

THE SYDENHAM-BOYLE THEORY OF MORBIFIC PARTICLES*

by

KENNETH D. KEELE**

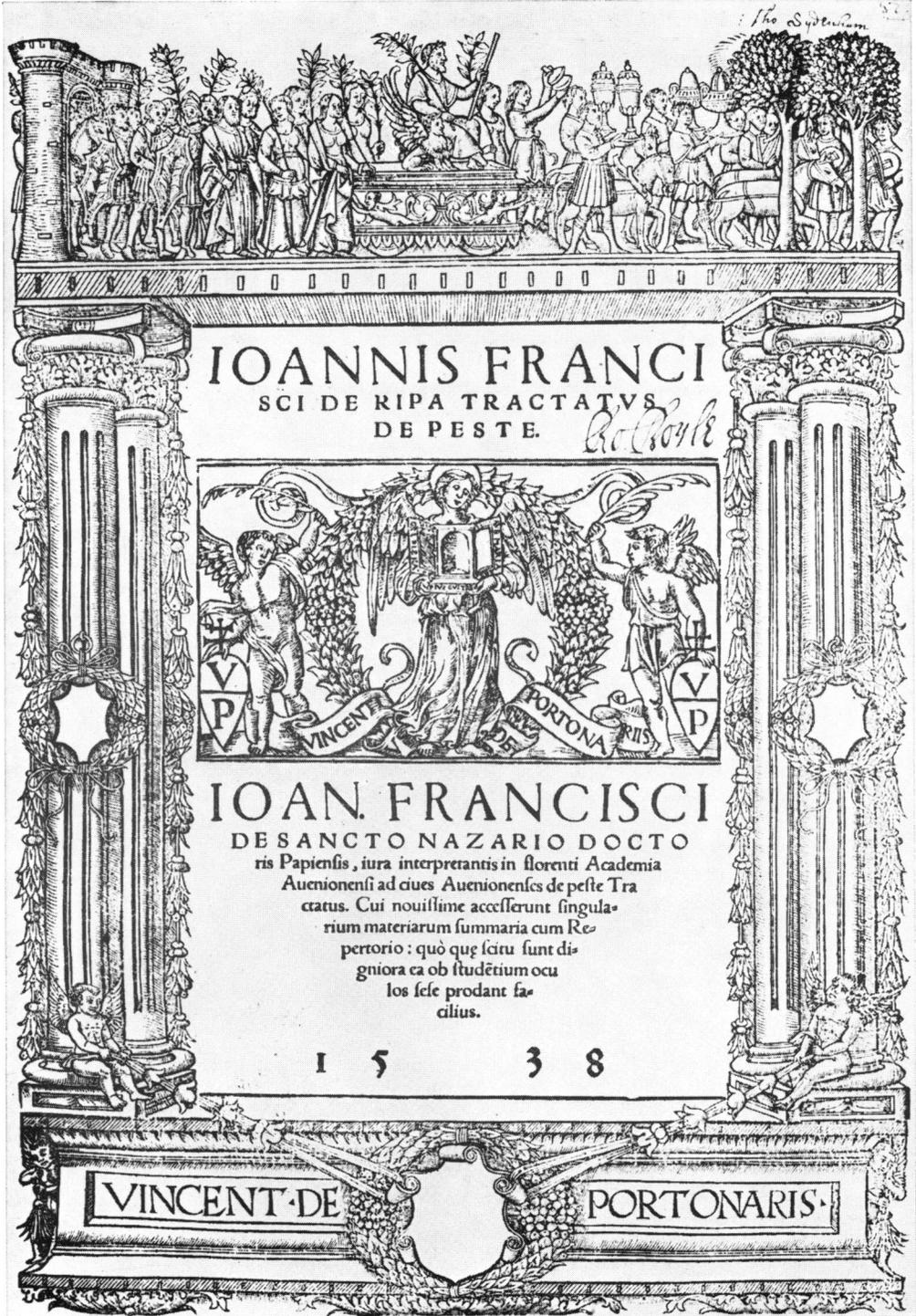
NOT LONG after the sense of pleasure at the privilege of being invited to give this Sydenham Lecture, I found myself troubled by my own attitude to what I knew of Sydenham. Like many others I had been introduced to Sydenham as the English Hippocrates, the clinical observer untrammelled by theory, and turning to Sydenham's *Medical observations* I had expected to find something similar to the clinical works of Hippocrates. This expectation was rudely shattered by its opening chapters, for instead of finding clinical descriptions I found a mass of speculative theoretical statements about "morbific particles", "peccant matter", etc., in disease. This was not what I had expected from this great clinician who not only took Bacon's inductive principles as his guide but repeatedly protested loudly against medical speculation. How did our English Hippocrates reconcile so unhippocratic an account of disease with his brilliant clinical descriptions? Here was my problem; and the invitation to give this Sydenham Lecture challenged me to solve it. Today I would like to define the problem further and offer my solution to you.

