THE ETIOLOGY OF RICKETS:

AN EXPERIMENTAL INVESTIGATION.

BY

D. NOËL PATON, M.D., F.R.S.,

REGIUS PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF GLASGOW;
AND

A. WATSON.

(From the Institute of Physiology, University of Glasgow.)

(Abstract.)

SINCE 1907 investigations upon experimental rickets in dogs have been carried on in this laboratory, first by Leonard Findlay,¹ then by Renton and Madge Robertson,² and subsequently by Noël Paton, Findlay, and Watson.³

These last experiments showed that while all the pups of two litters kept in the laboratory upon an abundant supply of whole milk and oatmeal porridge developed rickets, two pups from each of the litters kept in the country on skimmed milk and oatmeal remained free of the disease.

The present series of observations* shows that pups kept in the laboratory develop rickets even on an abundant supply of milk fat (as much as 7.5 or even 11 grams per kilo) and oatmeal porridge, but that those on the same amount of separated milk (0.2 to 0.7 gram of milk fat) and porridge develop the disease more rapidly. The energy value of the separated milk diet was necessarily lower than that of the full milk diet (207 to 267 calories as against 270 to 437 calories), and hence it is possible, as is suggested by the observations on infants by Hess and Unger,⁴ that a low energy intake may predispose to the disease, although it is not a causal factor.

To test this the next experiment was arranged so that pups of three litters, which were available at the time, should have the diet increased proportionately to their increase in weight, and that the energy intake should be kept ample throughout the period of growth, but that, while one series of pups should have the energy supplied largely from whole milk—fresh and dried—with bread, another should have it from dried separated milk and bread, another from lard, which the Vitamin Committee⁵ of the Medical Research Council class as a fat free of their anti-rachitic vitamin, and the last series from dried separated milk and bread. Scrupulous care as to cleanliness was observed throughout this experiment.

The result was that all the pups, with one exception, reached fifteen to eighteen weeks free of rickets, although those upon the separated milk and bread diet had only 0.3 to 0.6 gram of milk fat per kilogram per day.

The basis of Mellanby's⁶ experimental work is that separated milk up to 250 to 350 c.cm. and white bread, even with linseed oil, yeast, and orange juice, will not prevent the onset of rickets in pups between six and twelve weeks of age, while whole milk will prevent it, and upon this is based the practical recommendation of the Vitamin Committee,⁵ p. 99, that full cream milk should be used by children for the prevention of the disease.

Butter is placed with cod-liver oil (p. 102) as the substance richest in "fat-soluble A or anti-rachitic factor," but both of the two pups in our series to which butter was administered in large quantities developed rickets, while its administration failed to cure or to prevent the advance of the disease in another.

Our experience indicates that by attention to strict cleanliness it is possible to rear pups free from rickets in a laboratory. It is easy to rear them in the open air, even on a diet poor in milk fat. The work of Morpurgo on white rats, and the study of an epidemic of rickets among foxhounds in Adelaide by Bull,⁷ taken along with our results, point to the probability that a bacterial infection of the same non-specific character as that which the investigations of McCarrison have shown to be the causal factor in goitre, plays an important part in the etiology of the disease.

A point of considerable interest demonstrated in our observations is the more rapid growth of the pups kept in the open air.

* A detailed account of the experiments is published in the April number of the *British Journal of Experimental Pathology*. The expenses of the investigation were defrayed by the Medical Research Council.

CONCLUSIONS.

1. In young dogs, under ordinary laboratory conditions, a liberal allowance of milk fat up to even 14 grams per kilo of body weight neither prevents the onset of rickets nor cures it when it has developed.

2. Pups kept largely in the open air may escape the development of rickets on an intake of less than 1 gram of milk fat per kilo body weight.

3. With scrupulous care as to cleanliness it is possible to rear pups free of rickets in the laboratory on an intake of only about 0.5 gram of milk fat per kilo of body weight, along with bread, provided that the diet affords an adequate supply of energy.

4. The energy value of the diet, however supplied, quite apart from the presence of any hypothetical anti-rachitic factor in milk fat, would seem to play a part in controlling the development of rickets, but that it is only a contributory part is shown by the development of rickets in pups with a high energy intake when they are confined in the laboratory without scrupulous care as to cleanliness.

5. Milk fat may be reduced to about 0.3 gram per kilo of body weight, if its place is taken by an equal amount of lard, without the onset of rickets.

6. The results of these observations do not support the conclusion of the Accessory Food Factors Committee of the Medical Research Council that rickets is a deficiency disease due to lack of an anti-rachitic factor associated with milk fat.

REFERENCES.

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A TUBERCULOSIS IMMUNIZING VACCINE.

BY

NATHAN RAW, C.M.G., M.D., M.R.C.P., M.P.,

PRESIDENT, TUBERCULOSIS SOCIETY OF GREAT BRITAIN.

OF all the serious infections of the human body tuberculosis is the most hopeful, both as regards its prevention and also its cure, provided that treatment can be commenced early enough and continued long enough to give the affected tissues time for repair.

In spite of an enormous amount of research, continued in all parts of the world, we have reluctantly to admit that we have not yet obtained a specific remedy which will effectively destroy tubercle bacilli in the body. We must therefore rely on producing a sufficient immunity in the tissues to resist the attack by virulent tubercle bacilli. This immunity can be obtained:

1. By increasing the natural resistance by means of increased nutrition and sound hygienic conditions.
2. By producing an artificial active immunity in the tissues to the tubercle bacillus itself.

Increased care in infant welfare, better wages to the industrial classes, good nourishing food, a pure milk supply, the prevention of overcrowding, and, above all, good housing conditions and the segregation, of open cases of pulmonary tuberculosis, will obviate to an increasing extent the possibility of direct infection; but all this will take many years to accomplish. In the meantime I feel strongly, from my experience of treating many thousands of cases of tuberculosis in hospital, that we have at our disposal a scientific means by which we can secure some immunity to the bacillus, and certainly of preventing the extension of the disease in the human body when once introduced. Fortunately for civilization, the tubercle bacillus is a parasite and not a saprophyte. It has no existence outside the living body, otherwise the whole community would be endangered.

In the *BRITISH MEDICAL JOURNAL* of 1903 I published a preliminary note, the gist of which was that human and bovine tuberculosis were separate and distinct infections, producing a different set of symptoms in the human body. The lesions caused by the human bacillus (direct infection)