"An Enquiry into the Causes and Effects of Variolae Vaccinae"

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The Cape Western Branch of the South African Medical Association (B.M.A.) is indebted to Dr. G. D. Reitz of Stellenbosch for the donation of a copy of a second edition of "An enquiry into the Causes and Effects of Variolae Vaccinae, discovered in some of the Western Counties of England, particularly Gloucestershire, and known by the name of The Cow Pox," by Edward Jenner, M.D., F.R.S., etc., published in the year 1800; printed by Sampson Low, No. 7, Berwick Street, Soho: and sold by Law, Ave-Maria Lane and Murray and Highley, Fleet Street. On the cover page the name of one of its earlier owners, Dr. Roentgen, London, with the date 1843, is inscribed. The volume is neatly bound in full tree-calf with gold tooling. It is printed in old style Roman type on wove paper and is well illustrated by hand-coloured engraved plates. The volume is in a very good state of preservation and forms a valuable acquisition to the library.

The treatise was dedicated in the year 1799 to King George III in the following words:

TO THE KING.

SIR,

WHEN I first addressed the Public on a Physiological subject, which I conceived to be of the utmost importance to the future welfare of the human race, I could not presume, in that early stage of the investigation, to lay the result of my Inquiries at your Majesty's feet.

Subsequent experiments, instituted not only by myself, but by men of the first rank in the medical profession, have now confirmed the truth of the theory which I first made known to the world.

Highly honoured by the permission to dedicate the result of my Inquiries to your Majesty, I am boldened to solicit your gracious patronage of a discovery which reason fully authorizes me to suppose will prove peculiarly beneficial to the preservation of the lives of mankind.

To a Monarch no less justly than emphatically styled the Father of his People, this Treatise is inscribed with perfect propriety; for, conspicuous as your Majesty's patronage has been of Arts, of Sciences, and of Commerce, yet the most distinguished feature of your character is your paternal care for the dearest interests of humanity.

I am, Sir,

SIR,

With the most profound respect,

Your Majesty's most devoted

Subject and servant,

EDWARD JENNER.

Berkeley, Gloucestershire.
Dec. 20th, 1799.

We have been favoured with the opportunity of studying the volume and feel that certain observations made by Jenner should once more be brought to public notice in his original words, as they have stood the test of a century and a half of practice. We have been impressed by the care with which Jenner made his observations, the scientific and logical manner in which he marshalled his facts, and the sound and reasonable conclusions at which he arrived.

It may not be generally known that as early as 1721, Lady Wortley Montagu, the wife of the British Ambassador in Constantinople, brought a strain of modified smallpox virus from the East to Britain with which many were vaccinated in order to obtain immunity against the more severe forms of the disease. This practice of conferring immunity continued until Jenner's method became acceptable, and he himself constantly used smallpox virus to prove the immunity established against smallpox by vaccination with cowpox virus. The fact that cowpox conferred immunity against smallpox infection had been known many years before Jenner conducted his experiments, and it is said that the Duchess of Cleveland in 1670 remarked that she had nothing to fear from smallpox since she had had cowpox.

Jenner opens his observation with the following paragraphs:

"There is a disease to which the Horse, from his state of domestication, is frequently subject. The Farriers have termed it the Grease. It is an inflammation and swelling in the heel, from which issues matter possessing properties of a very peculiar kind, which seems capable of generating a disease in the Human Body (after it has undergone the modification I shall presently speak of), which bears so
strong a resemblance to the Small Pox, that I think it highly probable it may be the source of that disease.

In this Dairy Country a great number of Cows are kept, and the office of milking is performed indiscriminately by Men and Maid Servants. One of the former having been appointed to apply dressings to the heels of a Horse affected with the Grease, and not paying due attention to cleanliness, incautiously in milking the Cows, with some particles of the infectious matter adhering to his fingers. When this is the case, it commonly happens that a disease is communicated to the Cows, and from the Cows to the Dairy-maids, which spreads through the farm until most of the cattle and domestics feel its unpleasant consequences. This disease has obtained the name of Cow Pox.