First I must say that I am glad to find that I am not alone in being troubled by Sydenham's theoretical speculations. As long ago as 1797 James Currie, a fine clinician, who used the clinical thermometer in cases of fever, wrote,¹ "That he [Sydenham] recorded symptoms with great accuracy; and that he was a more cautious reasoner than his predecessors or contemporaries are facts that are indisputable. But though he affected not to theorize he was a theorist in every page of his works." Turning to more recent times I find that that distinguished contemporary medical historian, Oswei Temkin,² has shared this discomfort by comparing Hippocrates' works on *Epidemics* with our English Hippocrates' *Medical observations*, so displaying an unexpectedly marked contrast between their very different concepts of disease.

Turning to Sydenham's works themselves, I would first draw your attention to the fact that Sydenham dedicated his *Methodus curandi febres* of 1666 to Robert Boyle, acknowledging his influence in the undertaking particularly, since Boyle had accompanied him in visiting the sick. It is relevant to my theme to note that Boyle when in London lived with his sister, Lady Ranelagh, next door to Sydenham in Pall Mall. This intimate and neighbourly friendship with Boyle lasted for the rest of Sydenham's life. In my opinion, it relates significantly to Sydenham's medical theory. I shall return to it later.

*The Sydenham Lecture, given at Apothecaries' Hall on 21 November 1973.

**Leacroft House, Leacroft, Staines, Middlesex.



Title-page of Joannes Franciscus de Sancto Nazario's *Tractatus de peste* (Lyons, 1538) showing the signatures of Sydenham and Boyle. (By courtesy of the Wellcome Trustees).

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I shall now have to burden you with some rather lengthy quotations from Sydenham himself in order to clarify the nature of his medical theory of acute and chronic diseases, particularly fevers. To begin with I would like to share with you the passage that for so long troubled me, i.e. the opening paragraph of Sydenham's *Medical observations*.³ Here he writes:

As far as I am capable of a judgement the dictates of reason are as follows; namely that a disease however much its cause may be adverse to the human body, is nothing more than an effort of Nature, who strives with might and main to restore the health of the patient by the elimination of morbidic matter. . . . These maladies arise partly from the particles of the atmosphere, partly from the different fermentations and putrefactions of the humours. The first insinuate themselves amongst the juices of the body, disagree with them, mix themselves up with the blood, and finally taint the whole frame with the contagion of disease. The second are confined within the body longer than they ought to be, its powers having proved incompetent first to their digestion, afterwards to their excretion. Nature has provided a method for the elimination and exclusion of the peccant and foreign matter which otherwise would undo the whole fabric of our frame.

The secondary part played by the Galenic humours in acute diseases, according to Sydenham, is emphasized in his preface to the edition of 1676 where he writes:⁴

Humours may be retained in the body longer than is proper: Nature being unable to begin with their concoction and to end with their expulsion. They may also contract a morbidic blemish (labem) from the existing atmospheric condition. Finally they may act the part of poisons from the influence of some venomous contagion. From any of these causes the said humours become exalted into a substantial form or species of disease. . . . Putting all this carefully together we find strong reasons [firmis rationibus] for believing that a Disease is a species, equally cogent with those we have for believing a plant to be a species which springs from the earth, flowers and dies.

