More direct evidence, however, has taken the place of speculation. Russell⁸ emphasizes the importance of the facts that the symptoms of the various stages of the epileptic fit are closely mimicked by those following heart-block in Stokes-Adams disease; that uraemic convulsions are indistinguishable from those of epilepsy and are almost certainly due to cerebral oedema, consequent increase of intracranial tension being followed by temporary failure of the cerebral circulation; that in some recorded cases of value temporary cessation of the heart's action (disappearance of radial pulse) has immediately preceded the development of a fit. A number of direct observations of the human cortex during an epileptic convulsion have been made by surgeons (Horsley,¹⁰ Kennedy and Hartwell,¹¹ Leriche,¹² Horrax¹³). Sudden blanching of the cortex and pial vessels, and arrest of cerebral pulsation, is at once succeeded by pronounced hyperaemia and venous engorgement during the convulsive movements, according to the mean of the recorded observations. Reference might also be made to the apparent association of fits with disorder of the cerebral circulation in certain cases of Raynaud's disease, of which a number have now been reported (see a paper by H. J. Norman¹⁴).

While it would be unwise to ignore the cumulative effect of these differing lines of evidence, I do not think, after having given much consideration to the problem, that they can fairly be taken as showing anything more than that changes in the cerebral circulation accompany, in all probability, the march of events in an epileptic discharge. In my opinion Russell is justified in concluding that, even if vascular disorder is causal, it only carries the pathology of epilepsy one stage further. But I am not convinced that the association constitutes a causal relationship. The cerebral and general circulation is under the control of a vasomotor centre in the medulla oblongata; alterations in the whole cerebral vasomotor apparatus may be caused by dysfunction of that centre. Sudden loss of consciousness may not be of vascular origin, though accompanied by vascular change; the same pathological stimulus may act both on the bulbar vasomotor centre and on cortical neural elements themselves. That this would appear to be the case in respect of the unconsciousness following trauma is strongly suggested by the recent experiments of Knauer and Enderlen¹⁵; and although the analogy with epilepsy is remote, it is well not to lose sight of the possibility of the circulatory phenomena of the fit—as observed when the cortex is exposed—being no more than a sequel to a central neural disturbance of function at the level of the medulla.

If, however, we are sufficiently convinced by the evidence sketched in outline above, we should still be at the stage of pure speculation in regard to the question of how transient cerebral anaemia—in some cases only, not in all—causes neural mechanisms to discharge; we should have to imagine a local cerebral anaemia for the phenomena of Jacksonian epilepsy; and I submit that many cases of local and sudden cerebral anaemia, as in monoplegias of embolic or thrombotic origin, are unaccompanied by any discharging phenomena whatever. Nor is the solution of the problem facilitated by ascribing the motor discharges to anoxaemia. Imperfect oxygenation recurring periodically, locally, and seemingly vanishing after an attack—how is such a process to be imagined? And how will any such theory account for the aura of a fit, which, as has been stressed above, unquestionably appears to partake of the nature of a normal, orderly, regularized, non-excessive function of a given sensory mechanism? Is neural activity accompanied by anaemia in the cerebrum of the normal individual?

The truth is that the gulf between the vascular and the neural is almost as impassable as that between the physical and the psychical. In this lecture, intentionally, no allusion has been made to clinical varieties of epilepsy of an unusual kind; if, however, the phenomena of so-called "epilepsia partialis continua" are considered, they may justifiably be used as an argument for the improbability of "discharging lesions" being based on persistence of an abnormal vascular state; they appear to resemble much more these of continuous excitation of a reflex neural arc by a persisting neural stimulus.

It seems to me reasonable to suppose that the crescendo character of the symptoms of the epileptic fit is due to

direct action of a neural system on collateral and lower neural systems; if a vascular factor is involved, I have tried to show the possibility of it itself being of neural origin. In some instances this may have a bulbar locus; in others there is as clearly a transcortical commencement for the attack. We come back, therefore, to the view indicated at the outset: any constellation of nerve cells in the neuraxis may become unstable; hence physiological varieties of "fit" are to be expected. It is evidently more correct, clinically and physiologically, to speak of "the epilepsies" than of "epilepsy," and this fact by itself should lead us to avoid giving our patients the impression that once a diagnosis of epilepsy is made it is tantamount to pronouncing their doom. On the contrary, increasing latitude in our conception of the condition should lead to modification of therapeutic pessimism.

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DIETETIC CONDITIONS WHICH INFLUENCE THE CALCIUM CONTENT OF SALIVA:

THE POSSIBLE SIGNIFICANCE OF THESE FACTS IN TUBERCULOSIS.

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Introduction.

