A skiagram of his spinal column showed clear evidences of osteoarthritis. There was considerable outgrowth of new subperiosteal bone, and to some extent it was laid down around the neural openings. It is reasonable to suppose that pressure upon the nerves at their points of exit, with resulting oedema, played a considerable part in the collective group of symptoms.

The sacro-iliac joints as a source of iliac pain I have already referred to, and I need not repeat how important is the recognition of this association.

I might allude to other sources from which iliac pain may arise—the peritoneal and fascial stretching associated with an incipient inguinal hernia, for example—but I feel I have already drawn a complicated picture, and I do not wish to add to its complexity. It has been my desire to remind you of the importance of analysing in a more or less logical way any case of chronic iliac pain with which we may meet, and I have attempted to remind you of the physiological and anatomical considerations upon which such an analysis must be based.

NOTE ON THE ETIOLOGY OF PELLAGRA.

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SOME extremely interesting statistics of pellagra as it occurs in South Africa have recently appeared in a paper by Dr. E. H. Cluver.¹ Dr. Cluver describes an "outbreak" of pellagra in the Durban prison command, which comprises three groups of prisoners in separate institutions—the Central Gaol, the Point Prison, and the Congella Prison. In the first, for European and short term prisoners, 1.9 per cent. were affected; in the second and third, for long term hard-labour prisoners, 3.8 and 8.2 per cent. respectively.

It is of interest to consider whether the valuable tables of the rations supplied to the prisoners provide any evidence in support of either the vitamin deficiency or protein deficiency theories of the etiology of the disease. Four different ration scales are described—C and D, for short term (under three months) and long term coloured prisoners not natives of South Africa; E and F, for short and long term natives respectively. Prisoners receiving D and F do hard labour.

In a paper published in 1921² I drew attention to the fact that if the available protein (gross protein less loss in intestine) be reduced to the value of meat protein by the application of K. Thomas's figures for the "biological value" of protein from different sources, diets in which the value so obtained fell below 40 grams daily for non-labour communities and 45 grams for labour communities were likely to lead to pellagra in the consumers. There seem to be good reasons for doubting the validity of the method of determining the biological value employed by Thomas; nevertheless, the relationship of the value of protein in a diet so deduced to pellagra incidence is quite definite and cannot be accidental.

In Table I given below the protein content of Cluver's four diets has been investigated in this manner, the value of the mixed proteins expressed in grams of animal protein being shown in the line indicated by the letters B.V.

TABLE I.—The Protein Value of the Durban Prison Rations.

Ration Scale.	C.	D.	E.	F.
Gross calories	2,700	2,860	2,500	3,750
Gross protein	80	76	60	119
Protein from maize*	21	40	52	61
Protein from meat*	5	9.8	0	9.8
B.V. of protein	29.5	28.5	14	38
Cases of pellagra among recipients	2	7	10	44

* Gross amount; B.V. estimated from gross protein less 33 per cent.

The loss of protein in the intestine from a diet containing such indigestible materials as whole maize and beans is considerable. H. E. Roaf and I³ determined the average loss from the intestine on a somewhat similar diet supplied to the Turkish prisoners of war in Egypt in 1918. The observation was carried out on a squad of five men over a period of days. It was found that 33 per cent. of the protein intake failed to be absorbed. In estimating the available protein from the gross protein in the four diets one-third has therefore been deducted for non-absorption. The "biological value" is estimated from that figure.

It is evident that the value of the protein in all these four diets falls below the minimum safe value of 40. They are all, in fact, diets which would have been expected to result in pellagra among the recipients.

It seems scarcely justifiable to feed any type of prisoner for as long as three months on a diet so bad as E, issued to short term native prisoners. It consists entirely of maize with 450 grams daily of mixed vegetables. The general health of the recipients of this diet is not mentioned; the considerable daily amount of vegetables no doubt saved them from much. Although this diet is exactly adapted to produce pellagra, it is, even so, surprising that no fewer than 10 cases developed within less than three months from the time they commenced its consumption. The diet has a protein value almost identical with that used by Goldberger and Wheeler⁴ in the Rankin farm experiment; the calorie value is considerably less. In that experiment six out of eleven convicts forming the experimental squad developed the disease; it was not, however, until seven months after the beginning of the experiment that definite symptoms suggestive of pellagra were seen. The fact that two persons were admitted to the prison already suffering from the disease suggests that pellagra is less rare in South Africa than is supposed. It is also possible that individuals of the poorer class of natives, already sufficiently ill nourished, suddenly placed on such an exceptionally deficient diet as E, developed pellagra sooner than would otherwise have been the case. The still more perplexing fact that the disease had not been observed before in any of the three institutions, although the diets had been in force for some years, will be referred to later.