Sydenham then takes plague as his example of acute disease:⁵

for the sake of proving the truth of the above-made statement. . . . Is [plague] ought else but a symptom-complex that Nature puts into play in order that through the natural eliminations such as abscesses or some other form of eruption she may expel from the body those miasmatic particles that we have taken in along with the air we breathe. . . . Often she calls in the aid of fevers for the isolation of the foul [inquinatas] particles from the remainder of the blood and then by a further process she expels [either by diarrhoea, sweat, or by eruption] the particles thus isolated. . . . [By this violent motion of the blood,] it becomes an absolute necessity either that the death or recovery of the patient is determined rapidly. . . . for Nature must either expel the morbidic material [materiam morbidicam] by a crisis or become exhausted [fatiscat] in the struggle. This is the sort of disease we call Acute. . . . Occasionally however the parts that contain the Material of disease [Morbi Materia] are by their nature incompetent to determine a fever towards it and so unable to effect a full separation of the morbidic matter. Occasionally also the material fastens upon a part wholly unable to get rid of it at all. . . . as is the case with the morbidic matter impacted in the nerves of paralytics and with the pus in the cavity of a thoracic empyema. . . . Now in all these diseases the morbidic matter either never attains its proper coction or else attains it slowly and the diseases which arise from such material [hujusmodi materia] are properly called chronic.

Thus Sydenham distinguished the two groups of acute and chronic diseases. Acute diseases being his main interest, he further discusses their aetiology and defines an epidemic as follows.⁶ "Some [acute diseases] are engendered through occult and inexplicable changes in the atmosphere. These taint the human body [hominum corpora] but they depend upon the peculiar crases of our blood and humours only so far as these occult atmospheric influences have made an impression on them.

Such maladies continue their devastation during the continuance of the mysterious atmospheric constitution [illa aeris constitutione] but not longer. These diseases are called epidemics." From this passage we obtain our first clue as to what Sydenham had in mind when he used his well-known term, "epidemic constitution".

To define the atmospheric condition governing an epidemic constitution he carefully observed all the observable meteorological variables—what he called "manifest atmospheric changes of different years". In this he had the aid of a number of contemporary friends. Meteorological studies were made about this time (1663–1667) by his friend Robert Hooke using such new instruments as the thermometer, the anemometer, the hygroscope and barometer, all of which are included in Hooke's paper on "Making a history of the weather" (1667).⁷ Hooke there emphasizes the importance of correlating such observations with the effect of weather on our bodies; "what aches and distempers in the bodies of men; what diseases are most rife, colds, fevers, agues, etc." Christopher Wren⁸ also had embarked on a history of the seasons which included a "General description of the year whether contagious or healthful to men or beasts, with an account of epidemical diseases"; and in 1666 Sydenham's friend John Locke began his register of the weather which he did not abandon until 1683. Robert Boyle's studies on the air were by no means limited to the discovery of Boyle's Law. We shall return to them later.

The aid which Sydenham must have received from these superb observers enabled him to say in his chapter on epidemic diseases,⁹ "Much and diligently as I have observed the different characters in respect of the manifest atmospheric changes of different years with a view to detecting therein the reasons for the discrepancy amongst epidemic diseases I confess that I cannot find that I have proceeded one single inch on my way. Years that coincide in appreciable atmospheric characters differ in their diseases and vice versa."

Thus in his pursuit of the epidemic constitution he was led to the following remarkable conclusion,⁹ "This is how it is. There are different constitutions in different years. They originate neither in their heat nor cold, nor wet, nor drought, but they depend upon certain hidden and inexplicable changes within the bowels of the earth. By the effluvia from these the atmosphere becomes contaminated and the bodies of men are predisposed and determined as the case may be to this or that complaint. This continues during the influence of this or that constitution."

That this view of the production of morbid particles determining the constitution of epidemic diseases was no passing whim of 1676 is demonstrated by its appearance on several occasions. It is most clearly (and unexpectedly) expressed in Sydenham's *Treatise on gout* of 1683. Here he writes:¹⁰

Whether the inward bowels of the earth undergo various changes by the vapours which exhale therefrom so that the air is tainted, or whether the atmosphere be changed by some alterations induced by some peculiar conjunction of any of the heavenly bodies, it is a truth that at particular times the air is stuffed full of particles which are hostile to the economy of the human body, just as at other times it is impregnated with particles which disagree with the bodies of different species of brute animals. At these times whenever we draw in with our breath such noxious and unnatural miasmata, mix them with our blood, and fall into such epidemic diseases as they are apt to engender, Nature calls in fever as her usual instrument for expelling from the blood any hostile materials that may lurk in it. Such diseases are usually called epidemic.

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Similar views are again expressed in the *Schedula monitoria* of 1686¹¹ where Sydenham describes a new fever occurring in 1685 after the two years during the winters of which the Thames was frozen solid. Again he takes the opportunity of dissociating his new syndrome from any of the “manifest changes in the properties of the atmosphere which had taken place during the last two winters”, and repeats his conviction that “changes in a constitution arose from some certain secret and hidden alterations taking place within the bowels of the earth and pervading the atmosphere . . .”.

