milk and bread and evaporated milk (see table). Possibly this is due to the young being less fit, as well as of lower weight, at birth.

Lactation.

Lactation cannot be studied satisfactorily from this series of experiments. If the young are of low weight at birth, and the mother rat fails to rear them all, it is incorrect to assume that the diet is responsible. Obviously two factors are involved: the diet may be unsuitable for lactation, or the primary factor may lie in the poor condition of the young at birth—that is, a faulty diet during gestation. Since the young were all below average weight at birth, it is possible that the fault lay in the condition of the young, and not in the mother's milk supply. As will be seen from the table, some of the young were successfully reared, but not all.

To compare the three diets from the point of view of lactation, other experiments were made, as follows:

Stock does were selected and were given a good mixed diet during gestation. The milk diets were started as soon as possible after the birth of the litter; three mother rats were given each diet, and all were able to rear six young per litter. Examples of the growth curves of the young are given in Fig. 2.

It will be seen that the young whose mothers had the evaporated milk did not grow so rapidly as the others. Also, these babies were less fit—they were limp to the feel, and their coats were less good. However, they were all successfully weaned at the usual time.

Statistical Comparison of the Three Milks as Food during Lactation.

	Dried Milk (Sample A).	Fresh Cow's Milk.	Evaporated Milk (Sample G).
Average weight of one baby rat on second day	5.26 grams	5.04 grams	4.91 grams
Failures in rearing any one litter	2 failures out of 15 litters	6 failures out of 15 litters	7 failures out of 18 litters
Number of times all six young reared	6	3	4
Highest weight of one baby at 21 days	47 grams	42.75 grams	38.5 grams
Lowest weight of one baby at 21 days	30.33 grams	28.8 grams	26.0 grams

COMMENTS AND CONCLUSIONS.

From the experiments described in this paper it is obvious that dried and evaporated milks possess quite different dietetic values, and that the dried milk approximates more closely to fresh cow's milk than does the evaporated variety. Although only one sample of each kind of milk was used in this work, experiments previously reported prove that dried milks are superior to the evaporated ones as regards vitamin B content. To sum up—

1. The dried milk (Sample A)* compared with fresh cow's milk:

(a) The initial rate of growth of the young rats was more rapid, but the final weight attained was practically the same.

(b) The weight of the young on the second day was slightly better—that is, dried milk appears to be a better food for gestation.

(c) The suckling rats had thicker and silkier coats if the mothers were fed on the milk diet throughout their lives, but when the milk diet was only fed during lactation (that is, a good mixed diet given during gestation) there was no apparent difference in the sucklings.

2. The evaporated milk (Sample G)* as compared with cow's milk:

(a) The rate of growth of the young rats was less rapid and the final weight attained was less.

(b) The weight of the young at birth was less satisfactory.

(c) The weight of the young at weaning was lower. This applied equally to the baby rats of mothers fed on a good mixed diet during the gestation period, or on the milk diet throughout their lives.

Thus, the dried milk (Sample A) appeared to be quite equal in dietetic value to fresh cow's milk; if there was any advantage, it was in favour of the dried variety.

The evaporated milk (Sample G), however, compared less favourably with the fresh cow's milk.

It must be remembered, however, that a restricted diet, such as bread and any form of milk, is not as good as a mixed and more varied diet.

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THE ETIOLOGY OF PERNICIOUS ANAEMIA.

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SINCE Addison in 1849, in a paper read before the London Medical Society, described idiopathic anaemia, later called pernicious anaemia, a large number of theories have been advanced relative to its etiology. Hunter's hypothesis is that it results from oral sepsis with subsequent streptococcal infection of the stomach, and there can be no doubt that pyorrhoea is at least a contributory cause. It may account for the toxin to which the combined lateral and posterior degeneration of the cord, occurring in about half the cases, is due. The latter is a true degeneration of nerve fibres affecting both the axis cylinders and the myelin sheaths, and not a sclerosis such as occurs in disseminated sclerosis. The fact that this degenerative change in the posterior and lateral columns occurs in other wasting diseases and may antedate the anaemia or be unaccompanied by the anaemia, lends weight to James Collier's argument that the toxin affecting the cord is not necessarily the cause of the anaemia, but that the anaemia and the cord changes may be the results of a pathological process responsible for more than one toxin. Other investigators are of opinion that pernicious anaemia is due to intestinal toxæmia. Herter blames the *Bacillus welchii*, while Adami suspects the *Bacillus coli*.

