information not being sufficiently explicit to allow of a satisfactory deduction. Some of the results reported, doubtless, were induced by inoculation with the products of septic decomposition and not with the specific virus of the disease.

I have neither seen nor heard of any case parallel to the following; which came under my observation after it had been inspected by several. The particulars of the case I noted down at time of my visit, from the dictation of the patient and the corroborative testimony of Mr. Rayner, his surgeon.

On December 3rd last, while the patient, Mr. H. M. Hancock of Uxbridge, veterinary inspector, was superintending the autopsy of a bullock which had recently died of cattle-plague, which was being performed by his assistant. Mr. Hancock accidentally received on the back of his hand a puncture from the point of the knife, while the operator was occupied in removing the skin in the vicinity of the scrotum. The injury, being slight, was disregarded, but washed as soon as practicable, and thought of no more. On Dec. 8th, five days afterwards, a small, slightly elevated, hard pimple, was seen and felt on the site of the puncture. This gradually advanced till the ninth day from the puncture—the fourth day from papulation; when the enlarged papule became distinctly vesicular. There were but slight constitutional symptoms at that time. On the next day—the tenth from the receipt of the puncture, the fifth of papulation, and the second of vesiculation—he called upon his surgeon, Mr. Rayner of Uxbridge, who, upon seeing the hand, asked the patient “if he had not been handling the udder of a cow, for he could recognise a cowpock vesicle of the ninth day.

“The vesicle was then distended with lymph; its margin elevated and rather brown; centre depressed, and also rather brown; and it was surrounded with a large bright areola. There was considerable tumefaction extending from the knuckles above the wrist. The absorbent vessels were visibly inflamed and painful, and much uneasiness was felt in the axilla. The pulse, naturally slow, was accelerated. There was much fever, pain in the back and limbs, severe headache, anorexia, etc., which symptoms continued to increase to the end of the two following days, when the diffused areola had extended up to the elbow.”

On December 18th—fifteen days after the puncture, and ten days after papulation—the patient was seen in London by Dr. Quain, Professors Spooner and Simonds of the Royal Veterinary College, and also by Dr. Murchison. “The local inflammation and the constitutional symptoms had then partially subsided; the vesicle contained a rather turbid, brownish fluid, and all the indications of a declining vaccine vesicle.”

On December 20th, I visited Mr. Hancock at Uxbridge—the eighteenth day of puncturation, the thirteenth of papulation. There was then evident declining oedema of the integuments of the back of the hand, extending up to the elbow, with a slight blush of redness near it. The vesicle, which was still poulticed, was depressed in the centre, puckered at the margin, but still raised on a firm base. It certainly exhibited the appearances I have often observed, at a corresponding stage, on the back of the hand of milkers infected with casual cowpock. A similar vesicle I have depicted in Plate v, Fig. 2, of “Further Observations on the Variolæ Vaccinæ” (*Transactions of the Provincial Medical and Surgical Association*, vol. x, 1842).

The conclusion drawn from the appearance of the vesicle was corroborated by the history of its development. Its late appearance after the puncture; its tardy and gradual papulation and vesiculation;

the period of the advent of the areola; its extent and period of decline—all corresponding to these phenomena when induced by the casual inoculation of the milker by the cow affected with vaccinia. Still it must be regretted that lymph was not abstracted at a time when it would have been available in settling all doubts as to its reality.

In the few cases in which I have attempted inoculation with the nasal discharge in cattle-plague, on subjects not having previously undergone variola or vaccine, the results have been negative—the production merely of evanescent papules.

ON THE NATURE, CAUSE, AND TREATMENT OF TUBERCULOSIS.

By HORACE DOBELL, M.D., Physician to the Royal Infirmary for Diseases of the Chest, etc.

THE greater part of my leisure during the last sixteen years has been devoted to a study of the natural history of pulmonary consumption and other forms of tuberculosis, and to collecting, assorting, comparing, and testing the facts recorded by others, directly and indirectly connected with the subject.

