

INFANTILE SCURVY : ITS HISTORY

BY

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As early as the sixteenth century and still more in the seventeenth century the clinical picture of scurvy was acquiring a distinctness which it had never had before in the minds of medical men. In 1534 Euricius Cordus, a physician of eminence, as well as a poet, had written on the scurvy, and five years later the Professor of Medicine (and of Greek!) at the University of Ingolstadt, Johannes Agricola, devoted part of his writings to this subject. There is no reason to assume that scurvy came into existence at that time; indeed, it is quite certain that it must have occurred as soon as man discovered ways of subsisting without fresh meat and milk and the fruits of the earth, and especially when his journeyings by sea became extended so that he was more dependent upon long-preserved foods. Writers in the seventeenth century—which was particularly prolific in works on scurvy—still anxious to maintain the Hippocratic tradition, were at pains to show that Hippocrates had referred to scurvy, without naming it, as an affection of the gums or mouth associated with enlargement of the spleen, and that Galen, more explicitly, had described it under the names of *στομακάκη* and *σκελοτύρβη*, by emphasizing the oral manifestations and the weakness and difficulty in walking due to that affection: and they had no doubt that Pliny had meant scurvy when he described (Nat. Hist. Bk. xxv., c. 6) how the soldiers of Germanicus, campaigning on the Rhine, suffered, after the campaign had lasted two years, with loosening of the teeth and weakness in the limbs, and how a remedy was discovered for this in eating a plant called *Herba Britannica*, thought by modern writers to be the *Inula Britannica* of Linnaeus, or possibly some variety of sorrel. I have searched amongst many of the early writings on scurvy for any mention of its occurrence in infants or in children. It is not surprising that writers dealing with the disease, as many did, almost exclusively as an affection of soldiers and sailors, should make no mention of children. Gradually it came to be recognized that scurvy occurred also amongst the civilian population on land, but even then there is little separate mention of its occurrence in children. This can hardly be because it did not occur in them, for although breast feeding was prolonged, in most countries in the sixteenth and seventeenth centuries, to at least two years of age, and no doubt to some extent reduced the chance of scurvy in infancy, it must be remembered that the mother or foster-mother herself must often have been suffering from lack of fresh food, so that her milk must have lacked antiscorbutic value. The great factor in the wide prevalence of scurvy before the end of the

eighteenth century was the absence of fresh food during the winter. Of all the antiscorbutic foods which reduced the incidence of scurvy in later times, by far the most important, especially as being available throughout the winter, was the potato. Introduced into this country by Sir Walter Raleigh in 1585, it was still only a luxury in 1626, and, although the Royal Society urged its cultivation in 1663, it was not until the latter part of the eighteenth century that it began to be cultivated on a large scale. For the most part the population, especially the poorer sort, subsisted through the winter upon foods very poor in antiscorbutic value; in Belgium and in Spain the potato came into use a little earlier.

The essential relation of scurvy to diet, however, was unknown when the physicians of the sixteenth and seventeenth centuries tried impotently to mitigate this terrible disease, which, as they imply, even if they do not state, affected children and adults alike. A writer in 1609, Schenk, says that scurvy is sometimes found in several members of a family, and adds significantly, '*Partim quod eodem victu sint usi*,' i.e., because they have lived on the same diet, and apart from referring to '*pueri*' as affected by it, he mentions casually of a particular form of supposed antiscorbutic treatment, that he had used it for a tender infant, '*tenello infanti*.'

Probably the scanty reference to the occurrence of scurvy in infancy and childhood is due chiefly to the fact that these early writers described the disease without distinctions of age, indeed, some of their statements imply this, e.g., Balthazar Bruner in 1658, in a treatise, *De Scorbuto*, says, '*Saepe totas familias invadit*,' and mentions that in children the oral symptoms were more frequent than the limb symptoms; and another writer of the same date, Henricus Brucaeus, says that it '*attacks persons of any age*,' '*cujusvis aetatis et sexus*.' What wonder if medical men, seeing whole families stricken with the scurvy, concluded that it must be either contagious or inherited if, indeed, they did not, with less logic, attribute it, as Eugalenus did, to the Devil!