THE study of the etiology of dental caries and other defects of the teeth has usually centred around the chemical, physical, and bacteriological condition of the mouth, and, among other factors, saliva has been considered of importance in this connexion. However, in spite of the large amount of work by Miller, Röse, Pickerill, Marshall, Howe, Bunting, and many others, no relationship has ever been proved between the alkalinity of the saliva and the immunity to caries, as those upholding the acid-decalcification theory of caries might have hoped to establish.

Less work has been done on the calcium content of saliva, yet it is likely to be important. Among other possibilities it may hinder the removal of calcium from the teeth on the production of acid, or it may help in the hardening of the enamel after eruption, if this takes place, or it may aid in the arrest of caries.

The experimental work of May Mellanby¹ has proved that the structure of dogs' teeth, and probably also of human teeth, can be controlled by diet and environment. Foods rich in fat-soluble vitamin (for example, cod-liver oil, egg-yolk, milk, and most animal fats) tend to help the formation of well calcified, regularly arranged teeth, while other foods (for example, cereals, and especially oatmeal) tend to cause the development of badly formed teeth. Thus the total effect of a mixed diet is the outcome of a battle between these different dietetic influences.

On the basis of these facts Mrs. Mellanby and I started, three years ago, a clinical investigation to determine whether there is any relation between diet of the above-mentioned type and dental caries. Some evidence was obtained that a diet rich in fat-soluble vitamin not overburdened with cereal tends to prevent the onset and spread of dental caries more rapidly than does one containing little fat-soluble vitamin and more oatmeal and other cereal. These findings were published in a preliminary note (together with J. W. Proud, L.D.S.) in the *BRITISH MEDICAL JOURNAL* of August 30th, 1924.²

The investigation now to be described was carried out with the idea of seeing (1) whether there is any relation between the amount of calcium in the saliva and the rate of development and amount of dental caries, and (2) whether it is possible readily to alter the calcium in the saliva, especially by varying the diet in factors other than the calcium. As the work progressed, it was realized that many of the figures for calcium in the saliva were low compared with those obtained by other workers, and the possibility of this being due partly to tuberculosis was therefore considered.

In regard to the first point. The work carried out by Rose³ seems to indicate that, if anything, there is less calcium in the saliva of those people with fewer carious teeth; but that, if the amount of calcium in the ingested food is raised, then the calcium in the saliva may be in some cases also raised. Recently P. P. Laidlaw and Spencer Payne have worked out an accurate method for estimating small amounts of calcium,⁴ and have also studied the calcium content of the saliva of people whose mouths vary from the point of view of carious teeth. No constant relationship, however, was found between the amount of caries and the calcium in the saliva. As will be shown later, the amount of calcium in the saliva may vary from week to week with small alterations in the diet, and probably also with other unknown conditions, depending on the metabolic state from the natal or even pre-natal period up to the day of observation. It would not be expected, therefore, to find a close relationship between the calcium of saliva, as observed on one or two occasions, and the amount of dental caries at that time. On the other hand, Mrs. Mellanby and I showed (in the paper referred to above⁵) that by raising the amount of fat-soluble vitamin in the diet we were able to delay the spread of caries. I shall now show that by increasing the fat-soluble vitamin in the diet the salivary calcium is raised. There would, therefore, seem to be some connexion between the quantity of calcium in saliva and caries, but to prove this definitely a more prolonged investigation would have to be made.

The second part of this inquiry—namely, the effect of diet on the salivary calcium—has given very definite results which will now be described.

Method of Estimating the Calcium.

The saliva was obtained by asking patients to spit into glass tubes three minutes after their mouths had been washed out with water. Various ways of estimating the calcium were employed, and the results recorded were obtained by two methods: (1) the alizarin method described by Laidlaw and Payne (L. and P.);⁴ (2) the Kramer-Tisdall method (K.T.).⁵ In practically all cases in which estimations were made by both methods the results agreed.

The Effect of Small Specific Differences in the Diet on the Amount of Calcium in the Saliva.

The amount of calcium in the salivas of patients having different diets was estimated. The diets were those described in the paper already referred to in the BRITISH MEDICAL JOURNAL of August, 1924.² The principal differences between the diets may be summarized as follows:

Diet A contains most milk (1½ to 2 pints), cod-liver oil 6 drachms, and an egg daily, but no oatmeal.

Diet B contains least milk (¾ pint), no cod-liver oil and no egg, but 3 oz. of oatmeal, and olive oil (6 drachms).

It will be seen that diet A contains most calcifying vitamin and diet B the least, and that diet B is also peculiar in containing a large amount of oatmeal.

1. *Diet A.*—Twenty children were given diet A (more vitamin) and their salivas contained an average of 10.68 mg. of calcium in 100 c.cm.

2. *Diet B.*—Nineteen children were given diet B (less vitamin and more cereal) and their salivas contained an average of 4.68 mg. of calcium in 100 c.cm.

The following table gives examples of children fed on diets A and B.