Hurst¹ says that it is now generally agreed that Addison's anaemia is caused by a haemolytic toxin produced by some infection in the alimentary canal, and states his belief "that this infection cannot take place unless free hydrochloric acid is completely absent from the gastric contents." He claims that the achlorhydria is neither caused by the same toxin which produces the anaemia nor is it secondary to the anaemia, but that it is an essential predisposing factor. He quotes Ryle and Bennett² to show that 4 per cent. of healthy young men have achlorhydria. It will be interesting to see whether these men in due time develop pernicious anaemia. Hurst sums up his views as follows: "The achlorhydria allows the bacteria which produce the haemolytic toxin, and which probably have their primary focus in the mouth, to pass through the intestines without being destroyed by the HCl which ought to be present."

I have endeavoured to approach the subject of pernicious anaemia from a new standpoint. I agree that an unknown toxin is probably the cause, but can find no proof of this. Therefore I have tried to postulate a theory with a non-toxic basis. It is possible that in this disease two independent processes are at work—an abnormal blood regeneration by the bone marrow and an increased blood destruction. Which of these processes is the primary one?

The general opinion seems to be that the main factor is the toxic effect upon the bone marrow, resulting in the production of immature cells, which are unable to resist the forces of blood destruction and become disintegrated in the blood stream or destroyed by the phagocytic cells in the liver, kidneys, and other organs. The hypothesis I prefer is that the primary factor is the phagocytic action of the liver and kidneys, and that the bone marrow change is secondary, the latter being due to an increased and urgent

demand for red cells to replace those destroyed. As a corollary to this I ventured to suggest to myself that the cause of the increased destruction was not an unknown toxin, but an unknown substance normally present in blood, the diminution or absence of which renders the blood increasingly liable to phagocytosis by the epithelial cells of the liver, etc., and I assumed this substance to be a constituent of bone marrow or a complex circulating in the blood.

In an endeavour to prove this theory, I attempted to extract an active substance by treating 2 kilograms of ox bone marrow with 80 per cent. alcohol, and later with 95 per cent. alcohol, and obtained no result. This was probably to be expected. I now applied this alcohol-fractional precipitation method, used by Banting in Toronto for the preparation of insulin, with slight modifications, to ox blood. I am indebted to Dr. Calvert of the Medical Unit for his assistance in the extraction.

Preparation of Extract.

To 8 litres of fresh ox blood 5 litres of 95 per cent. alcohol, previously cooled to 3° C., were added with constant stirring. The mixture was allowed to stand for two hours and filtered through thick Chardin paper. To the filtrate was added one and a half times its volume of 95 per cent. alcohol. The liquid, placed in a cool room overnight, was refiltered next day, giving a perfectly clear yellowish solution. The alcohol was distilled off *in vacuo* at a temperature of 45° C. in a water-bath. The following day the turbid liquid residue was redistilled *in vacuo* until the volume of the aqueous solution, the fat having separated out, was reduced to 250 c.cm. It was then filtered free from fat in a Buchner funnel and the residue shaken up in a separating funnel to dissolve any fat that might be left. After this the aqueous solution was made up to 80 per cent. with absolute alcohol and allowed to stand overnight in a cold room.

On the fourth day a thick yellowish solution had formed; it was decanted off and made up to 93 per cent. with absolute alcohol. This was allowed to stand in ice overnight. By the following day a precipitate had separated out. The 93 per cent. alcohol was siphoned off, about 50 c.cm. being left covering the precipitate. The latter was then centrifuged down, washed once with alcohol and once with ether, and then transferred to a vacuum desiccator over sulphuric acid.

The 8 litres of ox blood yielded 1.45 grams of a blood extract which I called "sanguinin." The substance is light brown in colour and very readily soluble in water. The solution, which is yellowish, I made up in the following dilution: 1 c.cm. of the solution = 10 mg. of sanguinin.

Experiments.

Intravenous injections were given into the marginal veins of the ears of two rabbits.

Experiment 1.—In the first rabbit 2 c.cm. (20 mg.) of sanguinin was injected. Fifty minutes after injection the blood sugar equalled 0.128 per cent., and ninety minutes after 0.140 per cent., showing that there was no appreciable amount of insulin present in the injection of blood extract given. Blood counts taken on the following dates showed:

1923.	Red Cells.	White Cells.	Haemo-globin.	Colour Index.
Dec. 4, just after injection ...	5,496,000	5,200	70%	0.64
Dec. 8, 4 days ..	6,440,000	7,400	65%	0.5
Dec. 10, 6 days ..	5,512,000	5,100	80%	0.78

In ninety hours the red corpuscles had increased by nearly a million per cubic millimetre, the whites by 2,200, and there was a fall of 5 per cent. in haemoglobin. The latter may have been due to there being too great a demand for haemoglobin to cope with the increase in the number of red cells. The general deficiency of haemoglobin was due to the animal being kept in confinement.