It might seem strange that with so near a guess at the truth as was made by Schenk and others, who regarded diet as an important factor, physicians in the sixteenth and even in the seventeenth centuries considered contagion and heredity as possible sources of scurvy; Gregorius Horstius, for instance, at the same date as Schenk, stated that diet was a potent factor in the production of scurvy, and yet goes on to say that children, as a result of heredity become predisposed to scurvy (*nativa dispositio scorbutica lienis a parentibus in filios propagatur*), and that infants might contract the disease from kissing. Similar views were expressed by Gideon Harvey, physician to Charles II, in 1675, in a verbose and tedious treatise on '*The Disease of London, or a new Discovery of the Scorvey*,' where he seems to imply its occurrence in infants. He says it is contracted '*by means (1) of the Semen of the Parent and its plastic Faculty; (2) of the Uterin Blood; (3) of the Milk assuged by the Infant; (4) of the Contact of the Lips of the Mouth*

and ambient Skin of the Body, whereby the Scorbutic *μασμα* is transferred to the Child by being Kissed or Hugged by the Parents and lying by them in Bed.' The title of his treatise is interesting as suggesting that 'the Scorvey' was common in London at that time.

In the study of medical history, however, there is a fallacy always to be remembered, that until the clinical and pathological manifestations of a disease have become so clearly defined that its differentiation from other diseases is reasonably reliable, a name may cover morbid entities which are entirely distinct from one another. Already in 1686 Thomas Sydenham,* with his clinical acumen, had perceived that the name of scurvy was being applied to conditions which were essentially different, and instances gout, rheumatism, and the vague initial symptoms of various diseases. Avowedly syphilis and scurvy had been thought to be akin, and it is easy to see how infantile syphilis might have been and almost certainly was, confused with infantile scurvy. Purpura also was a source of confusion; Martin Lister,† in 1694, describes in some detail four cases of 'Scorbutus' in children aged respectively 5, 10, 6 and 8 years, but his description suggests that they were not really cases of scurvy, but of what would now be called primary purpura, one of them a fatal purpura hæmorrhagica.

The first clear description of Infantile Scurvy was given by Francis Glisson in his *De Rachitide* in 1650.

The Scurvy complicated with this Affect (rickets) hath these signs:—

- (1) They that labour under this affect do impatiently endure Purgations; but they who are only affected with the Rachites do easily tolerate the same.
- (2) They are much offended with violent exercises, neither can they at all endure them. But although in this affect alone ther be a kind of slothfulness and aversion from exercise, yet exercise doth not so manifestly, at least not altogether so manifestly hurt them as when the Scurvy is conjoyned with Rachites.
- (3) Upon any concitated and vehement motion they draw not breath without much difficulty, they are vexed with divers pains running through their Joynts and these they give warning of by their crying, the motion of the Puls is frequent and unequal, and sometimes they are troubled with a Palpitation of the Heart or threatened with a lypothymie, which Affects are for the most part soon mitigated or altogether apaised by laying them down to the rest.
- (4) Tumors do not uncommonly appear in the Gums.
- (5) The urin upon the absence of the accustomed Feaver is much more intens and encreased.

Such was Glisson's description of Infantile Scurvy; which he says 'is sometimes conjoyned with this Affect (the rickets). It is either hereditary or perhaps in so tender a constitution contracted by infection, or lastly, it is produced from the indiscreet and

* *Observationes Medicae*, 1686.

† *Sex exercitationes Medicinales*, 1694.

erroneous Regiment of the Infant, and chiefly from the inclemency of the Ayr and Climat where the Child is educated.* For it scarce holdeth any greater commerce with this Disease then with other Diseases of longer continuance, wherein after the same manner the Blood in time contracteth, yet it must be granted, that this Affect doth somewhat the more dispose to the Scurvy in regard of the want of motion and exercise.'