Here I would like to pause. I have, I hope, quoted Sydenham sufficiently to demonstrate that he did theorize, and that freely. I am aware that in presenting this theoretical aspect of Sydenham’s work I have contravened his reiterated declarations regarding the uselessness of hypotheses; and I have ignored his observations at the bedside. My justification for doing so lies in the simple fact that Sydenham did indeed write these passages and many more like them.

I feel that the problems raised by these theoretical statements of Sydenham can be resolved if we can find answers to two key questions: (1) Did Sydenham use this concept of morbid particles in obtaining those brilliant delineations of clinical syndromes upon which his fame rests? and (2) what was the origin of his idea of those “changes in the inward bowels of the earth” producing atmospheric morbid particles?

The short answer to the first question is yes; frequent examples are to be found in his clinical descriptions of fevers, for example smallpox. It was these that led Currie to refer to Sydenham as a “theorist on every page”. But it is best illustrated by an example which I am all the more happy to use since it also well illustrates how he focused his clinical acumen on the effects of treatment as well as diagnosis of disease. I refer to his use of quinine in the form of Jesuits’ bark for “agues” or “intermittent fevers” some of which were due to malaria.

In 1679 Sydenham replied to a question in a letter from Dr. Brady on the use of Peruvian or Jesuits’ bark in these words:¹² “Jesuits’ bark has been famous in London for the cure of intermittent fevers for upwards of five and twenty years and that rightly . . . A short time back, however, it went out of use being condemned on two grounds and those not light ones. Firstly when given a few hours before the paroxysm, as was the usual practice it would sometimes kill the patient at once. This happened to an alderman of London named Underwood, and also to a Captain Potter. Now this terrible effect of the powder, though rare, frightened the more prudent physicians, and that rightly.” The second reason for lowering the general opinion of the bark was the frequency of relapse. Sydenham faced both problems squarely—the danger to life and the frequency of the relapse. “Guard against these,” he wrote, “and I could cure the patient perfectly.” “In respect to the danger to life I laid it less to the bark than to its untimely [minus opportune] administration. During the days when there is no paroxysm a vast mass of febrile matter accumulates in the body. Now in this case if the powder is taken just before the paroxysm we check the method by which Nature gets rid of the morbid material so that being kept in it endangers life. Now this I thought I could remedy by checking the generation of any new febrile matter. Hence I gave the powder immediately after the paroxysm. This allayed the succeeding one. Then on the days of intermission I repeated it at regular intervals until a further paroxysm impended. Thus by degrees I brought the blood under the healing influence

of the bark." He adds that if the bark fails it is because "all that can remain must be the germ of the disease waiting for time to ripen". By keeping the blood "saturated with febrifuge" he solved this second objection to the use of bark, the occurrence of relapses.

Thus not only did Sydenham use his concept of "morbific matter" in describing his method of treatment with Jesuits' bark but he justified it on the grounds of preventing this morbific matter from generating afresh. In short he allotted to the morbific matter the property of life. How vividly his words recall to our twentieth-century mind the development of the rings, rosettes, and merozoites of the malarial parasite.

This example of Sydenham's use of the concept of morbific material, coupled with his above-quoted descriptions of fevers such as plague, the mode of production of empyema and paralysis, reveals that when Sydenham likened diseases to plant species he intended a deeper analogy than that merely between symptom patterns and botanical identification. He saw diseases as generating, growing and ripening in the body. And when he repeatedly spoke of Nature striving to restore the health of the patient by eliminating morbific particles, he saw himself as explaining and amplifying the Hippocratic concept of the *vis medicatrix naturae*.

There remains our second question; how did Sydenham get the idea of "changes in the inward bowels of the earth, which by their effluvia stuffed the atmosphere with these morbific particles?" That air might be the source of disease was one of the oldest medical concepts. It was clearly expressed in the Hippocratic work, *Airs, waters, and places*. But though the humoral qualities of hot, cold, moist and dry, as for example in marshy waters, are considered, there is no mention of morbific particles. The Hippocratic works on epidemics are strictly clinical and attribute disease to the patient's constitution rather than external agencies. The occurrence of telluric effluvia appears in Aristotle's *Meteorology*. Here vaporous and smokey exhalations from the earth are mentioned as responsible for the formation of metals and "stones in the earth". No medical importance is attached to them by Aristotle. Geber in the eighth century, though physician to the famous Caliph of the Arabian Nights, Haroun al Rashid, merely modified Aristotle's concept so that these terrestrial exhalations produced the sulphur, mercury, and salt of the alchemists; he does not mention the possibility of such exhalations producing disease. Galen, though he stressed the importance in disease of the qualities of heat, cold, wet and dry, in their actions on the humours, also acknowledging that air might be infected with putrid exhalations from corpses and marshes, did not talk of telluric vapours as their source.

