not made them out, but our hospital results are not anywhere near as good as the figures of private cases. I tell all my breast cases to come and see me after the operation, and I try to keep an eye upon them every so many months. I do not believe 20 per cent. of them are alive and well after five years. Surgeons will give many instances of people alive and well after the five years mentioned, but I believe the bulk of these are private patients; I myself have them up to seventeen years. But in private, whatever the delay may be, we see them, as a rule, far earlier than we see the hospital cases.

For my own part I freely admit that in the best cases I have the operation on the breast in the first place was not done with any idea of cancer, but always for chronic mastitis, and the cancer found later and the whole breast removed. That is the secret of the best of my cases, and that is how the importance of avoiding delay became impressed upon me. I believe that if operations for cancer of the breast could be carried out at this time there is no reason why we should not have 75 per cent. alive and well at the end of five years.

In the last twenty years the operation on the breast has quadrupled its gravity, but I do not think it has as much as doubled its benefit to the patient, and much even of that benefit is due to earlier operation, for the dread of operations is less now than it was. The extent of the operation has reached its limit, and if our results are to improve, as I am confident they can, then it must be by earlier diagnosis; and earlier diagnosis along the lines I have just indicated is bound to come.

I know the objection that will be raised is that many early cases would be operated upon in which no malignancy was found, and therefore the operation need not have been performed and is therefore unjustifiable. But the preliminary operation is a comparatively slight one; it leaves no visible scar, and if nothing serious is found the patient's mind can be set at rest; she is rid of the mass, and she is all the better for being rid of it. Does not getting rid of the mass and the giving of a definite diagnosis compensate and justify the proceeding? Think, too, what we gain every time we do find a cancer. How many cases of obscure abdominal disease undergo an exploratory operation and nothing is found? but the operation is not held to be unjustified. How many cases of obscure abdominal trouble are operated upon, and an apparently normal appendix removed? But it is not therefore said that the operation was unwarranted. How many times are gall stones diagnosed and at the operation no gall stones are found? We all know these cases, but we do not say that we have done more than take proper precautions.

Those who were at hospital twenty-five or more years ago can recall how few were the operations for gall stones or for appendicitis then seen. We were only beginning to operate upon these cases, and now they are more than common. Before that time exploratory operations upon the abdomen were unheard of; now they are a matter of common practice, and are carried out on quite slight grounds—the suspicion of gall stones or appendicitis, enteroptosis, chronic constipation, slight obstructive pains the cause of which is obscure; they are exploratory and diagnostic, and therefore considered necessary for diagnosis. The likelihood of cancer is certainly present, but it is not the formidable bugbear it is when we are dealing with the breast. Nothing is thought of exploratory abdominal operations, but the same people will often object to having an exploratory operation performed on the breast, though no one could compare the severity and seriousness of the two operations.

Believe me, the same change which has come in your lifetime in the case of appendicitis and gall stones is going to come in the case of the breast, and exploratory operations will in time be common, and greatly to the benefit of the patient. It may be a new doctrine now, but in a few years it will be the ordinary teaching of all medical schools, and the "wait and see" policy will be a thing of the past; it will be that policy which will be called unjustifiable, and the more we think of it the more unjustifiable it is from every point of view.

THE CAUSATION AND PREVENTION OF RICKETS.*

BY

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RICKETS is a disease of civilization, and is so frequently found in the large cities of America and Europe that it is doubtful whether the children of the poorer classes ever wholly escape it. Good evidence of a seasonal variation in the incidence of rickets has been shown by many observers—Schmorl, Hansemann, and others. It reaches its height in the winter and declines in the summer. Palm was the first to correlate this seasonal variation with the incidence of sunlight, and thus to anticipate by many years wider discoveries.

CAUSATION.

Many theories have been advanced to explain the cause of rickets: overfeeding, starvation, intestinal intoxication, defective hygiene, disorders of the ductless glands, and acidosis. The first great impetus to the modern intensive study of rickets was given by the work of Mellanby in this country in 1918. He varied the diets of young growing puppies until he found diets that would invariably produce rickets. To these diets he added various substances, and noted if any effect was produced in the process of calcification. He experimented on a large number of puppies and brought out many interesting facts. His most important conclusion was that rickets was really a deficiency disease—that is, it was caused by the absence from the food of a vitamin, and that the particular vitamin concerned was vitamin A or something closely associated with it. He found generally that fats richest in vitamin A were the most potent in preventing rickets, cod-liver oil being by far the best.