Unfortunately Dr. Cluver does not supply any information as to the percentage of pellagra cases among those receiving the four different ration scales. It may probably be assumed that the coloured foreign long term prisoners on ration scale D were very much fewer in numbers than the native long term prisoners on scale F. The conditions of labour appear to have been the same in the two cases; the incidence of pellagra among the coloured foreign prisoners, owing to the lower value of the diet (whichever of the two views of the etiology of the disease is adopted), should have been greater than among the native convicts.

That labour has an important influence in increasing the liability to pellagra is an undoubted fact to which I have drawn attention (loc. cit., p. 32), the apparent reason being that labour raises the need of the protein requirement (loc. cit., p. 54). The relatively large number of cases on diet F must be ascribed to the influence of labour on a community receiving a diet which, judged of by its protein value, would have been pellagrous even without that influence. It may be noted that of the 44 cases on diet F, 8 were originally on diet E, and were therefore probably non-labour.

From what has been said it is evident from the analysis of the four diets in regard to their protein value that the protein deficiency theory of pellagra provides a reasonable explanation of the result. Dr. Cluver very naturally accepts without comment Goldberger's view that the primary cause of pellagra is a deficiency in the P-P (B2) accessory factor in the diet. It is the purpose of this note to show that this theory is by no means conclusively proved, and that diets responsible for the Durban prison outbreak in fact supply strong evidence that the defect was not in the vitamin content but rather in the value of the protein.

In a paper⁵ read at the International Congress of Tropical Medicine in Cairo, which will be published shortly, I have endeavoured to analyse the data brought

forward by Goldberger and others upon which the theory is based. It would obviously be impossible to discuss the question in a short note such as this except in a very incomplete manner. The view is based mainly on the results of ten experimental diets supplied to groups of female patients, inmates of the Georgia State Sanitarium. In all except two of these diets the high or low value of the protein appears to provide a sufficient explanation of the curative or non-curative effect. The two exceptions are diets by which cure and protection were effected in one case by the addition of 50 grams of yeast⁶ extract (or dried yeast), in the other by the addition of 1,200 grams of tomato juice⁷—the basic diet being of very low nutritive value.

Apart from the fact that the supplements in the quantity given contain, in addition to the vitamin content, a large amount of other material, there are circumstances about these two diets which suggest the need of further investigation. That the curative effects of such diets is due to the B2 factor is deduced from experiments on rats and dogs, on the assumption that the peculiar dermatitis of rats and experimental "black tongue" in dogs are the analogues of pellagra in man.

The original experiments of Goldberger and his co-workers (ref. ⁶) have been repeated by Chick and Roscoe,⁸ Findlay,⁹ and others, and there is no doubt that a characteristic dermatitis is produced in rats by deprivation of vitamin B2. It cannot, of course, be expected that in animals so different from man as the rat and the dog the symptoms of a deficiency disease would be identical. There are, however, characteristic differences in the condition seen in rats which suggest some doubt as to the identity with pellagra, and circumstances in regard to the condition in dogs which, in my opinion, make the identity with the human disease very improbable. In the pellagra-like condition in rats, except in Findlay's experiments, alimentary tract symptoms appear not to have been seen. The dermatitis in rats is not related to exposure to light, while in man this is with rare exceptions the only direct exciting cause of the cutaneous symptoms. In man pellagra does not affect the urinary tract; in the rats haematuria seems to be a constant symptom.

The condition now known as "experimental black tongue," owing to its supposed identity with Stuttgart disease, known as "black tongue" in the United States, was first observed by Chittenden and Underhill¹⁰ in 1917 to result from improper feeding in dogs. The disease is characterized by the appearance of a pustular eruption on the mucous membrane of the cheeks, gums, and lips, gangrene of the tongue, with subsequent sloughing and acute gastro-enteritis. The cutaneous symptoms appear to be in the nature of localized inflammations resulting in subcutaneous abscesses. Goldberger and Wheeler¹¹ consider that the condition is due to feeding on materials deficient in vitamin B2; they find, however, that, although it is curable even in an advanced stage by raw lean beef, it is not curable, except in the early stage, by the administration of yeast or yeast extract. Underhill and Mendel,¹² on the other hand, conclude from their experiments that the condition is due to the absence of carotin from the food, and can be cured by the daily administration of 5 mg. of that substance, while it is not cured by the administration of either lean beef or yeast.

Black tongue resembles in some of its symptoms the descriptions of acute or typhoid pellagra, but it has no resemblance to the form of pellagra seen in Egypt. It seems, therefore, that while it is possible, in spite of certain characteristic differences, that the deficiency disease of rats corresponds to pellagra in man and is produced by the same cause, it is unlikely that this is so in the condition of experimental black tongue in dogs.