The ideas which led to this plan of work were set forth in a paper which I read to the Abernethian Society of St. Bartholomew's Hospital in 1848, and afterwards published in the *London Medical Gazette* of 1851, “On the Class of Medical Literature most needed in the Present Day.”* The object was to bring together in an epitome all the most reliable facts concerning tuberculosis, and, from a careful study of them as a whole, to frame hypotheses which seemed capable of co-ordinating and explaining large numbers of the principal facts; then to select the one which included the largest number, and to contrive some crucial experiments to test its correctness.

This plan of procedure was carried out with the effect of annihilating one hypothesis after another, each time suggesting some apparently better arrangement of the facts and some more appropriate ideas with relation to them, until, at length, one hypothesis, with certain possible variations, appeared to grow nearer and nearer to a complete theory.

I have again and again been on the point of publishing this view of the causes of tuberculosis; but have hesitated from a feeling that, before doing so, it ought to be brought up to the completeness of a theory; and my attempts to give it this completeness having always failed to satisfy me, I have been thus deterred from bringing it forward. I have, however, gradually become impressed with the belief that this incompleteness may have been due in some measure to my own want of a sufficiently profound knowledge of physiology and organic chemistry, and of the leisure necessary to acquire this knowledge and to carry out experiments in physiological chemistry. I have hoped to engage the assistance of those whose acquirements in this respect are better than my own, and who, being less occupied with the practice of medicine, have more time for the required class of work. In this hope I have been, at present, disappointed, both because the number of such men is limited, and because they have their heads and hands preoccupied with their own studies, and are naturally unwilling to leave these and apply themselves to such as may be suggested by other persons.

The reasons which have deterred me so long would deter me still from venturing to bring my hypothesis before the profession, were it not that having, during the last two years, published in the *Lancet* (Sept. 10,

* These papers, as corrected and reprinted in 1857, may be obtained from Messrs. Churchill.

1864, June 10, 1865, Nov. 11 and 18, 1865), the practical results of a crucial experiment, without giving any account of the hypothesis on which it was based, and these results having attracted the attention of my medical and scientific brethren, and given rise to many inquiries, I find myself called upon, in simple courtesy, to give some answer to these inquiries. Under these circumstances, and as the views which I entertain, whether they prove true or not, are at least the result of an inquiry conducted on philosophical principles, I feel that I cannot do better than lay them before the profession for discussion.

The hypothesis may be briefly stated as follows.

Tuberculosis is due to defect in the action of the pancreas on the fat taken as food (especially the solid fat). The supply of properly prepared fat is cut off from the blood: 1, by the fats not being brought into a proper condition by the pancreas; 2, by loss of absorbing power in the small intestine, due to the contact of unhealthy pancreatic juice and of defectively prepared food with its mucous membrane. Thus the blood becomes deficiently and defectively supplied with fat-elements from the food; is unable to afford those required for direct combustion; does not replace those taken up during interstitial nutrition; but, on the contrary, takes up more to compensate the deficient supply from the food. This having gone on up to a certain point, the fat-elements of the albuminoid tissues are seized upon, and these tissues are minutely disintegrated in the process. This disintegrated albuminoid tissue is nascent tubercle; and this process of disintegration is tuberculation.

Tuberculation will take place first wherever the following combination of conditions is most marked.

1. Greatest activity of interstitial nutrition.

2. Smallest amount of fat-elements able to be spared by the tissues.

3. A double process going on, consisting of: (a) ordinary interstitial nutrition in albuminoid tissue; (b) interchange of oxygen and carbonic acid, or carbonaceous matter through this tissue.

The tubercle thus formed may be allowed to remain on the spot where it is formed, constituting a *primary deposit at the point of origin*, and this will especially occur when formed under the three conditions just specified; or, it may not be allowed to remain on the spot where formed, but be at once carried away by the lymphatics in a minutely divided condition, and either arrested in the lymphatic glands or carried on into the blood to be deposited from it, constituting a *primary deposit distant from the point of origin*; or, having been primarily deposited in either of these ways, it may be taken up by the lymphatics and deposited in the lymphatic glands, or carried into the blood and deposited from it, constituting a *secondary deposit*.