The first clear description of this telluric factor that I have found is that of Mezeray reported by Boyle,¹⁸ according to which the great plague of 1346 "than which none had been observed more furious, began two years before in the kingdom of Cathay by a vapour which was most horribly stinking which broke out of the earth like a kind of subterranean fire . . . and infected the air in a wonderful manner." Such theories did not of course exclude the attribution of disease to such causes as the wrath of God and astrological conjunctions, factors favoured by Paracelsus. Even Fracastoro in 1546 with his intuition of live seminaria or seeds responsible for contagious disease declared that "premonitory signs occur in the heavens, air, water or the earth" leading to putrefaction. New interest in the atmosphere followed the appreciation of atmospheric

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pressure by Torricelli and Pascal. And Hooke (1664) studying the effects of refraction of air on the light rays emitted by the sun and moon, suggested that some of these changes may be due to terrestrial vapours rising from the earth into the air.

Not until we turn to the works of Robert Boyle do we find both Sydenham's terminology of "morbid particles", and their source of origin in the "bowels of the earth" clearly described. As early as 1660 Boyle¹⁴ had suggested that "air may be often generated as terrestrial particles minute enough to be carried up and down, and ascend into the atmosphere". In 1663 in his paper on the usefulness of natural philosophy Boyle writes,¹⁵ "He that considers what not infrequently happens in distempered bodies by the metastases of morbid matter, may enough discern that diseases that appear very differing may easily be produced by a peccant matter of the same nature". He elaborates the theme that a variety of symptoms so produced may equally well respond to "the same searching medicine endowed with qualities destructive to the texture of the morbid matter where ever it finds it." Boyle is applying his well-known corpuscular theory to medicine when he says¹⁶ "a greater proof of the power of steams upon the body may be taken from the propagation of infectious diseases, which being conveyed by insensible effluvia from a sick into a healthy body are able to disorder the whole economy of it . . . thus you will cease to doubt that corpuscles though so small as to be below the sense should be able to perform great matters upon human bodies." Perhaps the most important of Boyle's statements about morbid matter is,¹⁷ "And the cures that seem performed by Nature herself show what is possible to be done by natural means to evacuate the morbid matter or alter its nature". This sentence, published in 1663, is a paraphrase of the opening paragraph of Sydenham's *Medical observations* of 1676. In the same chapter Boyle suggests that the action of Jesuits' powder is "either to proscribe the morbid matter or so alter its texture as to make it harmless". Fulton in his *Bibliography of Robert Boyle* notes his recognition of the *vis medicatrix naturae*, quoting a passage from Boyle's essay on "Vulgarly received notion of nature", 1686, in which he asserts that Nature¹⁸ "watches for the Concoction of Peccant Matter before she rouses Herself up to expel it by a crisis."

Moreover, Boyle (and Sydenham) took the view that¹⁹ "the generality of former physicians have ascribed too much to the humours under the notion of their being hot and dry, cold and moist, or endowed with such other elementary qualities, and have taken a great deal too little notice of the saline and sulphurous properties of things." This reference to the sulphurous properties of things leads us to our second question regarding the source of Sydenham's ideas of changes in the bowels of the earth. Boyle says a great deal about this in his *Treatise on some unheeded causes of the insalubrity and salubrity of the air*. It is doubtful when this essay was originally written, as in the preface Boyle tells the reader that he lost the original notes and published some sheets that he found in 1685. Boyle also tells how he had always intended to devote special attention to the important subject of the salubrity and insalubrity of the air. He then writes,²⁰

Having observed that among the six principal causes of healthfulness or insalubrity of the air namely climate, soil, the situation of the place, the seasons of the year, the reigning winds, and especially subterranean steams. . . I observed there was one, viz. the last named about which I thought I could offer something that I had not met with in the books of physicians.²¹ . . .

This sixth and last thing upon which the salubrity and insalubrity of the air depends is the impregnation it receives from subterranean effluvia. . . . Some of them arise from the crust or superficial parts of the earth; the others have a deeper original ascending out of the lower parts and as it were, bowels of the terraqueous globe.

