XVIII. NOTE ON ANAEMIA, UROBILINURIA AND INTESTINAL HAEMORRHAGE IN RABBITS IN CONSEQUENCE OF EXCLUSIVE NUTRITION WITH COW'S AND GOAT'S MILK.

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DURING many years, physicians believed that the anaemia which develops if men or animals are exclusively fed with milk is caused by lack of iron, in consequence of which the formation of haemoglobin would become insufficient (*milk-anaemia by decreased formation*).

Afterwards [Czerny, 1912; Kleinschmidt, 1916] it was recognised, that in addition to the forms of anaemia just mentioned there are cases in which the clinical picture proves an increased destruction of red blood corpuscles. Here the organism makes strong but unsuccessful efforts to compensate for the increased loss of haemoglobin, so that the highest degrees of anaemia may be observed (*milk-anaemia by increased destruction*).

Now it has been noted in Holland, Germany, Austria and Switzerland, that in infants under one year old exclusive feeding with goat's milk is more frequently followed by severe anaemia than exclusive feeding with cow's milk [Scheltema, 1916; Korteweg, 1916; Brouwer, 1922, 1923, 1925]. Particularly goat's milk gives rise to those types of anaemia in which the symptoms of increased destruction and formation of erythrocytes are apparent [Brouwer, 1922, 1923].

The direct causes of these "milk-anaemias by increased destruction" are unknown. Probably they would be discovered if one succeeded in provoking these milk-anaemias in experimental animals. The experiments here to be described were intended to investigate this point in young rabbits, especially with a view to the goat's milk-anaemia of infants.

It must however be mentioned that, though we succeeded in causing severe anaemia, the symptoms which occur so frequently in anaemia by goat's milk (polychromasia, basophile granulation, normoblastosis, megaloblastosis) were not found. In the stained blood film preparations (Pappenheim) only a moderate anisocytosis and a slight anisochromia could be seen. After the death of the animals, we found with the aid of the method of Tirmann-

Schmelzer-Hueck only very little iron-containing pigment in the spleen and in the liver. Moreover, there was no apparent difference between the consequences of feeding cow's milk or goat's milk.

Therefore it remains uncertain whether experiments with rabbits are suitable to contribute to the solution of problems concerning anaemia caused by goat's milk. Perhaps some other animal, *e.g.* the dog, would be better. In 1924 Beumer and Wieczorek [1924] believed that they had shown that in this animal feeding with goat's milk leads much sooner to a severe anaemia than feeding with cow's milk.

Nevertheless, our investigation has been interesting because some symptoms were noted which indicate, that after all in our experiments the anaemia is totally or at least partially caused by an increased loss of erythrocytes.

For this research four young rabbits were taken from two litters (age three to four weeks), and of these in both cases two were fed with raw cow's milk and two with raw goat's milk. Moreover, wood shavings were given in the first experiment; they were omitted in the second experiment.

The cages were provided with screen bottoms of galvanised iron gauze to prevent access to faeces. Unfortunately, notwithstanding the protecting layer, the iron wire rusted somewhat, so that the possibility that small amounts of this metal were ingested cannot be excluded.

The cow's milk was derived from a herd of several animals; the goat's milk from one single animal. The fat percentage of the cow's milk was 2.9 to 3.3; that of the goat's milk 5 to 6.5.

The experiment with the first four animals was made in winter, when the lactating animals were receiving a winter ration; the experiment with the second four in summer, when the cows and goat ate as much grass as they liked.

In five of these eight cases a severe anaemia developed in the course of some weeks to some months. In this lapse of time the haemoglobin content declined to ± 25 (Sahli) and the number of red blood corpuscles below three millions. This anaemia was accompanied by slight, moderate or even severe urobilinuria¹. All the animals died after one to several months, and the same occurred with the animals in which only a slight anaemia or no anaemia at all developed.

In the animals fed with cow's milk, death occurred in the first experiment after 46² and 53 days and in the second after 58 and 105 days; and in the animals fed with goat's milk respectively after 21, 82, 73 and 80 days.

¹ As liver and spleen contained very little haemosiderin, the direct mutual dependence of anaemia and urobilinuria could not be proved. *A priori* the possibility that abnormal liver-function may be the cause of the urobilinuria cannot be denied. Indeed, by microscopical examination some fatty degeneration in the centres of the liver lobules and in the layer immediately underneath the liver capsule was unmistakable. It seems however improbable that this explains the urobilinuria.

² In the rabbit that lived 46 days, intussusception of the small intestine was found *post mortem*, probably the direct cause of death.

Loss of weight, loss of hair and deformations of the bones of the extremities were frequently observed during the last weeks.

After death in the animals with anaemia, the caecum and the beginning of the colon contained a brown-red coloured, semi-fluid mass. The latter consisted of remnants of foodstuffs and more or less destroyed blood. These high degrees of anaemia and intestinal haemorrhage developed in the first experiment in all four cases, in the second only once in an animal fed with cow's milk. One might believe that the wood shavings, by irritating the intestinal wall, promote the development of haemorrhage and in consequence the anaemia, but the case where no wood shavings were given proves that such irritation is by no means necessary.

Ulcers or other symptoms of inflammation of the intestinal wall were not found. Undoubtedly the blood originated from "capillary bleedings" as may be found in scurvy in a number of organs. Nevertheless the diagnosis of scurvy could not be supported by macroscopical examination of the deceased animals or by studying the microscopical appearance of the junctions of the bony and cartilaginous parts of the ribs. Indeed, some investigators [Nelson, Lamb and Heller, 1922] hold that rabbits need none or very little of the antiscorbutic factor; moreover, the food (raw milk) contained undoubtedly a certain amount of vitamin C¹.

It cannot be stated positively that the intestinal haemorrhages were the only cause of the anaemia. It was often observed that the faeces of the living animals were darkly coloured; but the blood-reaction was very faint (benzidine reaction), in distinction to what was found in the caecum-content after death.

SUMMARY.

Not only in human milk-anaemia, but also in experimental milk-anaemia (by cow's or goat's milk), one should not only make allowance for *decreased* building up of haemoglobin. For a symptom (*urobilinuria*) may be found that indicates (but not yet proves) an *increased* loss of red blood corpuscles; and in the deceased experimental animals (rabbits) an *increased* loss of red blood by capillary haemorrhage into the intestinal cavity was observed.

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¹ In winter, by giving sugar beets to the milk-giving animals, the presence of vitamin C in their fodder was secured.