It seems strange that Glisson's recognition of scurvy in association with rickets remained a dead letter for 200 years. Glisson was obviously writing from shrewd clinical observation; moreover, he recognized what was not fully appreciated until Barlow stressed the point in his communication to the Medico-Chirurgical Society in March, 1883, that rickets is no essential concomitant of infantile scurvy.

Even such careful clinical observers of diseases of infancy and childhood as George Armstrong, Heberden and Underwood make no mention of the condition which Glisson had described so faithfully. Perhaps in some degree this omission was due to the gradual diminution in the frequency of scurvy which must have occurred as the antiscorbutic value of vegetables and fruit came to be more and more recognized, and especially when potatoes came to be more generally available. As early as 1646 a Jesuit monk, Baptiste Ferrari, had published at Rome a work on the cultivation and use of the orange, and a German writer, John Drawitz, in 1647, had reported that sailors were 'speedily and effectually cured of the Scurvy by eating oranges,' and in 1694 Martin Lister (*loc. cit.*) wrote that 'the chief remedies for this disease are teaspoonfuls of orange-juice and lemon-juice.' In 1778, De Mertans, in a paper communicated to the Royal Society, describing the terrible incidence of scurvy amongst the children in a Foundling institution in St. Petersburg, recognized not only the antiscorbutic value of vegetables, but its diminution after cooking. 'I am convinced,' he says, 'that all the greens used in our kitchens are much more antiscorbutic when they are raw than after they have been boiled in water or have gone through any other preparation by fire.' He states particularly that none of the children 'were ever seized with the scurvy under two years old'; in this connection it is noteworthy that some at least of the younger children were boarded out with foster nurses, 'La plus part des petits à la mamelle étoient en nourrice à la campagne.' Even Lind, in his exhaustive and masterly work on the scurvy in 1754, has no mention of its occurrence in infants; the only instance mentioned in a child is in a boy aged 10 years. Lind, in his very full bibliography, does not include the name of Glisson.

With the increasing understanding of the essentials in the prevention and treatment of scurvy the disease must have become less prevalent. In the latter half of the eighteenth and earlier half of the nineteenth centuries the evil day of dried patent foods for infants had not yet dawned, so that the most potent cause of infantile scurvy in the latter

* 'Educated' is of course used here in its literal sense of 'brought up,' not of scholastic training.

half of the nineteenth century was not yet in operation, and this disease must, therefore, have been seen much less frequently in infants than in the time of Glisson. He had made two important observations with regard to infantile scurvy: (1) that it was sometimes associated with the rickets; (2) that the rickets bore no essential relation to it. These were ignored or forgotten, and later writers fell into confusion on the relationship. In 1795 S. T. Soemmering* propounds the view that 'Scurvy in adults is akin to, if not identical with, the disease which they call Rickets in infants, the one disease differs from the other exactly in proportion as the infantile body differs from the adult'; he regarded rickets and scurvy as one and the same disease, merely modified by age. A still more retrograde error was put forward by Antoine Portal† in his work on Rickets, 1797, where he regards rickets as a symptom of various diseases, such as gout and syphilis, and has a section, 'Du Rachitisme occasionné par le vice Scorbutique,' in which he describes a case which may have been scurvy in a girl of 10 years, but in which he gives no proof whatever of the rickets which he considers to have accompanied it. Montfalcon, who quotes this case in the *Dict. des Sciences Med.*, 1820, says 'On a vu dans d'autres cas, assez rares toutefois, une pareille complication du rachitis et du scorbut,' but gives no instances.