I know it is frequently observed and granted that marish grounds and wet soils are wont to be unhealthful because of the moist and crude vapours that the stagnating waters send up too copiously into the air. And on the other side dry soils are generally looked upon as healthy. But yet I think that besides what can be justly ascribed to the moist vapours or dry exhalations . . . in many places the healthfulness and insalubrity of the air may be ascribed to other sorts of effluvia from the soil . . .²³ . . . It is possible that though in a small compass of time the noxious effluvia that rove in the air may be too thinly dispersed to insinuate themselves in any considerable number at the pores of the skin yet by continual contact of the air which may last for many months or years there may be opportunity for a considerable number of morbid particles to insinuate themselves . . . and having once got entrance they may by the capillary vessels pass to larger vessels and so get into the mass of blood and by its circulation be carried to all parts of the body. . . . These observations make it probable that mineral exhalations may not only affect human bodies by being drawn into the lungs with the air they swim in, but insinuate themselves into the pores of the skin . . .²⁴ . . . I think it very possible that divers subterranean bodies that emit effluvia may have in them a kind of propagative or self-multiplying power. I will not here examine whether this proceed from some seminal principle which many chemists ascribe to metals and even stones, or, which is perhaps more likely, to something analogous to a ferment such as in vegetables enables a little sour dough to extend itself through the whole mass, or such as when an apple or pear is bruised makes the putrefied part by degrees to transmute the sound into its own likeness.

In a section headed—"It is likely that epidemical diseases are in great part produced by subterranean effluvia",²⁴ Boyle suggests that, "among the many various effluviating bodies that the terrestrial globe may conceal in its bowels some whose reeks ascend plentifully into the air may occasion an excess of heat, cold, moisture". He suggests that effluvia which are in themselves harmless may, "from their combinations" produce "corpuscles of a new and very morbid nature . . . which whether breathed in with the air in respiration or carried up and down by the blood or other liquors of the body may pass by other parts of it without doing them any harm and attacking this or that determinate part producing there some disease. The short duration of some epidemics may result from all the morbid exhalations ascending all at once or being rapidly dispersed." Boyle emphasizes that great quantities of subterranean noxious minerals exist, "many unknown to us, on which account it need be no wonder that new diseases appear, some of short some of long duration according to the duration of the production of the morbid effluvia."

These fragments of Boyle's corpuscular theory of disease supply the context in which Sydenham's frequent references to effluvia and morbid particles should be considered. Sydenham however, confesses that he was not as happy about his theory as his observations, saying,²⁵ "I have told the truth, the whole truth and nothing but the truth and if others will make similar observations they will add their voices to mine. In the meanwhile I ask the pardon and submit to the arguments of better judges than myself for all the errors of theory."

To my mind Boyle's account both clarifies and amplifies the significance of Sydenham's theory. So closely are the two accounts interwoven that it seems highly improbable that the two men developed them independently, particularly when we know that they were so closely associated as friends and neighbours. And there is one fascinating piece of evidence of their mutual co-operative work on infectious diseases. In his

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lengthy account of plague Boyle tells how he pursued the matter procuring and consulting “some uncommon authors”. It would appear that he gave one such “uncommon” work, *De peste*, by Joannes Franciscus de Ripa (1538), to Sydenham, for its title-page holds the unique distinction of bearing the signature of both men. Yet neither mentions the other in relation to this corpuscular or morbid particle theory of fever. Why not? I would suggest for the good reason that both of them appreciated that it remained hypothetical, lacked observational backing, and was “open to the censure of the great Bacon” whose principles of induction they both admired. Would it have been possible for them to extend their speculations to observational verification? Boyle himself made observations under the microscope in 1663, writing of²⁸ “A strange observation made in Italy by Panarola, a famous physician in Rome who by the help of an excellent microscope is said to have described in vinegar small living creatures which he takes to be worms . . . Causing a somewhat hollow bottom of pure crystalline glass to be fitted to my microscope I prosecuted the enquiry myself and at length was so lucky as to discover these little creatures . . . These swimming creatures be not exactly of a size, some seem slenderer than any sort of living ones . . . And I remember that having looked in a good microscope upon one of them and a cheese-mite much about the same time, the fish appeared so slender that we judge it not much thicker than one of the legs of the mite.”