Twelve patients on the ordinary hospital diet, which is intermediate, as regards the amount of calcifying vitamin, between diets A and B, contained an average of 7.79 mg. of calcium in 100 c.cm. of saliva.

DIET A.				DIET B.			
Patient.	Calcium.	Method.	Weeks on Diet.	Patient.	Calcium.	Method.	Weeks on Diet.
B. R.	Mg. 9.50	L. & P. K.T.	8	G. C.	Mg. 6.00	L. & P. K.T.	104
	9.78				5.40		
S. H.	9.80	L. & P. K.T.	16	C. W.	4.50	L. & P. K.T.	12
	8.69				3.18		
V. P.	11.07	L. & P. K.T.	16	L. E.	5.70	L. & P. K.T.	8
	11.63				5.84		
S. R.	12.60	L. & P. K.T.	52	I. R.	2.46	L. & P. K.T.	23
	12.49				2.82		

Alterations in the Calcium Content of Saliva as the Result of Changes in the Diet Alone.

1. Some patients on admission to hospital were found to have an average of 3.07 mg. of calcium in 100 c.cm. of saliva. Their diets were unknown. They were now given diet A, with the result that the average amount of calcium was increased from 3.07 to 7.07 mg. in 100 c.cm. of saliva—for example, in the case of B. R. the amount of calcium was increased from 4.1 to 9.5 mg. in eight weeks.

2. Some patients who had been having diet B for ten weeks had an average of 4.47 mg. of calcium in their saliva. Later they were given diet A, and then the calcium was increased from 4.47 to an average of 12.07 mg.

3. Other patients on diet B, with an average of 5.15 mg. of calcium in the saliva, were given the ordinary hospital diet, and their calcium was increased, but only to an average amount of 8.95 mg.

4. Some patients on diet A, with an average of 12.02 mg. of calcium in the saliva, were later given diet B, when the amount of calcium was only slightly diminished—namely, from 12.02 to 11.67 mg. These patients were kept on diet B for four weeks only, as when this part of the investigation was attained the conclusion was reached that the general health of the patients on diet B was not so good as that of those on diet A. It is known that vitamin A can be stored in the body, and, presuming that this substance is of some importance in varying the percentage of calcium present in the saliva, it is possible that the quantity stored in the lengthy period during which diet A had been given was not sufficiently depleted to cause an alteration in the amount of calcium in the saliva in the four weeks on diet B.

Other Factors in Addition to Diet which might have Influenced the Results given above.

The average amount of calcium in the saliva of the children on admission to hospital was only 4.77 mg. in 100 c.cm. This is low compared with the figures obtained by other workers, which vary between 6 and 12 mg. per 100 c.cm. Therefore, various factors were considered which might be the cause of this low calcium content.

1. *Tuberculosis.*—The children all suffered with tuberculosis of bones or joints, in which varying degrees of decalcification had occurred. It was found that in most cases those children who had suffered from the disease longest had the smallest amount of calcium in their saliva on admission to hospital. The following are examples:

R. I. had had disease of the vertebrae for ten years; it had produced marked bony destruction, and was active on admission; his saliva contained only 0.90 mg. of calcium in 100 c.cm.

H. L. had had tuberculosis of the sternum and tarsus for three years, with sinus formation; his saliva contained only 1.60 mg. of calcium in 100 c.cm.

H. A. had had active disease of the hip-joint with abscess formation, but no bony destruction, for three months. His saliva contained 6.88 mg. of calcium in 100 c.cm.

However, there is no reason to believe that this factor was of primary importance in altering the relative amount of calcium in the salivas of the children in the diet groups; since this disease was common to all, and those children with the least active tuberculosis were usually put on diet B, and those who were suffering most severely from this infection were put on diet A.

2. *Water*.—All the patients were drinking Sheffield water, which has a low calcium content. To test this point the amount of calcium of a few Sheffield persons was obtained and compared with the amount found in a few London residents. The average quantity of calcium in the salivas of the ten Sheffield persons was: adults 8.07 and children 7.19 mg. in 100 c.cm. of saliva. The average quantity of calcium in the saliva of the ten London cases was: adults 10.61 and children 9.34 mg. in 100 c.cm. of saliva. Röse³ carried out investigations with the idea of relating the extent of caries to the calcium content of the drinking water in different districts. He found that, on the whole, the children living in districts where the water was hard suffered less from caries than those living where the water was soft. The amount of calcium in the saliva of these subjects, however, was often less when the water was hard than when it was soft. Röse states that the full influence of a calcium-rich diet is only seen after several generations. It was found in the present investigation that the addition of calcium phosphate, calcium lactate, and calcium carbonate over a short period to the dietary of patients had no effect on the calcium content of the saliva.

3. *Age of the Patients*.—No definite relation was noticed between the age of the patient and the amount of calcium in the saliva.

