 120° C. one of the animals died after 1, another after 4 months; both had lost considerably in weight, but did not show any neuritis. The third animal had, after 4 months, lost in weight; but otherwise it was apparently healthy. I made two experiments, each on four chickens.

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3. *Archiv für Hygiene*, 1906, vol. LVIII.
In the first experiment two animals were fed on beef boiled for \( \frac{1}{2} \) hour at 100° and afterwards for 1 hour at 120° C., two control animals got the same beef, boiled for \( \frac{1}{2} \) hour at 100° C. All boiling was done in an ordinary autoclave; the beef was always minced and was found to be thoroughly boiled. The result is shown in the Table below. After 3—4 weeks the weight of all animals had increased. But afterwards their appetite diminished and their weight slowly decreased. At last the animals took very little food, became very emaciated, and died, or were killed, as shown in the Table. During the last 3—4 weeks all the animals showed a pronounced inclination to lie down.

At first sight it might appear that the result of this experiment was negative, i.e. that there was no difference between the two couples of chickens. The difference was, however, very marked. In the first place, both animals fed on 120 degrees beef, showed very pronounced oedema under the skin of the lower limbs as well as of the abdomen and throat. Both of them, also, had moderate hydropericardium. These alterations were, however, not marked in the two other animals, though the subcutaneous tissue of the one that lived longest, was somewhat watery. In the second place both animals fed on 120 degrees beef showed a very extensive degeneration of the nerves of the lower as well as of the upper limbs, the number of affected fibres being very great, both in the nerve trunks and in their finer ramifications. On the other hand, the radial nerve of the one that lived the shortest time of the controls, as well as the sciatic and peroneal nerves from the one that lived the longest time of the latter, contained but few degenerated fibres; most of them were to be found in the latter animal.

### TABLE.

Chickens fed on beef boiled at 100 and 120° C.

<table>
<thead>
<tr>
<th>Weight of animals in grams</th>
<th>day 1st</th>
<th>day 7th</th>
<th>day 16th</th>
<th>day 23rd</th>
<th>day 30th</th>
<th>day 37th</th>
<th>day 44th</th>
<th>day 51st</th>
<th>day 58th</th>
<th>day 65th</th>
<th>day 72th</th>
<th>day 79th</th>
<th>day 86th</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 degrees beef, 1st chicken</td>
<td>700</td>
<td>770</td>
<td>880</td>
<td>1000</td>
<td>1020</td>
<td>1000</td>
<td>930</td>
<td>940</td>
<td>935</td>
<td>885</td>
<td>—</td>
<td>865</td>
<td>killed</td>
</tr>
<tr>
<td>100 degrees beef, 2nd chicken</td>
<td>910</td>
<td>890</td>
<td>1080</td>
<td>1210</td>
<td>1220</td>
<td>1160</td>
<td>1120</td>
<td>1080</td>
<td>1080</td>
<td>840</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>120 degrees beef, 1st chicken</td>
<td>910</td>
<td>890</td>
<td>1080</td>
<td>1210</td>
<td>1220</td>
<td>1160</td>
<td>1120</td>
<td>1080</td>
<td>1080</td>
<td>840</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>120 degrees beef, 2nd chicken</td>
<td>750</td>
<td>740</td>
<td>890</td>
<td>950</td>
<td>1000</td>
<td>890</td>
<td>900</td>
<td>870</td>
<td>870</td>
<td>720</td>
<td>570</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Some few degenerated fibres often appear in the nerves taken from quite normal animals: this I can state from observations on guinea-pigs.
and rabbits. Hence the difference between the two couples of chickens was in reality very marked.

In the second experiment two chickens were fed on beef boiled \( \frac{1}{2} \) hour at 100° C.: the other two were this time fed on the same meat, boiled for \( \frac{1}{2} \) hour at 110° C. The boiling was, as before, done in the autoclave, and the beef, which was cut in small pieces, always proved to be thoroughly boiled. This time all the animals ate well and increased in weight, until one of them, fed on 110 degrees beef, and having apparently been well, suddenly was found paralytic in the cage the 49th day after the beginning of the experiment. It died 5 days afterwards showing emaciation, some hydropericardium and somewhat watery subcutaneous tissue, but no distinct oedema. Microscopically, the larger nerves as well as their finer ramifications were extremely degenerated, both in the lower and upper limbs. In addition, the muscles of the extremities and the heart showed fatty degeneration. In the white substance of the spinal cord there were also some, though not many degenerated fibres.

The remaining three animals continued to increase in weight, until they were killed on the 68th day. None of them seemed ill, but the nerves of the second 110 degrees animal contained a moderate number of degenerated fibres in the larger trunks and their ramifications in both the lower and upper limbs. In the two 100 degrees animals only the sciatic nerves contained some few degenerated fibres. It therefore seems evident, that beef may produce polyneuritis in chickens, even when boiled at a lower temperature than the 120° C. commonly employed in the manufacture of tinned meat.

Both the chickens fed on 110 degrees beef increased less in weight than the other two. The day before one of them became paralytic it had only increased 515, and the other 525 grams since the start, against 835 and 775 grams of the controls. And when the remaining three animals were killed, the surviving chicken fed on 110 degrees beef had increased 865 grams since the start against 925 and 1100 grams for the controls.