By 1859 scurvy had so far receded from the foreground of medical perspective that not only had Glisson's observations on infantile scurvy been forgotten, but even the possibility of scurvy being associated with rickets was regarded as something unknown. In that year Prof. Möller‡ reported three cases of 'Acute Rickets,' and whilst denying that ordinary rickets was inflammatory, admitted that these acute cases reminded one decidedly of an 'osteitis.' In 1862 he recorded more fully two cases in children, aged respectively 14 months and 21 months, one of which died and showed a subdural haemorrhage. In the other case the purple swelling of the gums specially attracted his attention, and he noted, 'Sehr bald nahm es eine völlig scorbutartige Beschaffenheit an.' Even then, with this resemblance before him, he did not recognize that it was actually scurvy, and after months of unsuccessful treatment, 'endlich, wegen der Aehnlichkeit mit dem Scorbut, Citronensaft und frische Gemüse versucht, alles ohne den mindesten Erfolg.' And then comes warm weather and the child's recovery is attributed to fresh air! The lemon juice and the fresh vegetables get no credit; and Möller concludes that the acuteness of symptoms in such cases is due to abnormal rapidity of growth in the bones, and that the resemblance to scurvy is merely external and symptomatic. 'Was ubrigens die durch solche Knochenblutungen entstehende Aehnlichkeit mit Scorbut betrifft . . . so halte ich sie nur für eine rein äusserliche symptomatische.'

* *De morbis vasorum absorbentium*, 1795.

† *Observations sur la Nature et sur le traitement du Rachitisme*, Paris, 1797.

‡ *Konigsberger Med. Jahrbücher*, I, 1859, and III, 1862.

It seems hardly appropriate that, as sometimes happens, infantile scurvy should be called 'die Möller-Barlowsche Krankheit,' for Möller failed to recognize the scorbutic nature of the disease, the very point which Barlow's investigations established. After Möller, cases of this affection continued to be described as 'Acute Rickets,' with no inkling of scurvy, until Ingerslev* in 1871 recorded a case of scurvy in an infant aged 15 months. Ingerslev has not received the credit he deserves: he not only gave a graphic description of this case, but he was quite clear as to its being scurvy: 'det var dog tydeligt en skorbutisk Tilstand,' he says; and unlike other writers before and after him, he makes no confusion between it and rickets, indeed he does not even mention rickets. He points out that good hygiene was powerless to prevent it in presence of faulty diet: lack of vegetables was the fault, 'det just er Savnet af Vegetabilier som giver Anledning til Skorbug,' but he thought that vegetables might be antiscorbutic rather by affording a mixed diet than by any special virtue.

In 1876 the nature of this affection was still in doubt in this country. Sir Thomas Smith had under his care at the Children's Hospital, Great Ormond Street, a fatal case, and it was at Barlow's suggestion that the condition found post mortem was called 'Haemorrhagic periostitis,' a term which Barlow himself later condemned as inappropriate. In November, 1878, and in July, 1882, Dr. W. B. Cheadle described cases under his care with full recognition of their scorbutic character, and that they were instances of 'Scurvy supervening on rickets.' He propounded the deficiency origin of the disease: 'There is an invariable factor. . . . This essential factor it has been proved over and over again is the absence of certain elements in food.' In 1881, however, so acute a clinician as Gee, then colleague of Dr. Cheadle, at Great Ormond Street, still failed to recognize these cases as scurvy, for he reported five cases under the name of 'Osteal or periosteal cachexia,' observed between 1878 and 1880. 'Quandoque bonus dormitat Homerus'!

In 1883 the nature of this affection was finally settled by pathological evidence brought forward by Barlow, then Assistant Physician to the Children's Hospital, Great Ormond Street. His paper 'On cases described as Acute Rickets, which are probably a combination of Scurvy and Rickets, the Scurvy being an essential and the Rickets a variable element,' was read before the Medico-Chirurgical Society of London† and accompanied by an exhibition of pathological specimens illustrating the condition in three fatal cases, on March 27, 1883. Between 1883 and 1894, when Barlow delivered his Bradshaw Lecture on 'Infantile Scurvy and its relation to Rickets,' he had had 33 cases under his care, and was able to add some important clinical details to the picture of infantile scurvy, giving a completeness to it which has left very little to be added by subsequent observers. The pathology of scurvy remained an unsolved problem. Barlow stressed, what earlier observers had already recognized,

* Et Tilfaelde af skorbug hos et Baru. Hospitals—Tidende, Aug. 2. 1871.