Thus the disease makes its progress from the Horse (as I conceive) to the nipple of the Cow, and from the Cow to the Human Subject.

Morbid matter of various kinds, when absorbed into the system, may produce effects in some degree similar; but what renders the Cow Pox virus so extremely singular is that the person who has been thus affected is for ever after secure from the infection of the Small Pox; neither exposure to the variolous effluvia, nor the insertion of the matter into the skin, producing this distemper.

The first two cases recorded by Jenner are quoted verbatim as they form the basis of his investigation and are typical of the sixteen cases which he observed before he conducted his first vaccination with cowpox virus.

CASE I.

JOSEPH MERRET, now an Under Gardener to the Earl of Berkeley, lived as a Servant with a Farmer near this place in the year 1770, and occasionally assisted in milking his master's cows. Several horses belonging to the farm became to have sore heels, which Merret frequently attended. The cows became affected with the cow pox, and soon after several sores appeared on his hands. Swellings and stiffness in each axilla followed, and he was so much indisposed for several days as to be incapable of pursuing his ordinary employment. Previously to the appearance of the distemper among the cows there was no fresh cow brought into the farm, nor any servant employed who was affected with the Cow Pox.

In April, 1795, a general inoculation taking place here. Merret was inoculated with his family; so that a period of twenty-five years had elapsed from his having the Cow Pox to this time. However, though the variolous matter was repeatedly inserted into his arm, I found it impracticable to infect him with it; an efflorescence only, taking an erysipelatous look about the centre, appearing on the skin near the punctured parts. During the whole time that his family had the Small Pox, one of whom had it very full, he remained in the house with them, but received no injury from exposure to the contagion.

It is necessary to observe, that the utmost care was taken to ascertain, with the most scrupulous precision that no one whose case is here adduced had gone through the Small Pox previous to these attempts to produce that disease.

Had these experiments been conducted in a large city, or in a populous neighbourhood, some doubts might have been entertained; but here, where population is thin, and where such an event as a person's having had the Small Pox is always faithfully recorded, no risk of inaccuracy in this particular can arise.

CASE II.

SARAH PORTLOCK, of this place, was infected with the Cow Pox, when a Servant at a Farmer's in the neighbourhood, twenty-seven years ago.

In the year 1792, conceiving herself, from this circumstance, secure from the infection if the Small Pox, she Nursed one of her own children who had accidentally caught the disease, but no indisposition ensued—During the time she remained in the infected room, various matter was inserted into both her arms, but without any further effect than in the preceding case.

The following footnote to Case IV is of particular interest as it do not forms the first description of immune reaction, which at present is a subject of controversy.

It is remarkable that variolous matter, when the system is disposed to reject it, should excite inflammation on the part of which it is applied more speedily than when it produces the Small Pox. Indeed it becomes almost a criterion by which we can determine whether the infection will be received or not. It seems as if a change, which endure through life, had been produced in the action, or disposition to action in the vessels of the skin; and it is remarkable, too, that whether this change has been effected by the Small Pox, or the Cow Pox, that the disposition to sudden cuticular inflammation is the same on the application of variolous matter.

Jenner describes his first vaccination with virus from an active cowpox pustule thus:

CASE XVII.

The more accurately to observe the progress of the infection, I selected a healthy boy, about eight years old, for the purpose of inoculation for the Cow Pox. The matter was taken from a dead pustule, on the hand of a dairymaid, who was infected by her master's cows, and it was inserted, on the 11th of May, 1796, into the arm of the boy by means of two superficial incisions, barely penetrating the cutis, each about half an inch long.

On the seventh day he complained of uneasiness in the axilla, and on the ninth he became a little chilly, lost his appetite, and had a slight head-ache. During the whole of this day he was perceptibly indisposed, and spent the night with some degree of restlessness, but on the day following he was perfectly well.

The appearance of the incisions in their progress to a state of maturation were much the same as when produced in a similar manner by variolous matter. The only difference which I perceived in the limpid fluid arising from the action of the virus, which assumed rather a darker hue, and in that of the efflorescence spreading round the incisions, which had more of an erysipelatous look than we commonly perceive when variolous matter has been made use of in the same manner; but the whole died away (leaving on the inoculated parts scabs and subsequent eschars) without giving me or my patient the least trouble.