Soon after the publication of Mellanby's work the American investigators, McCollum, Simmonds, Shipley, and Park, and Sherman and Pappenheimer, showed almost simultaneously and independently that rickets could be produced in the rat by diets that were abnormal in their inorganic constituents. Their investigation showed that apart from any vitamin deficiency the essential thing in the production of rickets was to impoverish the diet in the raw materials of the skeleton—that is, in calcium and phosphorus. They found that rickets could be produced by diets poor in phosphorus or in calcium, or by diets that contained these elements in unbalanced amounts. More especially was it shown that a diet with a minimum amount of phosphorus could be made a rickets-producing one by the addition of excess of calcium. Although bone owes its rigid structure to its calcium phosphate content, most previous workers on the subject had, curiously enough, confined their attention to the part played by calcium in bone formation only. It is obvious that calcium without sufficient phosphorus to combine with it is useless to the organism for bone formation, and the work of the American investigators gave this point due consideration. Sherman and Pappenheimer more particularly proved that the form in which the phosphorus was given—that is, as a simple inorganic phosphate or as an organic phosphate in various types of combination—was important. They showed generally that soluble inorganic phosphates were more efficient in preventing rickets.

This work on rats paved the way for extensive work on the part played by deficiency substances in the etiology of rickets. Cod-liver oil was introduced as a specific for rickets by the Frenchman Bretonneau. Trousseau and other physicians had convinced themselves of its effectiveness by clinical observation. By means of a histological test—the so-called lime test—McCollum, Simmonds, Shipley, and Park showed that cod-liver oil caused a remarkable deposition of lime salts in the cartilage of the rachitic rat close to its junction with the metaphysis. Howland and Park demonstrated also, by means of the x rays, the

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deposition of lime salts in the bones of rachitic children following administration of cod-liver oil. The specific action of cod-liver oil in curing and preventing human rickets has been established by many observers, more particularly by Chick and her collaborators in an extensive investigation in Vienna.

Although Mellanby was inclined to believe that the antirachitic principle of cod-liver oil was fat-soluble A, other observers began to doubt it. Findlay, using butter-fat, claimed that though it was rich in vitamin A yet it was poor as an antirachitic agent. Sherman and Pappenheimer first showed clearly that a diet deficient in vitamin A only would not produce rickets. This was confirmed by other investigators.

McCollum, Shipley, Simmonds, and Park compared the action of butter-fat and cod-liver oil, and came to the conclusion that the latter contained in abundance a substance that was antirachitic but which had no specific action on growth or the prevention of keratomalacia. McCollum, Simmonds, Becker, and Shipley proved that the antirachitic substance was distinct from fat-soluble A vitamin. Hopkins has shown that fat-soluble A vitamin is destroyed by combined heat and oxidation. McCollum and his co-workers treated cod-liver oil in this way until, as shown by tests on animals, it had lost its power to promote growth; this oil was found, nevertheless, to be potent as an antirachitic agent. This conclusive experiment settled once and for all the non-identity of vitamin A and the unknown antirachitic agent.

RADIANT ENERGY.

In 1919 the German physician Hulschinsky reported that he had cured cases of rickets in children by radiating them with the light from a quartz mercury vapour lamp. The action was not local, radiation of one limb healing the rickets of both limbs. This important observation was confirmed by many workers.

The quartz mercury vapour lamp emits rays rich in the ultra-violet region, and it was proved that the active rays were these short invisible ones. Window glass cuts off these rays, and Hulschinsky found that he could not cure rickets if the light of his mercury vapour lamp was filtered through glass. The active rays were the ultra-violet ones. Hess and his co-workers extended these observations and showed that ultra-violet light would cure and prevent rickets in rats. They also proved that other sources of ultra-light—the carbon arc and cadmium spark—were active against rickets. By means of selective filters they were able to cut off different portions of the spectrum, and arrived at the conclusion that the active rays were those having a wave-length of 300 μ or shorter.

Hess and his co-workers and McCollum and his also showed that the rays of the sun would prevent rickets in rats. The sun's rays, it may be mentioned, extend down to about 290 μ in the ultra-violet region. If the sunlight is filtered through glass then it does not protect against rickets. Miss Chick and her co-workers proved the protective power of sunlight on a large number of children in Vienna fed on rachitic diet. The experiments we describe confirm and amplify the fact that ultra-violet light is specific in protecting against experimental rickets in rats.