† See p. 223 for this original paper.

the importance of fresh food in the prevention and treatment of scurvy, but chemists were searching in vain for the *causa causans* of scurvy. It was only when Holst and Frölich in 1912* first showed that animals could be rendered scorbutic (they used guinea pigs) that advance became possible in the investigation of the causal factors in scurvy, and since that time a host of observers have been at work determining experimentally, by tests upon animals susceptible to scurvy, the degree of scorbuticity of various foods, the presence or absence of the antiscorbutic factor in particular foods, and the conditions which affect its potency. Following the lead of Sir Gowland Hopkins, it had become usual to name the particular deficiency which rendered a food scorbutic, deficiency of vitamin C, and various facts had been ascertained with regard to this hypothetical vitamin C, but still it remained unfound, until, in 1928, Györgyi† isolated a crystalline substance from the adrenal cortex of the ox, and also from orange and from cabbage, to which he gave the name hexuronic acid: a substance with powerful antiscorbutic activity. Further chemical investigations were made by Cox, Hirst and Reynolds in 1932, leading to a change of name. The substance was re-named 'ascorbic acid,' or, as some Continental writers name it, 'ascorbinic acid.'

This chemical substance, ascorbic acid, is now very generally accepted as the essential antiscorbutic factor. Its artificial synthesis seems already to have become an accomplished fact, which may have some practical bearing upon the prevention of infantile scurvy in the future.

Valuable and interesting as these laboratory investigations of the last few years have been, it is not to them that we can attribute the decrease of suffering and also of mortality from infantile scurvy which is so evident in the past half-century. This is due to the demonstration of the scorbutic nature of the disease by Sir Thomas Barlow, and the clear description of its clinical features by him and by Dr. W. B. Cheadle, making its recognition gradually more universal; their insistence at the same time upon its amenability to one treatment, and one only, the administration of the element deficient in the scurvy-producing diet, by giving fruit juice, potato, and fresh meat juice, has been the means of preventing and relieving a large amount of infant-suffering.

One point which must strike everyone familiar with the disease, as seen in recent years, is the discrepancy between the average age of the cases recorded 50 or 60 years ago, and that of cases seen to-day. In that earlier period the cases recorded were mostly over a year old. Cheadle's three cases were respectively 16 months, 16 months, and 3 years old. Twenty out of Barlow's 35 collected cases were over a year old, whereas nowadays and, indeed, within the past twenty years, a case over a year old is quite the exception, the large majority being between six months and twelve months old. The meaning of this—as a study of those older cases shows—is that the disease, thanks chiefly to the writings and

* Holst, A., & Frölich, T., *Zeitschr. f. Hyg. und Infect.*, 1912, 72, 1.

† A. Szent Györgyi, *Biochem. Journ.*, 1928, XXII, 1387.

teaching of Sir Thomas Barlow, is diagnosed so much earlier, and the feeding corrected, on the lines emphasized by him, so much earlier, that the infant is saved weeks and months of the terrible suffering which an unrecognized case of infantile scurvy undergoes. The point stressed by Barlow, that scurvy is the essential and rickets only a variable manifestation in these cases, was not fully recognized for several years. The misleading term, 'scurvy-rickets,' is sometimes heard even to-day, and was in common use thirty years ago, perpetuating haziness of ideas as to the pathology and treatment of a condition which, as Glisson recognized, and Barlow finally established, is essentially scorbutic and responds not to anti-rachitic treatment, but only to antiscorbutic measures.

At the time when Barlow first demonstrated the scorbutic nature of the disease from pathological investigation, the mortality of infantile scurvy in the series of cases which he collected, was 1 in 4.5 approximately; as a result of the better understanding of this disease, and its more general and earlier recognition since his investigations were published, the mortality has fallen to about one-fourth of this proportion; in a series of 155 cases, under the present writer's observation, it was almost exactly 1 in 18.

The aim of medicine is not only to reduce mortality, but to reduce suffering, and in this latter respect a splendid contribution was made to medicine by those investigations which gave to infantile scurvy its alternative name, Barlow's Disease.