In order to ascertain whether the boy, after feeling so slight an affection of the system from the Cow Pox virus, was secure from the contagion of the Small Pox, he was inoculated the 1st of July following with variolous matter, immediately taken from a pustule. Several slight punctures and incisions were made on both his arms, and the matter was carefully inserted, but no disease followed. The same appearances were observable on the arms as we commonly see when a patient has had variolous matter applied, after having either the Cow Pox or the Small Pox. Several months afterwards he was again inoculated with variolous matter, but no sensible effect was produced on the constitution.

Here Jenner's researches were interrupted until the spring of the year 1798, when there was a severe outbreak of cowpox. He now vaccinated a series of cases, establishing the possibility of transmitting the infection from animal to man and from man to man. It is of interest that his son, Robert J. Jenner, eleven months old, was included in this series but did not take. Jenner proffers no explanation for this.

In order to establish that there was an acquired immunity to smallpox, he subsequently vaccinated all his cases with virus of that disease. A doubt still remained as to the potency of this virus, and in order to prove this he infected a susceptible patient and reports on this experiment as follows:

To convince myself that the variolous matter made use of was in a perfect state, I at the same time inoculated a healthy young son of it, who never had gone through the Cow Pox, and it produced the Small Pox in the usual regular manner.

These experiments afforded me much satisfaction; they proved that the matter in passing from one human subject to another, through five gradations, lost none of its original properties.

S. A. TYDSKRIF VIR GENEESKUNDE

375
He follows this first and most important part of his treatise with further observations on the subject, citing confirmation of his work by others and dealing with the objections of his opponents. He states that much criticism had arisen out of faulty technique and the method of inoculation. The following words of Jenner even to-day have point, and if remembered by all vaccinators, will go far towards saving their patients unnecessary suffering:

"I have the strongest reason for supposing that if either the surface or incisions be made so deep as to go through it, and wound the adipose membrane, that the risk of bringing on a violent disease is greatly increased. I have known an inoculator, whose practice was 'to dig deep enough (to use his own expression) to see a bit of fat', and there to lodge the matter. The great number of bad Cases, independent of inflammations and abscesses on the arms, and the mortality which attended this practice was almost inconsiderable; and I cannot account for it, on any other principle than that of the matter being placed in this situation, instead of the skin."

"Although it is very improbable that any one would now inoculate in this rude way by design, yet these observations may tend to place a double guard over the lancet, when infants, whose skins are just comparatively so very thin, fall under the care of the inoculator."

"Some of it was inserted into a scratch made so superficial that no blood appeared."

The vaccination then done was successful.

The need for careful preservation of lymph was recognised by Jenner, who stressed that the warm waistcoat pocket of the physician was not the best place for storage, in the following words:

"... which, in its fluid state was put into a phial, corked, and conveyed into a warm pocket; a situation certainly favourable for speedily producing putrefaction in it..."

"Those who had been inoculated in this manner being as much subject to contagion of the Small Pox, as if they had never been under the influence of this artificial disease, and many, unfortunately, fell victims to it, who thought themselves in perfect security."

He also remarks in his account on the preparation of lymph that—

"When kept several days in a state of moisture, and during that time exposed to a warm temperature, I do not think it can be relied upon as capable of giving a perfect disease..."

In his further observations, Jenner refers to two interesting conditions, one of which is to-day recognised as variola minor (alastrium, amas), and which he describes in the following words:

There are certainly more forms than one, without considering the common variation between the confluent and distinct, in which the Small Pox appears in what is called the natural way. — About seven years ago a species of Small Pox, spread through many of the towns and villages of this part of Gloucestershire: it was of so mild a nature, that a fatal instance was scarcely ever heard of, and consequently so little dreaded by the lower orders of the community that they scrupled not to hold the same intercourse with each other as if no infectious disease had been present among them. I never saw nor heard of an instance of its being confluent..."