Radiant energy, it must be concluded, is as important a factor in the cure and prevention of rickets as the unknown substance present in cod-liver oil and other oils. The children in city tenements in Britain are made rickety by a diet insufficient in antirachitic substances and by over-clothing and confinement indoors. Exposure of children more or less nude to sunshine or arc lamps would be of great benefit.

Iversen and Lenstrup and Howland and Kramer showed independently that the blood in cases of rickets is low in inorganic phosphorus. The inorganic phosphorus of normal children is about 5 mg. per cent.; in cases of rickets it may fall as low as 1 mg. per cent. In rickets complicated by tetany the calcium in the blood is below normal. These chemical changes in the blood are well established by a large number of investigators, and it can now be asserted that rickets is always associated with a

diminished content of calcium or inorganic phosphate or both in the blood. In rachitic children it is usually the inorganic phosphorus that is low.

Hess, examining the blood of children in New York, claims to have shown that there is a seasonal variation of inorganic blood phosphate; it falls during the winter, reaching its minimum in March, and rises again in the spring and summer till it is at its maximum in the late summer. This observation confirms in a striking way the opinion of Palm, expressed, as has already been mentioned, so many years ago, that rickets is due to insufficient sunlight.

If a cardinal symptom of rickets is a blood low in calcium or inorganic phosphorus, then cod-liver oil or ultra-violet light, if they are specific antirachitic agents, might raise the concentration of these substances in the blood when administered to cases of rickets. That this is so has been shown by many investigators. Hess was the first to demonstrate a rise in inorganic blood phosphate in the blood of rachitic children following ultra-violet light treatment.

Iversen and Lenstrup and Howland and Kramer have shown that cod-liver oil has the same effect. McCollum and co-workers produced rickets in rats by giving diets (1) poor in phosphorus, and (2) poor in calcium. Other rats on the same diets had cod-liver oil in addition. Howland and Kramer examined the blood of these rats, and showed that (1) were low in inorganic phosphorus, and that (2) were low in calcium. Those rats having cod-liver oil had the normal calcium and inorganic phosphate blood contents. The histological structure of the bones follows in a quite remarkable way the concentration of calcium and inorganic phosphorus of the blood.

It is well established, then, that rickets is a metabolic disease characterized by bones deficient in calcium phosphate, and accompanied by a diminished content in the blood calcium and of inorganic phosphate; that it can be cured both clinically and in experimental animals with certainty by administering cod-liver oil, and that the curative action is not due to vitamin A. It can also be cured with certainty by the action of ultra-violet light.

In what way do these two dissimilar agencies act? A consideration of the calcium and phosphorus metabolism may throw some light on this problem. The experiments of one of us (A. W.) described in this paper show that experimental rickets is accompanied by defective absorption of calcium and phosphorus from the intestinal tract and a very low uptake of these elements from the food supplied. Other observers, notably Paton, Sharpe, and Findlay, and Telfer have found that this is also the case with rachitic infants. Telfer has proved that the administration of extra calcium decreases the absorption of phosphorus, as shown by the urinary output; ingestion of fat also lowers the absorption of calcium, which is excreted in the faeces as calcium soaps. It is often urged against metabolism experiments that they are of too short duration and consequently are liable to gross errors. This cannot be said of the experiments described in this paper, in which the calcium and phosphorus metabolism was recorded throughout the experimental period of one month. In the rachitic rats A. W. did not get a negative calcium or phosphorus balance, and it is obvious that rickets is possible without the actual loss of calcium or phosphorus from the organism. Telfer finds that this is the case with rachitic infants. A. W.'s experiments show conclusively that both ultra-violet light and cod-liver oil greatly increase the absorption of calcium and phosphorus from the intestinal tract, and that this is followed by an increased retention in the skeletal structures as shown by bone analysis.

These results suggest very strongly that the primary seat of rickets is the gastro-intestinal tract—a view that is by no means new. In this connexion the experiments of Zucker, Johnson, and Barnett are of interest; when they made their rickets-producing diet acid it no longer produced rickets. They also examined the faeces of rachitic and non-rachitic rats, and found that the pH of the faeces of the non-rachitic rats was lower—that is, more acid—than those of rachitic rats on the same diet. If the intestinal contents are made acid it will prevent the formation of

insoluble calcium compounds, more especially the basic calcium phosphate, and so facilitate absorption of calcium and phosphorus in the blood stream. It has been suggested that the bacterial flora of the intestine may have some influence on absorption, and the experiments of Hill, Eidinow, and Colebrook, who have shown that radiation with ultra-violet light increases the haemobacterial power of both man and experimental animals, are of interest in this connexion. On the other hand, Korenchevsky was unable to produce rickets experimentally by bacteriological means. Findlay, who in a recent review of this subject is inclined to look with favour on the gastro-intestinal tract as the primary seat of rickets, was also unable to produce rickets by infecting the intestinal canal. He suggests that the digestive processes are impaired in rickets, and quotes some experiments that support this view.