It is of interest to consider, apart from the experimental evidence referred to above upon which the vitamin deficiency theory of pellagra is based, what evidence there is that such deficiency is not the usual or only cause.

In the paper mentioned above (ref. ³) I have endeavoured, by grouping the components of various pellagrous and other diets in a manner originally suggested by Hindhede according to their assumed vitamin content, to find out whether in such diets there is any correlation

between the amount of foodstuffs rich or poor in vitamins and the results in the communities receiving the diets. The only correlation is with the content in animal proteins, pellagra incidence being greater the less animal protein there is in the food. This is a well-known fact, and has frequently been quoted as evidence of the benefit of high value protein in the cure and prevention of the disease. Diets, of course, occur which are non-pellagrous but contain no animal protein.

It has been pointed out that the dietaries tabulated by Dr. Cluver might be expected to be pellagrous from the value of the protein content. It is proposed to compare these diets with some others and consider whether there is any evidence of a vitamin B2 deficiency which might equally or in part have been responsible for the result.

Aykroyd and Roscoe¹³ have recently published a valuable paper on the distribution of vitamin B2 in foodstuffs, from which it is possible to state roughly the relative value of different materials in this factor. They examined seventeen foodstuffs, both in regard to the growth-promoting property and the curative effect on the pellagra-like dermatitis of rats. They find that the two properties run parallel, indicating that the cessation of growth and the appearance of the specific dermatitis are the result of a deficiency of the same factor. The authors deal with the cereal and pulse products in a slightly different manner; by comparing, however, their Tables II and IV, and using the explanatory figures given in para. 3 (p. 490) of their paper, it is possible to determine the number of grams of different food materials which would contain an approximately equal amount of vitamin B2. I have ventured to estimate this for certain foodstuffs so as to show what number of grams of each would correspond in vitamin content to 1 gram of meat in its natural state. The following is the result of the estimate: meat 1; beans (dried) 1.2; whole maize (African) 1.5; milk (natural) 2; maize meal or wheat flour 2.8. Beans are assumed to be of the same value as dried peas; the amount of maize meal needed in the food to produce normal growth is stated by Aykroyd and Roscoe to be more than 65 per cent.; it is assumed for the purpose of this estimate that an amount equivalent to 100 per cent. would suffice.

It is necessary to state briefly the manner in which these figures have been arrived at from the authors' results. In their Table IV it is stated that the minimum amount of meat in its natural state required to produce normal growth in the rat is about 2.5 grams, of fresh milk 5 grams. In Table II it is stated that to produce a comparable result with vegetable foodstuffs there must be added to the basic diet (free of B2) 45 per cent. of dried peas, 50 per cent. of whole maize, and more than 65 per cent. of maize endosperm (100 of maize meal has, as above stated, been taken as sufficient). They state that 1 gram of dry food represents 14 per cent. of the daily ration. It will thus be seen that by dividing these percentages by 14 the daily required amount in grams will be obtained. For example, in the case of whole maize $50 \div 14 = 3.57$ grams. Dividing the figures so obtained by 2.5 (grams of meat needed daily) the amounts given above corresponding to 1 gram of meat are found.

It seems justifiable to assume that, applying the figures for the different food materials as factors, the comparative value of different diets in regard to their vitamin B2 content can be roughly estimated. This has been done in the subjoined Table II, the protein value being given also for comparison. Apart from rice and fresh vegetables the only components given are those which may be a source of the B2 factor. It will be remembered that Goldberger and his co-workers (ref. ⁶) describe an experimental diet with a supplement of 200 grams of lean beef which was curative and preventive of pellagra. There is no doubt that these observers considered that this amount, or rather less, contained all the required pellagra-preventing factor. This diet is therefore given in the first column of the table with two other diets following it which were known to be curative or non-pellagrous, and three more under the influence of which the recipients suffered from the disease. The figures given in this table need very little comment. It is obvious that, assessed on the basis of Aykroyd and Roscoe's results, the vitamin B2 content of

the food has no relation to the incidence of pellagra. The content in this factor is as high in the pellagrous diet as in the non-pellagrous. On the other hand, the pellagrous diets all have a protein value considerably below the minimum safe value of 40, while the non-pellagrous have a value considerably above this figure. All the diets have been analysed as described and are given as examples; fourteen other diets known to have been either curative or the reverse have been examined in a similar manner with the same result.

TABLE II.