The more strongly-heated beef produced therefore some underfeeding. This was—at least chiefly—due to the fact, that the animals did not eat this beef as readily as the less boiled one. This was evident from the quantities of beef eaten by each animal, which were this time weighed daily from the start. Adding together these quantities, the one 110 degrees animal had, the day before it got paralysed, altogether eaten 7685 and the other one 8980 grams; the corresponding figures with respect to the 100 degrees animals were 10,395 and 9210 grams. And when the three remaining animals were killed, the surviving 110 degrees animal had, since the start, altogether eaten 14,050 grams against 15,800 and 15,095 grams, for the two 100 degrees animals. But the figures given also show, that the difference was
comparatively small. It therefore seems impossible to ascribe the polyneuritis to an underfeeding in the ordinary sense of this word. This conclusion must also be drawn from the previous experiment. In connection with this subject it also may be mentioned, that Eijkman did not find any polyneuritis in chickens fed on so small quantities of unpeeled rice, that they died from starvation. Nor have I found any polyneuritis myself, experimenting in a similar way with pigeons. These animals, when left to themselves, eat 25—30 grams of dried peas or unpeeled barley daily. Instead of this quantity, I gave each of 12 pigeons 5—10 grams daily, with the result that they died after 5—7 weeks, but without any of them having polyneuritis. In spite of the pronounced emaciation and loss of weight mentioned above, which pigeons show when fed on peeled rice, barley, &c., and in spite of the loss of appetite, which I have repeatedly found accompanies these symptoms, the polyneuritis cannot in these cases either be due to an underfeeding in the common sense of this expression.

Before leaving the experiments on chickens, it may be added, that the beef always had been recently boiled. That is to say, the effect of the strongly-heated beef can only be ascribed to a decomposition of one or several constituents of the beef produced by the high temperature or high steam-pressure used in the boiling.

The foregoing experiments may in various directions need to be supplemented. For instance, I twice saw polyneuritis occur in poultry yards in Norway. The first time about 30 of 200 chickens died of paralysis. I only got one carcass for examination; this chicken showed a very extensive neuritis of the limbs. As to the food, I only know that the chickens chiefly, if not exclusively, had got coarsely ground Indian corn, which food, as far as I can judge from two experiments, does not produce neuritis in pigeons. As soon as the food on my advice was altered, the diseased chickens recovered, and the mortality ceased at once; but I do not know, in what direction the food was altered. The second time three chickens out of seven died, one after the other, with paralysis; before death their gait was unsteady and stumbling. I made the post mortem of one of them and found a very pronounced oedema under the skin of the throat, neck and head; there also was some hydropericardium. Microscopically, I found a moderate neuritis of all limbs. In this case, the animals were to a large extent fed on fresh potatoes, which food, as mentioned above, only produced a distinct neuritis in one out of 11 pigeons.

A further pursuit of the experiments of Eijkman and Grijns may also be of interest on account of the additional light they may throw upon the deterioration of food owing to strong heating. We have seen, that this is of importance in weighing the question of the nutritive value of tinned food. But the same applies also for instance to the steam-boiling of various articles of food, used in many modern hospitals.
This boiling is often done at an over-pressure of \( \frac{1}{4} \) atmosphere, i.e. a temperature of about 110° C., which boiling, when applied during \( \frac{1}{2} \) hour, produces, as we have seen, an alteration in the nutritive elements of beef.

Several chemical questions arise. For instance, which are, properly speaking, the nutritive constituents, the presence of which prevent, and conversely, the absence of which produce the disease? That such elements exist has been suggested by Grijns, and seems to be proved by Eijkman\(^1\) who was able to cure the malady by adding to the injurious food an aqueous extract of rice-bran.

I have, however, for the present abstained from trying to answer these and other questions concerning\( \textit{polyneuritis gallinarum} \), because the experiments mentioned above have not thrown any clear light upon the question, which has been to me the principal one, i.e. the etiology of ship-beri-beri. It is true, the experiments described have shown that more of the ordinary articles of food produced\( \textit{polyneuritis gallinarum} \), than appears from the papers of Eijkman and Grijns. The experiments also support the suspicion, mentioned above, as to the injurious effects of tinned meat and poor quality bread, used on long voyages. On the other hand, however, the experiments have not demonstrated in any convincing way the injurious effect of dried potatoes, though the latter, to judge from facts, seem to be often connected with the malady. It may further be added, that\( \textit{polyneuritis gallinarum} \) resembles tropical beri-beri much more than the ship-disease, neuritis being present much oftener than in ship-beri-beri. And finally, even if modified feeding of pigeons and chickens had produced a disease more like ship-beri-beri, the objection would still remain that we cannot, from experiments on poultry, draw any convincing conclusion concerning man.

I therefore discontinued the experiments on poultry and passed over to investigations on mammalia. These latter investigations have been carried out in conjunction with Dr Frölich, and some of the results will be discussed in the following paper.

\(^1\) Arch. f. Hyg. 1906, vol. LVIII.