The beneficial effects of exercise and a healthy open-air life are in great part due to a raised rate of metabolism, which must be followed by increased absorption from the intestinal canal, but, as shown later, rickets can be prevented in rats by ultra-violet radiation when these animals are kept in stagnant moist warm air. Mere increase of metabolism by exposure to cool open air does not suffice to prevent rickets on a deficient diet. A border-line diet, however, may well be made sufficient by increase of metabolism through exercise and open-air life.

It may be argued that the inability of the rachitic animal to maintain normal levels of calcium and phosphorus in its blood is not due to defective absorption but to other causes; these substances may be absorbed and excreted at a lower level owing to the animal's inability to make use of them—this inability to build up bone from supplies of material present being the root cause of rickets. The present state of knowledge does not permit us definitely to refute this view, but there is quite good evidence against it. The diets used for the experimental production of rickets do so by virtue of their deficiency either in quantity or in balance of calcium and phosphorus, and if this is rectified, then the animals do not develop rickets even if they are deprived of vitamins and radiant energy. Take, again, the experiments of McCollum and his co-workers on the effect of starvation in rickets; they took rats, which they rendered rachitic, and starved them for a few days and then killed them. Histological examination showed that the period of starvation was followed by a marked deposition of lime salts. The breakdown of the starving animal's tissues liberated phosphorus and calcium, which were promptly used to build up bone. This tends to show that it is not the rachitic animal's power of forming bone which is at fault, but lack of the raw materials—that is, calcium and phosphorus.

A consideration of the evidence given in this paper strongly suggests, then, that the primary cause of rickets is a low calcium and inorganic phosphate level in the circulating blood, and that this is due to defective absorption from the intestinal canal; and we favour this view.

Given the presence of adequate amounts of calcium and phosphorus in the blood, how does the animal convert this into bone? Until quite recently knowledge of this process was very meagre; recent work of Robison and his co-workers throws new light on it. They have shown that growing bones contain an enzyme capable of splitting hexose phosphates into inorganic phosphate. If strips of fresh young bone are placed in a solution of a calcium hexose phosphate insoluble calcium phosphate is deposited in the bone. Robison has further shown that a hexose phosphate is a normal constituent of blood, and that it occurs chiefly in the red blood corpuscle. This work is of great interest, but not yet advanced enough to consider specifically from the standpoint of the etiology of rickets. Both normal and rachitic bone contains the enzyme.

EXPERIMENTAL METHODS.

Our experiments were all carried out on rats. Except in a few early experiments when we used the diet described by McCollum, we used exclusively the diet 84 of Sherman and Pappenheimer. This has the following composition:

Patent flour	...	...	95 grams
Calcium lactate	...	...	2.9 "
Ferric citrate	...	...	2.0 "
Sodium chloride	...	...	0.1 "

It is a very deficient diet, poor in protein, practically free from vitamins, poor in phosphorus, and rich in calcium in relation to the phosphorus content. The ratio of calcium to phosphorus is about 4:1. It is the low phosphorus content together with the relatively large amount of calcium that gives this diet its rickets-producing character. The content of phosphorus, while being of itself ample, is not absorbed, and is mostly excreted in the faeces in combination with calcium. This diet produces, in fact, phosphorus starvation, and with the stock of rats we used it never failed to produce rickets.

The rats used were the ordinary white albino or black and white rats bred in the Institute. The stock rats were fed on oats principally, with occasional scraps from the canteen and a little greenstuff. The young rats were known to have a minimal quantity of vitamin A stored.