In the advance of these diseased processes, any part of the body in which nutrition is going on in albuminoid tissue may become both the source and seat of tubercle; and any part, whether albuminoid or not, if supplied with lymphatics or blood-vessels, may become the seat of tubercle.

Pure tuberculosis commences when fats, properly acted upon by the pancreas, cease to pass in normal proportions into the blood.

Tuberculation commences when albuminoid tissue is abnormally seized upon for its fat-elements.

A secondary state is superadded when tubercle has been carried into the circulation, which constitutes tuberculæmia or tuberculous blood-poisoning.

Tuberculosis may stop short of the production of tubercle (tuberculation), if the normal supply of fat, properly acted upon by the pancreas, be restored to the blood before the albuminoid tissues have begun to be disintegrated; and it will not return so

long as this supply is kept up to a normal standard. Tuberculosis may stop short, after the production of tubercle, if the normal supply of properly prepared fat be restored; but, in this case, the tissues must have become so poor in fat-elements that it will be difficult to escape the formation of fresh tubercle in the defective tissues, while the reconstruction of normal tissue is going on. A very rapid and superabundant supply of properly prepared fat to the blood will, therefore, be required.

The balance of fat-elements in the blood and tissues having been restored, tuberculosis will cease; but tuberculæmia, with all the difficulties due to the presence of foreign decomposable and absorbable matter in the tissues and blood, may remain.

In progressing tuberculosis, after the occurrence of tuberculation, tuberculæmia is added to and combined with the original disease. An ordinary case of consumption is a combination of these three states.

If the second portion (b) of the third condition specially favouring tuberculation—viz., “an interchange of oxygen and carbonaceous matters through tissues nourished by blood deficient in fat-elements”—can be provided for by supplying carbonaceous matters to the circulating medium of the part otherwise than by the normal processes and channels, a temporary protection from tuberculation will thereby be given to the tissues through which the interchange occurs.

If this part were previously the one in greatest danger of tuberculation, it will for a time give precedence to the part not so protected; e. g., the lungs may be thus protected by the introduction of oleine through the portal system, the small intestine and mesenteric glands taking precedence in the order of tuberculation from the want of such protection.

But, as nothing can permanently protect the albuminoid tissues from disintegration except solid fat properly acted upon by the pancreas, the protection by the means above described is only temporary; and, unless the normal conditions be soon restored, the previously protected part will become tuberculous at last. By these means, however, the succession in which parts ordinarily suffer may be changed; and if the normal state be restored in time, the part temporarily protected may permanently escape disease.

The defective function of the pancreas causing defective action upon fats may be temporary or permanent, and a tendency to such defect may be hereditary.

When the normal function of the pancreas has been restored, the mucous membrane of the small intestine may not have recovered its absorbing powers, and thus the fats, though properly prepared by the pancreas, may not enter the blood.

Defect in the function of the pancreas may be produced:

1. By any cause which for a prolonged period greatly reduces its activity, by diminishing the normal demand for carbonaceous matters in the blood.

2. By the action on the nervous system of powerful or prolonged depressing influences.

3. By inflammatory and other abnormal conditions of neighbouring parts.

4. By prolonged loss of absorbing power in the small intestine by which the function of the pancreas is rendered useless.

The normal function of the pancreas may be restored (within certain limits as to the duration of the existence of the cause of its defect) by means which make a healthy demand upon its active functions, remove the depressing influences from the nervous system, and permit the absorption of properly pre-

pared fats by the mucous membrane of the small intestine.