Calculating from Hooke’s measurements of a mite, the thickness of one of its legs which Boyle claimed to be able to detect would be about 20 microns. He could not therefore have visualized such protozoal morbid particles as the malarial parasite. Sydenham, however, stubbornly saw no value in the microscope for revealing his morbid particles. “Nature” he wrote,²⁷ “performs her operations on the body by parts so minute and insensible that I think nobody will ever hope or pretend even by the assistance of glasses or any other invention to come to a sight of them and to tell us what organically texture or what kinde of ferment . . . separate any part of the juices in any of the viscera.” He even scoffed at the description by Power and Hooke of a mite revealed by the microscope as contributing “very little towards the discovery of the cause and cure of disease”.

Thus both Sydenham with his “generating” morbid particles, and Boyle with his corpuscular effluvia of “self-multiplying power and seminal principle” came to the very frontier of a germ theory of disease. But one cannot say they crossed it. Both realized that their theories were speculative and unverified by observation; both remained uninfluenced by Leeuwenhoek’s descriptions of little animals sent to Robert Hooke from 1676 onwards.

However the medical harvest was rich. For looking back one cannot but feel that Sydenham’s theory of infectious disease was close to a germ theory, so close indeed that it facilitated rather than obscured his fine clinical observations of disease patterns. It clearly often underlay his observations and designs of therapy as instanced here in the case of quinine. Indeed it would appear that his morbid particle theory was the hypothetical thread upon which his clinical pearls of diagnostic and therapeutic description were strung.

I think we are justified in retrospect in taking the view that Sydenham was not only brilliant in his practice of medicine but that with the aid of Robert Boyle his theory

of morbid particles was brilliant also, particularly if we may equate part of Boyle's concept of environmental pollution from the "bowels of the earth" with pollution from the bowels of modern industry.

REFERENCES

1. J. Currie, *Medical reports on the effects of water cold and warm as a remedy in fever and febrile diseases*, Liverpool, Cadell & Davies, 1797, p. 138.
2. O. Temkin, 'Die Krankheitsauffassung von Hippokrates und Sydenham in ihren "Epidemien"', *Sudhoffs Arch. Gesch. Med. Naturw.*, 1928, 20: 327.
3. *The works of Thomas Sydenham*, trans. by R. G. Latham, 2 vols., London, Sydenham Society, 1848-1850, vol. 1, p. 29. (I have used this work for all quotations from Sydenham, hereafter cited as "*Works*". Where I have differed in translation I have inserted the Latin text from Thomas Sydenham, *Opera universa medica*, Leyden, 1754.)
4. *Works*, vol. 1, pp. 18-19.
5. *Ibid.*, pp. 30-31.
6. *Ibid.*, p. 31.
7. R. Hooke (1667). In Thomas Sprat, *The history of the Royal Society of London*, London, R. Scot, 1702, p. 173.
8. C. Wren, *ibid.*, p. 312.
9. *Works*, vol. 1, p. 33.
10. *Ibid.*, vol. 2, p. 138.
11. *Ibid.*, pp. 190-191.
12. *Ibid.*, pp. 11-12.
13. R. Boyle, *Complete works in five volumes*, ed. by Thomas Birch, London, 1744, vol. 4, p. 291. (All quotations from Boyle are taken from this work.)
14. R. Boyle (1660), 'New experiments physico-mechanicall touching the spring of the air and its effects', *ibid.*, vol. 1, p. 36.
15. R. Boyle (1663), 'The usefulness of natural philosophy', *ibid.*, vol. 1, p. 550.
16. *Ibid.*, p. 536.
17. *Ibid.*, p. 482.
18. J. F. Fulton, *A bibliography of the Honorable Robert Boyle*, 2nd ed., Oxford, Clarendon Press, 1961, p. 113.
19. R. Boyle, *op. cit.* (ref. 15), p. 474.
20. R. Boyle (1685), 'Some unheeded causes of the insalubrity and salubrity of the air', *ibid.*, vol. 4, p. 276.
21. *Ibid.*, p. 277.
22. *Ibid.*, p. 281.
23. *Ibid.*, p. 282.
24. *Ibid.*, pp. 284-287.
25. Sydenham, *Works*, vol. 1, p. 26.
26. R. Boyle, *op. cit.* (ref. 15), p. 436.
27. Quoted from K. Dewhurst, *Dr. Thomas Sydenham*, London, Wellcome Historical Medical Library, 1966, p. 92.