No attempt was made to select particular litters; the rats were taken at random from the Institute stock, animals weighing 40 grams, or as near as possible to this figure, being chosen. Each experimental group consisted of four animals; unless otherwise stated, they were kept in wooden boxes 14 by 9 by 7 inches, with perforated zinc lids; sawdust was used as bedding. The boxes were kept in a poorly lit room, what little sunlight there was having to come through plate-glass windows. The diet was mixed in the form of a stiff paste with distilled water and fed to the animals daily. Distilled water for drinking was supplied *ad lib*. Each rat was weighed at the commencement of an experiment and then weekly. The experimental period was twenty-eight days. At the end of this time they were killed and samples of blood taken for analysis; the bones were either examined histologically or they were x-rayed. In most cases the diagnosis was made from an examination of the x-ray photographs; although we used histological methods in some of the early experiments we found the x-ray method more useful. There is no doubt of the correctness of the diagnosis by this method, the difference between radiographs of rachitic and non-rachitic animals being most striking. Generally the inorganic phosphorus in the blood of the rats was determined at the end of each experiment, as was also the calcium and phosphorus of the bones. Young rats of about 40 grams weight put on the Sherman-Pappenheimer diet increase a little in weight and then decline, their appetite fails, and if left longer than twenty-eight days they usually die. If killed at the end of twenty-eight days gross rachitic changes are obvious and unmistakable. Typical experiments will be described here with the experimental results obtained.

We first tried the effect of exercise, or rather lack of confinement. One group of rats was kept in our standard size box, while another group was kept in a much larger box having four and a half times the floor and nine times the capacity of the small box. Rickets developed in all the rats in each box, so that confinement *per se* was not responsible for the development of the rickets.

Similar experiments were tried in which one group of animals were kept in the large box as before; but the box was kept out of doors for two hours daily, freely exposed to any winds and to a north sky in March, but shaded from direct sun. Rickets again developed. We are forced to the conclusion that exercise and open air but absence of direct sunlight have no specific antirachitic effect on young rats. It is possible that exposure to cold was disadvantageous. The influence of direct sunlight was next investigated. The rats were kept in the standard box, but at 12 noon each day they were transferred to an open-mesh wire cage and exposed on a high balcony facing south for two hours each day to whatever sun was available. The experiments were done in the spring and summer, but in this country the daily amount of sunlight is very variable. Our results varied, but we came to the conclusion that a minimum exposure of two hours to bright sun- or sky-shine five days a week was necessary to protect rats from rickets under the severe experimental conditions we have adopted in this research.

The rays emitted from two different known sources of ultra-violet light—the quartz mercury vapour and the open carbon arc—were next investigated. The rats were kept in their usual standard boxes; when it was necessary to expose them they were transferred to a small large-mesh wire cage and exposed for varying times to either the carbon arc or the mercury vapour lamp. The exposure varied from two hours daily to five minutes daily, and the distance from the lamps two to three feet. The quartz mercury lamp was a vacuum lamp taking 3.5 amperes at 200 volts. The carbon arc was a hand-fed lamp taking 5 amperes. The results are very striking provided the exposure is sufficient and not through glass, which filters out the active ultra-violet rays; radiations from this lamp will always prevent rickets from developing in rats on the standard diet we have used. The minimum exposure that will prevent rickets we found to be five minutes daily two feet from the mercury vapour lamp, and about thirty minutes

for the carbon arc at the same distance. We came to the conclusion that ultra-violet light is specific in its antirachitic effect. This will be emphasized in the experiments we are now going to describe.

This specific action of ultra-violet light seemed to us to conflict with the evidence of the incidence of rickets in tropical climates. Rickets is by no means unknown in the tropics, although it has been shown by chemical tests that the tropical sun is rich in ultra-violet rays. It is well known that the average mean temperature in the tropics is very high, and there is often present also a high degree of humidity. It seemed possible to us that this might influence in an adverse way the specific antirachitic effect of ultra-violet light, so we proceeded to investigate the question.

We first tried the effect of dry heat on young rats fed on a normal diet. A group of young rats was kept in standard boxes, the food consisting of the Institute stock diet—that is, whole cereals with a little greenstuff daily when available. From 5 p.m. to 9 a.m. the rats in their boxes were kept on the floor of the hot room, where the mean temperature was about 33° C. They spent the rest of the time in the outer hot room, where the mean temperature was about 23° C. This was continued for a period of twenty-eight days, when the rats were killed and examined for signs of rickets. No evidence of rickets was seen in any of the rats. Rickets, then, is not produced in rats fed on a normal diet and subjected to a high temperature for twenty-eight days. Another group of rats was fed on the same normal diet and kept in wire cages. These cages were suspended in large tanks with hot water just below but not touching the bottom of the cages. The water was regulated with a thermostat to keep a temperature of about 37° C. The rats thus lived in a very hot humid atmosphere. We found it very difficult to keep rats under these conditions, several dying of acute congestion of the lungs. A couple of rats lived under these conditions for forty days, and when killed they showed no signs of rickets. We came to the conclusion that, providing the diet is adequate, conditions simulating the tropics at their worst, but without any ultra-violet light, will not give rise to rickets in young rats.