This hypothesis having been constructed step by step to explain the phenomena of tuberculosis, I feel safe in asserting that there is hardly a well established fact connected with the origin, course, terminations, and therapeutics, of tuberculosis, which cannot be more satisfactorily explained by this hypothesis than by any other yet suggested. I have carefully compared all its parts with the best established views in modern physiology; and, so far as my knowledge and judgment are competent to decide, there is nothing essentially inconsistent with these views in any portion of it. At the same time, I am quite aware that there are many important points in physiology, unavoidably involved in every theory of nutrition, whether normal or abnormal, on which our knowledge is, at the best, vague and unsatisfactory. All that can be expected, therefore, in this respect, is that conditions shall not be required by a theory of morbid nutrition which are forbidden by the knowledge we have of normal nutrition. I believe it will be found that I have studiously kept within these limits; but, as I have already said, I am conscious of my deficiency in profound physiological and chemical attainments; and I am, therefore, the more desirous that my views shall be examined by those who possess these qualifications, in order that their truth may be strictly tested.

It is not my intention, then, to enter into a discussion of the purely physiological and chemical details of this hypothesis, but rather to direct attention to some of the most striking points in which it is consistent with the clinical history and pathology of tuberculosis, and especially to those in which it reconciles and explains apparently incongruous phenomena.

In the first place, it is necessary to impress the importance of the position occupied by fat in the processes of life; and I cannot do this better than by quoting the following statements by recognised physiologists, in which my own opinions are embodied.

"In considering fat as an important agent in the various phases of the metamorphosis of animal matter, we cannot, however, refer its action solely to mere contact or catalytic force; but we are constrained to assume that it co-operates in the metamorphic action, and experiences metamorphoses, combinations, and decompositions." (Lehmann's *Chemistry*, vol. 1, p. 269.)

Under certain circumstances and for a certain time, "animals can be maintained by a nourishment from which fat is entirely excluded"; and, when the increase of fat in their bodies is in excess of the substances soluble in ether taken as food, "the formation of fat is due to a process of life." (Letter from Professor Liebig to the author, April 3, 1853.)

"In all the forms in which albumen naturally occurs, it is combined with fatty matter." (Kirkes's *Physiology*, 3rd edition, p. 12.)

"The usual function of fat is unquestionably, like that of starch or of sugar, to keep up the heat of the animal. . . . We require the combustion of all the non-nitrogenous constituents of food to enable us to account for animal heat. . . . But it is, nevertheless, a fact that fat is always present in healthy muscle; and it is desirable to consider its relation to muscular action. . . . The experiments made by Bidder and Schmidt on starving cats, and by Bischof and Voit on a starving dog, throw light upon this subject. . . . When Bischof and Voit supplied their starving dog with fat, the waste of the body, as evidenced by the lessened amount of urea excreted, was diminished, because the fat supported the respiration, which before had partially to depend on wasting tissues.

The fat cast over them a protective influence, and limited their waste to the support of their own dynamic functions; and in this fact would seem to be the use of fat after it is stored up in the muscle. We allude to its chemical use; for its mechanical advantage in lessening friction and its possible histogenetic employment in the formation of cells are not under consideration. . . . A man in ordinary health and activity wastes daily 1750 grains of dry flesh or 7000 grains of fresh muscle, which would contain 150 grains of fat. . . . We refer to fat distributed in and inherent to healthy muscles, and not to masses of adipose tissue. . . . The chemical use of fat deposited within muscle may be to protect it from the assaults of oxygen during repose. A muscle, when at rest, gives out carbonic acid, which is, no doubt, partly due to the oxidation of its effete particles, but also to the oxidation of fat. . . . Tissues may, and do, evolve heat by transformation when required to do so." (Dr. Lyon Playfair, *The Food of Man in Relation to his Useful Work*: 1865.)

A part of the heat necessary to maintain a constantly elevated temperature in birds and animals, "depends upon the direct combination of certain elements of the food with the oxygen of the air by the combusive process. The quantity of carbonic acid that is generated directly from the elements of the food, seems to vary considerably in different animals and in different states of the same individual. . . . In man and other animals which can sustain considerable variations of climate, and can adapt themselves to a great diversity of habits, the quantity of carbonic acid formed by the direct combination of the elements of the food with the oxygen of the air differs extremely under different circumstances. It will serve as the complement of that which is formed in other ways." (Carpenter's *Principles of Physiology*, 6th edition, p. 265.)