The other General Vaccina following vaccination of which he gives an account—

"A few scattered pimples I have sometimes, though very rarely seen, the greater part of which have generally disappeared quickly, but some have remained long enough to suppurate at their apex. — The eruption I allude to, has commonly appeared sometimes in the third week after inoculation..."

The above extracts show that Jenner had made a very careful study of the methods and results of vaccination, and that after a lapse of 150 years there have been few alterations, except that arm-to-arm vaccination is no longer practised, but lymph is now obtained from animals. There is no record that Jenner ever used lymph direct from the cow to vaccinate humans.

Acute High Altitude Anoxia.

Fatality in air crews due to deprivation of oxygen during bombing operations at high altitude afforded this opportunity to study the gross and microscopic anatomy of acute anoxia in man as it occurs at low atmospheric pressure. Twenty-seven necropsies were performed during 1943 in one hospital on members of high altitude bomber crews in which death had been attributed to anoxia by the air force medical officers who investigated the cases. In no case was there a history of rapid ascent to high altitude. Widespread, severe capillary congestion was found. This was conspicuous and most constant in the pulmonary, renal, intestinal and cerebral capillaries. The skeletal muscle did not have this congestion. In a high proportion of cases the systemic venous and the portal circulations showed gross and microscopic congestion and the right ventricle was dilated. There was wide individual variation in the incidence, location and amount of edema and hemorrhage. An exception to this was the consistent occurrence of hemorrhage in the thymus and in the middle ears. Swelling of endothelial cells of capillaries of the renal medulla was observed. The presence of fat-free and glycerin-free vacuoles previously described in the myocardium, liver and less frequently in cells of other organs was confirmed. These vacuoles occurred with equal frequency in cases of anoxic anoxia (acute carbon monoxide poisoning), but were rarely found in the tissues in non-anoxic control cases.

(Kritzer, Captain R. A.: War Medicine, 6, 369, December, 1944.)

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Early Vitamin Deficiency and Blood Vitamin Levels.

It is frequently difficult to determine whether a patient has a true vitamin deficiency and can be restored to health by the intelligent use of diet supplemented with vitamins or whether he is a constitutionally inferior person in whom prolonged and excessive vitamin therapy would prove futile. The application of new methods of determining vitamin levels in the blood or urine may be of great importance, these investigators from Duke University School of Medicine say, if patients having unquestionable evidence of a vitamin deficiency should prove to have levels significantly lower than those of normal controls. This study, therefore, was undertaken to determine the relationship between the clinical picture of early vitamin deficiency and laboratory determinations of vitamin levels. The following studies were conducted: history, including a careful evaluation of the diet, physical examination with a neurological consultation, complete blood count, total proteins and A/G ratio, urinalysis, gastric analysis, proctoscopic and gastroscopic examinations, ileal studies, stool fat, prothrombin time, slit lamp examination of the eyes, glucose tolerance test, E.K.G and determinations of vitamins A and C, carotene, nicotinic acid, riboflavin, thiamin, pyridoxine, and pantothenic acid. Coloured photographs of the mouth and tongue were taken routinely. In some patients nerve biopsies were done. The patients, all hospitalised, were divided into two groups, those with definite signs of vitamin deficiencies and controls in the ward consisting of patients who gave no definite evidence of a deficiency state. In addition, there were normal controls consisting of students, technicians, dietitians and others, all of whom had been existing on an apparently adequate diet.

It was concluded from these studies that there appears to be a definite picture of mild or early deficiency as indicated by glossitis, papillary atrophy of the tongue, cheiriosis or peripheral neuritis, and the results obtained from laboratory examinations of vitamin levels. In the group of patients classified clinically as having a B complex deficiency, the levels of nicotinic acid, thiamin and riboflavin were significantly lower than those of normal controls. In this group, the plasma levels of A and carotene also lowered. In the normal group. Among patients showing physical signs of a deficiency of the B complex, the laboratory data indicate the prevalence of multiple deficiencies. As a result of these studies, the authors believe that the laboratory determinations of vitamin levels may become important aids in the recognition of mild or early vitamin deficiencies.