We then subjected rats fed on our rickets-producing diet to conditions of dry heat described above, giving half of them thirty minutes' exposure to the carbon arc daily while the other half acted as controls. All the controls developed rickets, while none of the rats that had the light treatment showed any signs of rickets. Even under these adverse environmental conditions ultra-violet light prevents the development of rickets.

Other experiments have been carried out rather different from those described above, but with the same object in view. The usual groups of experimental and control rats were kept in standard boxes on the standard rachitic diet, but the actual light treatment was given under adverse conditions. The light from the carbon arc was by means of an aluminium reflector so focused on the rats as to expose them to tropical heat; other rats were chilled by keeping them for thirty minutes in the cold room and radiating them with the mercury vapour lamp actually in the cold room; yet others were radiated in the hot room with the mercury vapour lamp; further groups were radiated while they were kept cool by a powerful air blast or oppressed by moist heat. The results were always the same: the radiated rats, however adverse the conditions of radiation, were all free from rickets.

We consider these results in general highly significant, and feel justified in making the broad generalization that, provided an animal is supplied with food just sufficient to maintain life and a little growth and a bare minimum of the bone-forming elements calcium and phosphorus, then if ultra-violet light be supplied in adequate amount rickets will not develop however unfavourable the animal's environment be.

We carried out some other experiments on rather different lines.

A favourite remedy with animal dealers and keepers is flowers of sulphur; they say that it tones up animals out of condition and generally helps to keep their coats glossy. Its use combined with treacle as a spring tonic for children is traditional. We therefore tried this as an antirachitic substance. The usual group of four rats were given the standard rachitic diet to which was added 25 per cent. of flowers of sulphur (arsenic-free); at the end of twenty-eight days the rats were killed and examined—they showed no signs of rickets. This suggested an important addition to our scanty list of antirachitic agents, so the experiment was repeated. In the second experiment the result was negative; all the rats developed rickets. We have tried sulphur many times, but conclude that it fails to prevent rickets as often as it succeeds. We are convinced, then, that it can in about half the animals prevent rickets, but its action is uncertain.

In view of the partly favourable action of sulphur we thought

it of interest to see if a purgative or an intestinal antiseptic had any antirachitic effects. We used magnesium sulphate as being a typical neutral purge, and thymol as a typical intestinal antiseptic. We also tried arsenic, this substance being a well known tonic and mentioned also in the literature as being beneficial in cases of rickets in children. Magnesium sulphate and thymol proved to be useless as antirachitic agents, all the experimental rats showing severe rickets. The arsenic group of rats all showed rickets, but it seemed to be of a much milder type than that in the controls.

In view of statements made by others we thought it advisable to try the effect of the gases given off by the carbon arc and also of air that had been acted on by the mercury vapour lamp. There was, we found, no protection from rickets, even when the rats breathed the fumes of the irradiated air for a couple of hours a day.

It was suggested to us that the skin was a depot of antirachitic substance, and that ultra-violet light acted on the skin and stimulated it to pour this into the circulation. We therefore tried feeding animals on the antirachitic diet with portions of skin from freshly killed normal rats. The normal rats were killed and then skinned, as much hair as possible was removed, and weighed portions of the skin were administered daily to the experimental rats. The rats consumed the skin avidly. We gave amounts varying from 0.5 to 2 grams of fresh moist skin daily per rat. The results were negative; in fact, the rats that had the 2-gram ration of skin had grosser rickets than the controls.

We carried out an experiment with results that now seem highly significant in view of recent work. A group of rats were taken, and instead of radiating them daily they were given one hour's exposure to the mercury vapour lamp weekly, four exposures being given in all. This sufficed to protect them completely from rickets, and it seemed to us at the time that the light had actually synthesized something in the rat's organism which it was able to store and use subsequently.