"The fatty matters of the blood are obviously destined to furnish the contents of the adipose and nervous vesicles, whilst their presence seems also to be required in the early stages of the production of cells generally. One of the principal sources of their expenditure, however, is that combusive process by which the heat of the body is maintained; and the amount deposited in the tissues as fat may be looked upon as the surplus of the quantity ingested that is not thus consumed. . . . The question of the capability of animals to produce fat has been much disputed. There seems, however, no reason for doubting that it may be generated, not only from the hydrocarbonaceous constituents of the food (sugar and starch), but also from the splitting up of the albuminous compounds." (Carpenter, *op. cit.*, page 341.)

"It is clear that fat exerts a protective influence over the albuminous tissues, sparing their consumption or oxidation by its own greater affinity for oxygen. . . . When fat is added to the food, its direct combustion takes up the oxygen, and prevents its action on the nitrogenous tissues." (Carpenter, *op. cit.*, p. 332.)

In the second place, I must point out that, although reliable observations on the blood in phthisis are very scarce, those which we have are consistent with my hypothesis. "In this disease, the saponified fatty matters of the blood decrease perhaps more than in any other." (Bequerel and Rodier's *Animal Chemistry*, Speer's translation, 1857.)

In the next place, all reliable analyses and observations of the nature of tubercle itself give results consistent with my statement, that it is albuminoid tissue disintegrated by the combustion of some of its fat elements.

From the analyses of Scherer, "tubercle may be

regarded as protein from which five atoms of carbon, one of hydrogen, and one of oxygen, have been removed." (Simon's *Chemistry*, translated by Dr. Day, p. 479.)

"Chemistry, equally with the microscope, has failed to point out any essential difference between 'grey miliary' and 'crude yellow' tubercle. Chemists are agreed in regarding tubercle as consisting of some modified protein compound or compounds with fat and earthy salts." (Dr. Fuller, *Diseases of the Chest*, etc., p. 355.)

"It exhibits no tendency to form perfect cells, but rather abortive corpuscles, which form slowly, and slowly break down. Elementary molecules are not formed capable of further development. . . . The tissue which is occasionally seen mixed with it in expectorated matter, is disintegrated lung (Andrew Clark), and only means that so much pulmonary structure has been destroyed." (Dr. Pollock, *Prognosis in Consumption*, p. 111.)

"The destructive change which takes place in tubercle is not a vital act, but is determined by a conversion of the chemical components arising out of an interchange of the elements." (Rokitansky, Sydenham Society's edition, vol. i, p. 299.)

In the fourth place, it must be observed that not only all the symptoms of confirmed phthisis, but the earliest appreciable symptoms of impending tuberculation, upon which physicians are generally agreed, are entirely consistent with my hypothesis. These latter have been briefly and pointedly stated by Dr. Pollock in his recent work. "A preexisting disorder of health is invariably present before there is any evidence of deposit in the lungs. . . . These are symptoms not referable to any disease of the lung, so far as the function of respiration is concerned, but clearly indicative of a general disorder of the system. . . . The earliest of all this group is emaciation." (*Op. cit.*, p. 39.)