4. *Hour of Collection*.—The amount of calcium in the saliva varied slightly at different times of the day in individual persons, but this variation was not constant.

5. *Rapidity of the Secretion of the Saliva*.—It was not found that the percentage amount of calcium varied appreciably with the rapidity of secretion.

6. *Hydrogen-ion Concentration*.—This varied between a pH of 6.5 and 7.5, and bore no relation to the amount of salivary calcium, nor to the degree of dental caries.

SUMMARY.

1. The amount of calcium in the saliva is influenced by diet. (a) A high calcium content of the saliva can be produced by a diet having a large fat-soluble vitamin content. (b) A low calcium content can be produced by a diet containing much cereal (especially oatmeal) and comparatively little fat-soluble vitamin, although the amount of calcium ingested in this diet may be the same as, or even greater than, in (a).

2. The calcium of the saliva is not increased by increasing the calcium of the diet over a short period.

3. Tuberculous children appear to have a lower calcium content of the saliva than normal children, and, on the whole, low resistance to the infection is accompanied by low calcium content. This relationship between resistance to infection and salivary calcium requires further investigation before it can be regarded as established.

4. It will be seen that the calcium content of the saliva is controlled by the same factors of special nutrition as those on which the calcification of teeth and bones also depend. If, therefore, caries of the teeth be influenced by the chemical composition of the saliva, then it is evident that the problem of dental caries is at least partially one of general metabolism. This point of view is corroborated by other results showing the relation of diet and caries, published elsewhere.

The expenses of this research were borne by the Medical Research Council and the Dental Board of the United Kingdom, to both of whom I wish to acknowledge my indebtedness.

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PLEURAL EFFUSION COMPLICATING PNEUMOTHORAX.

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PLEURAL EFFUSION is the most common complication of pneumothorax. If every patient with pneumothorax were examined daily with the x-ray screen there would be seen at some time or other in practically every case a small pool of fluid lying in the costo-diaphragmatic angle. Such small collections of fluid, however, are quickly absorbed; they come and go, and are of no importance. In speaking of pleural effusion I mean cases where the fluid at least covers the diaphragm and lasts more than a week, and I do not include those small transient effusions discovered accidentally by x rays.

Out of 309 consecutive cases in which I have successfully induced artificial pneumothorax for pulmonary tuberculosis an effusion formed in 128 (41.4 per cent.), and of these 47 (36.7 per cent.) are dead. Of the 181 cases in which no fluid formed, 57 (31.5 per cent.) are dead. Of the 128 cases the fluid remained clear in 92, and 27 (29.4 per cent.) of these are dead. In the other 36 cases the fluid was tuberculous pus, and 20 (55.6 per cent.) of them are dead. In time, no doubt, more of these cases will die of tuberculosis, but this applies equally to cases with and without fluid, so that the figures can be taken to show that, roughly speaking, cases which have clear pleural effusion do neither better nor worse than dry cases, but that if a tuberculous empyema forms the outlook is much more serious.

It should be clearly understood that these 309 cases do not include non-tuberculous cases, nor those where artificial pneumothorax was attempted but failed or was only partially successful. I have divided them into three groups: C1, where the disease was unilateral; C2, where there was some disease in the other lung but only slight; C3, where more than one-third of the better lung was affected. The last group consists largely of cases where artificial pneumothorax was induced as a last resort, and so the mortality is very high. Had the patients in this group lived longer many more would undoubtedly have developed effusion.

The following table shows the number of cases in the various groups which developed fluid.

	C1.		C2.		C3.	
	Cases.	No. Dead.	Cases.	No. Dead.	Cases.	No. Dead.
Total ...	126	24 (19%)	125	47 (34.8%)	48	33 (68.7%)
No effusion ...	78	13 (16.6%)	72	22 (30.6%)	31	22 (71%)
Clear fluid ...	35	5 (13.9%)	45	14 (31.2%)	11	8 (72.7%)
Pus ...	12	6 (50%)	18	11 (61.8%)	6	3 (50%)

In my series, effusion in the great majority of cases developed in the first six months and rarely occurred after the first year. The number of months after the induction of artificial pneumothorax when the effusion formed was:

1 to 3 months ...	45 cases
4 to 6 " ...	43 "
7 to 12 " ...	29 "
13 to 18 " ...	5 "
Over 18 months ...	6 "

Various explanations have been given to account for the frequency of pleural effusion in cases of pneumothorax. Irritation of the gas, its temperature, the repeated punctures of the parietal pleura, or the intrapleural pressure have all been described as playing a part in the production of fluid. In my opinion, however, these effusions are true tuberculous exudates, and in my experience they occur with equal frequency whether the gas is heated or not and whether air, nitrogen, carbon dioxide, or oxygen is used. We know that pleurisy is a common complication of pulmonary tuberculosis, and that it often leads to