In an attempt to gain further insight into the mechanism of the action of antirachitic agents, one of us (A. W.) studied the calcium and phosphorus metabolism of these groups of rats in special metabolism cages. Group (1) was fed on the standard rickets-producing diet only. Group (2) had the same diet with the addition of 0.2 c.cm. of cod-liver oil per rat per day. Group (3) had no cod-liver oil, but the rats were radiated daily for ten minutes two feet from the mercury vapour lamp. The experiments lasted the usual period of four weeks. During this period the weekly intake of calcium and phosphorus was determined, also the calcium and phosphorus excreted in the urine and faeces. The difference between the intake and combined urinary faecal excretion gives the amount retained.

	Calcium.	Phosphorus.
The controls retained	0.37 gram,	0.15 gram
The cod-liver oil group retained ...	0.58 "	0.26 "
The mercury vapour lamp group retained	0.51 "	0.20 "

These figures are the total retentions for each group of rats over the full experimental period of twenty-eight days. It will be observed that both cod-liver oil and ultra-violet light increase markedly the retention of calcium and phosphorus. In no case, however, was there any excretion of phosphorus in the urine. This means that in the rat under these conditions the inorganic phosphorus content of the blood is below the threshold level of the kidney both in the rachitic and non-rachitic animal. Calcification occurs when the inorganic phosphorus in the blood is below the threshold level of the kidney but higher than that of the blood of the rachitic rat as shown by direct blood phosphorus determinations. It will be remembered that the diet used is rickets-producing in virtue of its poverty in phosphorus. Let us now consider the calcium excretion: this being in considerable excess is excreted partly in the urine and partly in the faeces. The proportion of the total calcium excreted found in the urine was as follows:

In the controls	34.2 per cent.
In the cod-liver oil group	73.8 "
In the ultra-violet light group	65.7 "

While in the controls or rachitic rats only one-third of the total calcium excreted finds its way into the urine, two-thirds being excreted in the faeces, in the cod-liver oil and ultra-violet light-treated rats which are free from rickets, the figures are reversed—two-thirds of the calcium is excreted in the urine and one-third in the faeces. These figures strongly support the view that the antirachitic body in cod-liver oil and radiant energy in the form of ultra-violet light both act in the same way in preventing rickets, and that this mode of action is a facilitation of absorption of calcium and phosphorus from the intestine into the blood stream.

It is interesting to note that it is not necessary to have a negative balance—that is, a greater excretion than intake—of calcium or phosphorus before rickets develops. So long as there is enough calcium and phosphorus absorbed to satisfy the minimal demand for ossification, rickets will not develop. When absorption falls below this level rickets develops.

Since these pages were written Steenbock and Black, and also Hess, have published papers claiming that rickets can be prevented in rats by radiating the diet with ultra-violet light. Steenbock and Black radiate the whole diet, and claim that feeding this to the animal prevents the development of rickets. Hess radiates an inactive oil—cottonseed oil—and claims that feeding a little of this with the daily ration prevents rickets.

Independent confirmation of this important work seems necessary, so we have carried out some experiments with that object in view. We adopted the technique we have used throughout this work. Four groups of rats were taken, each rat weighing about 40 grams. Group 1 were fed on Sherman and Pappenheimer's diet 84 previously described. The diet, after being made up into a stiff paste with distilled water, was spread on a clock glass in a thin layer and placed under a mercury vapour lamp twelve inches from the burner and radiated for half an hour. It was then given to the rats daily for twenty-eight days, when the rats were killed and x-rayed. They showed no signs of rickets.

Group 2 were fed on the standard diet, and in addition received 0.5 gram daily of an inactive linseed oil that had been radiated half an hour twelve inches from the mercury vapour lamp. Fresh oil was radiated for each day's ration. The rats were killed after twenty-eight days and x-rayed. They also showed no signs of rickets.

In Group 3 the patent flour portion of the diet only was radiated as described above; after mixing with the other constituents it was given to the rats. At the end of twenty-eight days these rats proved to be free from rickets.

Group 4 were fed on the standard diet, and in addition they received a daily dose of radiated hardened cottonseed oil. This oil, which is really a solid fat, is a commercial product that we have used for other experiments on account of its complete freedom from fat-soluble vitamin A. It is the liquid cottonseed oil of commerce that has been hardened by the technical process of hydrogenation. It was radiated in the following way: the oil was melted into a transparent quartz flask; this flask was attached to a slow-running motor and slowly rotated between two mercury vapour lamps, six inches from each lamp, and radiated for a period of eight hours. It was then given to rats of Group 4 in daily doses of 0.5 gram per rat. On killing the rats at the end of the twenty-eight days they all showed on x-ray examination severe rickets. This was surprising in view of the previous result with linseed oil. Two explanations are possible: (1) the prolonged period of radiation at a temperature of 40° to 50° C. had destroyed any active substance formed earlier; (2) the process of hydrogenation had destroyed in cottonseed oil a precursor or substance which, when aided by ultra-violet light, becomes active.