	Curative or Non-pellagrous.						Pellagra Producing.					
	1		2		3		4		5		6	
	A	B	A	B	A	B	A	B	A	B	A	B
Meat ...	200	200	105	105					62	62	62	62
Milk ...			200	100			700	350				
Whole maize ...					50	33			285	181	285	181
Maize meal ...	140								230	82	230	82
Grits ...	48	90										
Wheat flour ...	70				125	43						
Wheat bread ...			600	130								
Pulse (dry) ...	14	12	50	41	170	141			40	35	200	166
Rice ...	28		75		470							
Vegetables ...	130*	?	150	?	170	?	113*	?	160	?	200	?
B.V. ...	48		51		50		23		29		38	
B2 value ...		302		376		217		350		350		491

1. Goldberger's preventive diet with meat supplement.
2. Kasr-el-Aini (Cairo Hospital) ordinary diet. Curative with rest.
3. Mean of six Indian gaol diets (McKay).
4. Pellagrous diet. Non-curative (Goldberger).
5. Durban prison diet D.
6. Ditto, F (Cluver).
- A. Daily weight in grams of certain components.
- B. Vitamin B2 value of the same as compared to value of meat.
- * Tomato juice. Other vegetables mixed.
- B.V. Net protein value in terms of animal protein.

The paper referred to above (ref. 5, now in the press) was written before the appearance of Aykroyd and Roscoe's observations. These observations appear entirely to support the conclusion which I arrived at from the consideration of other available data; the conclusion being: that in diets composed of natural foodstuffs the usual origin of pellagra is related to a deficiency in the protein value and not to a deficiency in the vitamin content.

There are, however, certain diets on which the pellagra incidence was very high and which are not only very deficient in protein value but also deficient in vitamin value. The following are examples:

	B.V.	B2 Value.	Pellagra Incidence.
Armenian refugee epidemic ...	23	192	Per cent. 23
Rankin farm experiment ...	15	144	55
Basic diet in Goldberger's experimental diet	10	102	40

The components (excluding sugar and fats) in the basic diet to which various supplements were added in Goldberger's experiments are shown in Table II, col. 1.

It is of interest to consider briefly whether there is any evidence that the effect of a protein deficiency may be accentuated by a coincident deficiency in the B2 factor.

During the past few years papers have been published by Reader and Drummond¹⁴ and by Miss Hartwell¹⁵ showing that, at any rate in the growing animal, vitamin B2 is essential to the effective metabolism of protein in the body. The last author has demonstrated, in addition, that the amount of this factor required varies with the nature of the protein, being least in the case of proteins of animal origin. It is therefore possible to believe that in the absence of a sufficiency of B2 in the food a secondary

protein deficiency would manifest itself, while with a sufficiency of the vitamin factor relative to the type of protein the value of the latter might be high enough. The deduction, therefore, which may be suggested from the relation of vitamin B2 to protein metabolism in its bearing on the etiology of pellagra is the following: "that among individuals living on the borderline of vitamin sufficiency the value of the protein intake would determine the pellagrous or non-pellagrous effect of the diet."

There may therefore be two alternative causes of the disease—a deficiency in the vitamin factor, or a deficiency in the value of the protein. From what has been said above, however, it seems unlikely that under ordinary conditions the content in the first factor is ever insufficient. It is possible to imagine unusual diets in which the assimilation or metabolism of proteins is interfered with by the absence of the B2 factor. This may, indeed, be the origin of the pellagra-like condition described in rats.

In conclusion, attention may be drawn to a rather paradoxical circumstance in connexion with the Durban prison outbreak, which required more explanation than Dr. Cluver gives. The ration scales are stated to have been unchanged for seventeen years, and it is suggested that pellagra was unknown in these prisons before November, 1927. The fact that at about the same date the public health authorities issued a circular drawing the attention of medical officers to the question of pellagra suggests that possibly undiagnosed cases may have occurred previously; just as the fact that two individuals were admitted to the prison already suffering from the disease suggests that pellagra is commoner among the poorer classes in South Africa than is supposed.

Nightingale, in 1913, described a somewhat similar outbreak which occurred in the Victoria Prison in Rhodesia; in that case the outbreak was traced to a coincident change in the rations, finely milled maize flour having replaced coarsely hand-ground millet. It certainly would be a very surprising fact, considering the value of the diets, if pellagra were unknown in the Durban prisons previous to 1927.

Apart from this case, there are many anomalous facts familiar to those acquainted with the epidemiology of pellagra: the geographical distribution of the disease, its absence or rarity in some countries and presence in others where the food conditions are not very different and the economic state of the poor must be the same; the occurrence of asylum cases in England and other European countries, in institutions in which the diets seem to be above reproach; the familial cases in children, such as those described by Box¹⁶ and Hutchison.¹⁷ These are among the facts for which a fully satisfactory explanation does not yet seem to have been found.

I believe that the essential cause of pellagra is a primary or secondary deficiency in the value of the protein intake relative to the individual requirement—a requirement which may be raised by various conditions. Observers, however, with large clinical experience of the disease are not all convinced that there is no other extrinsic factor, and the possibility ought perhaps not to be lost sight of that the food deficiency may be the necessary precursor or concomitant of such a factor.

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