Experiment 2.—Into a second rabbit was injected 5 c.cm. (50 mg.) of sanguinin. Blood counts taken on the following dates showed:

1923.	Red Cells.	Haemo-globin.	Colour Index.
Dec. 17, just before injection ...	4,016,000	83%	1
Dec. 21, 4 days after injection...	5,654,000	75%	0.66
Dec. 24, 7 days ..	6,280,000	90%	0.72
Dec. 31, 14 days ..	5,504,000	82%	0.82

Here again we find a fall in haemoglobin and an increase in red blood cells followed by a fall. It would appear that the sanguinin either temporarily stimulates blood formation or temporarily inhibits blood destruction.

A similar effect was observed on giving a series of intravenous injections to a patient with pernicious anaemia in a remission stage.

The patient was admitted to hospital on October 21st, 1922, with the following signs and symptoms: Lemon-yellow tinge of skin, glossitis, complete achlorhydria on three occasions; temperature rising to 100° F. at night; numbness and tingling in arms and legs, oedema of legs, and increasing weakness. All her teeth had been removed eight years previously, and her stools contained coliform bacilli only. The blood picture on admission was as follows: There was a great variety in the size and shape of the red cells, numerous megaloblasts, some showing mitosis. The red cells numbered 802,000 per c.mm., white cells 1,500, haemoglobin 20 per cent., colour index 1.2. Differential count: Polymorphs 32.5 per cent., small lymphocytes 51 per cent., large lymphocytes 7 per cent., eosinophils 5 per cent., myelocytes 3 per cent., hyalines 1 per cent.

The patient left hospital on December 15th for Christmas. She had greatly improved; the red cells numbered 2,436,000, white cells 1,400, haemoglobin 33 per cent., colour index 0.69. She attended afterwards as an out-patient, and periodical blood examinations were made without showing any appreciable difference in the blood picture.

As this seemed a suitable case for experimental purposes, owing to the blood being in a stationary condition, I gave her a series of intravenous injections of sanguinin at intervals of four days: 1 c.cm. (10 mg.) of sanguinin was given on September 30th and on October 3rd, 7th, 11th, and 15th. The blood counts, taken four days before, during, and subsequent to the injections, were as follows:

1924.	Red Cells.	White Cells.	Haemo-globin.	Colour Index.
September 26 ...	2,640,000	1,100	36%	0.68
October 7 ...	3,196,000	1,200	39%	0.61
October 11 ...	2,956,000	1,700	39%	0.66
October 15 ...	3,148,000	1,400	39%	0.61
October 22 ...	3,176,000	—	39%	0.61
October 29 ...	3,560,000	—	42%	0.6
November 5 ...	3,640,000	2,600	40%	0.55

Differential count: Polymorphs 29 per cent., large lymphocytes 10 per cent., small lymphocytes 59 per cent., eosinophils 4 per cent., fragile cells 2 per cent., and neutrophil myelocytes 1 per cent.

After the first injections she complained of sweating and of feeling tired, sleepy, and heavy in head, arms, and legs. After the later ones she said that they gave her fresh life and vitality and she missed them when they were omitted—probably a mental effect.

On December 1st, 1924, the count was as follows: Red cells 2,920,000, white cells 1,600, haemoglobin 40 per cent., colour index 0.69. Examination of the above figures shows that there was a rise in the red blood corpuscles of 1,000,000 per c.mm. in six weeks, followed by a fall in the succeeding three weeks. The white count of this patient has always shown a marked leucopenia, usually about 1,500 per c.mm. with a relative lymphocytosis. The colour index is characteristically high in the relapse and low in the remission stages.

Experiments with sanguinin (1 c.cm.) on blood pressure showed an immediate fall of about 20 mm. of mercury, but intravenous injections of distilled water (1 c.cm.) gave the same results, so the observation was of no value. I expected an increase in the blood pressure, on the assumption that there might be a percentage of adrenaline present in the blood extract. It is impossible to say how much of the undoubtedly improvement which has occurred in this patient since the injections were given is due to the sanguinin.

Conclusion.

The fact of importance which arises out of the above experiment is that an extract can be obtained from blood by means of the alcohol-fractional precipitation method. The substance is freely soluble in water, non-toxic, and has apparently some effect in increasing blood formation. The extraction process is a long and expensive one and the amount of sanguinin obtained very small. The failure to extract sufficient insulin to affect the blood sugar curve in the amount given to the rabbit is interesting, as is also the negative result obtained on examining the blood pressure.

It is not impossible that, by using other methods of extracting blood, further substances, probably of greater import than sanguinin, may materialize.

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