In Group 5 the calcium lactate, ferric citrate portion of the diet only was radiated for half an hour. The calcium lactate was radiated in the powder form, the ferric citrate and sodium chloride were dissolved in water so as to give a large surface for radiation. The radiated salts were then mixed with the patent flour and given to the rats in the usual way. The salts were radiated fresh daily. The rats were not protected from rickets. These results confirm the work of Steenbock and Black and Hess—that certain rickets-producing foodstuffs can be made antirachitic by radiation with ultra-violet light. Further investigations show that cholesterol, or a vegetable sterol, after radiation has very great antirachitic power.

Two other American investigators, McQuarrie and Kugelmasser, have published a preliminary account of an investigation in which they claim to have got startling results. Briefly, their work consists in making antirachitic substances like cod-liver oil or egg yolk undergo a process of oxidation, and during this process they claim that radiant energy is given off that will darken a sensitive photographic plate through a quartz screen but not through a glass screen. In other words, antirachitic substances undergoing a process of oxidation give off ultra-violet light. We have repeated their experiments but are unable to confirm their results or substantiate their claims. We have made many experiments in many different ways with different antirachitic substances, but have been unable to act on the most sensitive photographic plates either through quartz or glass screens when these were so arranged as completely to protect the photographic film from vapour arising from the substances in question. We found that certain samples of fused quartz, after being irradiated by ultra-violet rays, were able to act on a photographic plate. The quartz was rendered phosphorescent, and we think this may possibly explain why

McQuarrie and Kugelmasser obtained positive results through a quartz screen and not through glass.

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TWO DISEASES DUE TO FASHION IN CLOTHING:

CHLOROSIS AND CHRONIC ERYTHEMA OF THE LEGS.

BY

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I.—CHLOROSIS.

THOSE of us who were house-physicians at hospitals in London about 1890 saw much of chlorosis in girls and young women. Making blood counts in such cases and prescribing Bland's pills and other chalybeate preparations constituted a not inconsiderable part of the daily routine work on the medical side. Where are similar patients to be seen now? Did anyone suspect that the familiar features of chlorosis would ever almost completely vanish from the doctor's surroundings as they have? It is true that formerly in general practice countless troubles in women of all ages were attributed to "anaemia" without any blood count being made, and to doubt the correctness of the diagnosis was often to offend the patient. It is therefore quite natural that some modern physicians of a younger generation, experts in blood examination, especially those practising on the Continent, should question the alleged former frequency of chlorosis, suggesting that it was due to want of knowledge and insufficient or careless examination of the blood. But no one who was a house-physician in London about 1890 can admit the justness of such an accusation. Blood counts were made and the ordinary features of chlorosis were well known. Indeed, one could make the diagnosis with practical certainty when one passed girls and young women in the London streets, or even at the seaside, with the typical appearance of "green-sickness."

One remembers the characteristic pale, puffy face, the shortness of breath on climbing the stairs or other slight exertion, and, in the severer cases, obvious physical signs of cardiac dilatation. There were the out-patients who gave up their treatment at the hospital to take advantage of some charitable person's kind offer of a gratuitous holiday at the seaside. There they often tried to vie with their companions in "healthy" exercise and "enjoyment" of the open air, but with most unfortunate results. Chlorosis was certainly not due merely to insufficient food or want of open-air exercise. They soon returned to London and the hospital out-patient room, but in a condition far worse than when they left. They had lost during their holiday all that they had previously gained from the out-patient chalybeate treatment.

Some patients sought employment as cooks or helps in basement kitchens, so that they could avoid the frequent stair-climbing ordinarily required of domestic servants. In this way they escaped much of the dyspnoea on exertion, the "panting" on the stairs, and the "tea and bun" midday meal of many of the shop-girls of that period. They got plenty of meat, but often took very little green vegetables and fruit so as to save themselves from gastric flatulence—with the result that they increased their tendency to constipation, and often added to their other troubles recurring so-called "bilious attacks" and the kind of headaches largely due to intestinal autointoxication.

Psychasthenic and functional nervous symptoms in the more mentally active and (financially) "better-off" subjects