The next point to which I would direct attention is the occurrence of hæmoptysis in the early stage of phthisis. It so often happens that the first occurrence of hæmoptysis is followed by a steady descent of the patient, that, popularly, the hæmoptysis is looked upon as the cause of consumption. Although this is proved to be erroneous, it is a fact that, in a large proportion of cases, the first attack of hæmoptysis, even though slight in amount, is followed by marked symptoms of phthisis, and especially by loss of weight. The first Medical Report of the Brompton Hospital (1849) shows that hæmoptysis occurs in 63 per cent. of all cases of phthisis, and is more frequent in the first stage, as 3 to 1. Dr. Pollock says: "I have observed 351 cases of profuse hæmoptysis, of which 204, or more than one-half, occurred in the first three months of the illness." "An early profuse hæmoptysis is to be regarded as a bad prognostic; the softening being likely to take place early, and the remission in the progress of the disease to occur only at a period when already much structural mischief has taken place. "The prognostics to be derived from slight repeated hæmoptysis are, on the other hand, not favourable, this being the commencement of the ordinary form of phthisis." (*Op. cit.*, p. 139.)

This is entirely in accord with my hypothesis. For, so long as there is a sufficient supply of fat in the system to protect the albuminoid tissues, there is no reason why tissue should be invaded; but, as soon as this ceases to be the case, the first breaking up of organic structure will occur; and this is the moment at which hæmoptysis may be reasonably expected to take place for the first time. The first hæmoptysis, therefore, although in no sense the cause of the tubercle or of the emaciation, may, in

truth, often mark the point in the case at which the formation of tubercle begins, and also the point from which emaciation and other general symptoms of disease must advance in a marked degree, until the progress of tuberculosis is stopped.

A sixth and still more interesting point is the relation of tuberculosis to the menstrual function, with respect to the effect upon the carbon in the system. Menstruation in health has a definite relation to the quantity of carbonic acid discharged from the system by other means. From the occurrence of puberty to the cessation of menstruation, so long as healthy nutrition is maintained, everything which arrests menstruation increases the discharge of carbonic acid from the lungs; and the recurrence of menstruation reduces that discharge. It is evident, therefore, that the menstrual flux is a means of eliminating carbon. Now, it is well known that, previous to the appearance of local symptoms of tubercle, the catamenia usually become irregular, and gradually diminish in quantity until, as the disease goes on, they entirely cease; that permanent arrest of menstruation is a usual occurrence in confirmed and progressing tuberculosis; that any prolonged arrest in the disease is usually attended with a restoration of menstruation; that, when menstruation coincides with confirmed and progressing tuberculosis, all the symptoms of the disease are usually increased at the monthly period; that the cessation of menstruation during pregnancy is commonly accompanied by quiescence in the symptoms of tuberculosis; that a large number of cases of phthisis commence at the age of puberty; and (which appears at first very curious) that at this age, among those attacked, there is a large preponderance of males over females—"123 to 90." (Pollock, p. 295.)

As I read these facts, they have the following meaning. In females, the balance of their nutritive functions is so arranged that, at the age of puberty and during the whole generative period, there shall be, normally, a surplus of carbon in the system. At the age of puberty, this superfluous carbon protects them from some of the dangers of tuberculosis to which boys, who have no such surplus to fall back upon, are exposed. Thus, a girl at the age of puberty, deprived of some of the normal supply of properly prepared fats by a temporary arrest of the function of the pancreas, simply suffers a delay in the appearance of menstruation, appropriating her surplus carbon for the protection of the tissues; whereas a boy, similarly placed, has no such means of escape.

The disappearance of the catamenia when tuberculosis has set in is explained by the deficient supply of fat to the blood cutting off the surplusage of carbon for excretion. The latency of tuberculosis when the catamenia are retained by pregnancy, is explained by the saving thus temporarily effected in the expenditure of carbon. The restoration of the catamenia during periods of arrested tuberculosis is the expression of a return to the normal proportion of carbon in the system. With this clue, many other analogous phenomena may be easily explained. It is important to remember that, although the number of reliable experiments on the quantities of carbonic acid exhaled by the lungs in tuberculosis, as compared with the quantity in health, is not large; and that such experiments are open to many sources of fallacy; yet, so far as they go, they are to the effect that the exhalation of carbonic acid from the lungs is diminished in tuberculosis, which is, like the above facts, in accordance with my hypothesis. (*Annalen der Chemie und Pharmacie*, 1846, p. 23.)

[To be continued.]