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Epidemics and Infectious Diseases at the Time of Hippocrates. Their Relation to Modern Accounts*

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The chapters on Epidemic Diseases in the Hippocratic books soon will make strange reading. They will become unfamiliar to physicians of the Western world because of eradication of insect vectors, elimination of pathogenic bacteria and large scale immunizations. Moreover, chemotherapy is bound to change the natural course of these diseases. We no longer have the pessimistic outlook of Hippocrates that in most cases human nature cannot overcome these forces.[1] The Roman physician, Asclepiades once said that Hippocrates' books on epidemic diseases read like "a meditation on death".

The seven books on *Epidemics* would fill about 250 good sized printed pages. The first and third book are most likely from the hand of Hippocrates himself. One characteristic of these books is that diagnostic names were not assigned to the description of diseases even if numerous cases of the same clinical pattern were collected. The entire account resembles the diary of a travelling physician, who, after a days hard work, jotted down his observations on weather condition, location of cities, the particular

* This paper was given, in abbreviated form, as lecture at a Meeting of the Medical Historical Society of Western New York on January 24 1960 in Buffalo (N.Y.).

[1] Hippocrates, *Sämtliche Werke*, ins Deutsche übersetzt und ausführlich kommentiert von Robert Fuchs, München 1895, three volumes (later referred to as Fuchs 1, 2 or 3). Here: Fuchs 1: *Die kritischen Tage*, chapter II, 430 (also Kuehn, *Medicorum Graecorum opera quae extant*, Leipzig 1825, Vol. XXI: *Hippocrates*, T. 1, p. 149).

environment of the patients, and last but not least, gave brief notes of his clinical experiences. It appears very difficult and in many instances impossible to diagnose individual cases from such insufficient descriptions. But in some chapters the observations are somewhat summarized into new clinical entities. Identification of infectious diseases from these writings has to be made on the epidemiological observations, on account of type and length of the fever, on abdominal signs and symptoms, especially the size of spleen and liver, on the description of the appearance of stools and urine and the manifestations of skin and scalp. The assumption that the course of epidemic diseases has not changed much in this geographic area since Hippocratic times makes it easier to relate ancient accounts to modern descriptions of apparently similar cases. Great clinical acumen and thorough observation enabled HIPPOCRATES to outline the most important epidemic and infectious diseases by their symptomatology. We find in the Hippocratic books *On Epidemics* some descriptions of infectious diseases which represent localized pathology. Numerous authors have written extensively about and quoted from the texts such clinical pictures as colitis, erisypelas, diphtheria, mumps, meningitis, pulmonary tuberculosis (called Phthisis), puerperal sepsis and others. These chapters represent classical writings and make good reading. Other chapters represent generalized infectious diseases as tetanus, apparently cases of influenza, and other fevers which could be identified by their type and duration, as malaria.

Less agreement has been reached about other chapters. Some have not yet been identified with a known epidemic ailment. Of some a tentative diagnosis will be tried in this paper (Dengue, Undulant Fever). In other instances, interpretations diverging from previous literature will be discussed (Parotitis, Splenomegaly). Furthermore, descriptions of cases apparently representing Relapsing Fever and Typhus Exanthematicus have provoked considerable discussion. Some aspects of their clinical course which would support this diagnosis, have been neglected. This question will be discussed first because of the great historical importance of these diseases. If the diagnosis of typhus can be made plausible then we are able to recognize this disease as an important cause of the downfall of the might and wealth of Athens which, in connection with the Peloponnesian War and the spread of malaria through Greece, at this historical period, contributed to the decline of the dominant role of Greece in trade and culture.

Relapsing Fever

HIPPOCRATES spent much time on the isle of Thasos in the northern part of the Aegean Sea. During a local epidemic, he recorded the following case history of two brothers which is interesting because of a precise behaviour and duration of the fevers:

"They fell sick together at the same time and lay ill near the bungalow of Epigenes. The elder brother had a crisis on the 6th day, the younger on the 7th. Both suffered a relapse together at the same time after a remission of five days. After the relapse both had a complete crisis together on the seventeenth day. But the great majority (i.e., of the other patients during that epidemic) had a crisis on the sixth day with an intermission of six days, followed by a crisis after five days. Those who had a crisis on the seventh day had an intermission of seven days, with a crisis on the third day after the relapse."[2]

The writer mentioned some other combinations of the phases of this fever, but all add up to 17 days for the combined periods of fever and the afebrile interval. The text stated that none of those who recovered from the first attack of fever failed to suffer a relapse. At least this appeared the rule in most cases. Death occurred mostly on the sixth day of the illness. Nosebleed, diuresis and loose stools were considered as favorable prognostic signs. This epidemic was very wide spread and affected preponderantly young people. Its description resembles very much those of the modern Mediterranean type of Relapsing Fever, a louse born disease widespread in the Balkan area. Its tick born varieties are endemic in Africa, the Near and Far East and in the Western Hemisphere. The first phase of these fevers usually lasts four to seven days. A crisis ensues during which the temperature often abruptly drops more than 10°F. An afebrile interval of about five days is followed by a relapse which usually lasts five to seven days. The first two periods of fever and the interval often add up to a period of seventeen days. Cases have been published in which the first relapse ended on the eighteenth day, the second on the thirty-fourth day and another on the forty-fifth and sixty-ninth day. As in the Hippocratic account, these figures are almost exact multiples of the seventeen day period. Nosebleed, icterus and diarrhea, angina and parotitis are also mentioned as usual com-

[2] *Hippocrates*, with an English translation, W. H. S. JONES, London 1923, four volumes (The Loeb Classical Library, referred later as LOEB). Here: LOEB, vol. I, p. 177–179 (*Epidemics I*, 20 and 21).

plications. The mortality varies from 2 to 60% according to the state of nutrition and resistance of the patients.[3,4]

It is common knowledge that jaundice is such a frequent complication of recurrent fever that, during an epidemic, the differential diagnosis of other forms of jaundice is often overlooked, or at least very difficult to make. When observing the combination of jaundice with nosebleed, enlargement of spleen and liver and the typical pattern of the fever, the clinician usually can suggest a diagnosis of relapsing fever.

Modern authors reported that in severe cases, patients frequently die on the second day of jaundice in an acute state of collapse. This corresponds on the average to the seventh or ninth day of the illness, as mentioned by HIPPOCRATES.[5] But jaundice, so frequently recorded in the older writings, could also have been of viral or spirochaetel (Weil's disease) or other origin. Too many details, required by the modern observer, are missing for any further useful discussion. Also the higher incidence of relapsing fever in persons afflicted by malaria, tuberculosis or malnutrition may often have caused distortion of the classical picture. We even read in HIPPOCRATES that the epidemic in Thasos overcame many people who had been ailing previously for quite some time. Considering all these difficulties, the description of HIPPOCRATES compares fairly well with modern accounts of relapsing fever. An experienced author like MAC ARTHUR[6] also supports the assumption that this Hippocratic chapter fits the picture of louseborn relapsing fever. According to MAC ARTHUR, relapsing fever was not described again before the 18th century in Ireland.

Other diseases likely to be confused with relapsing fever are typhoid, typhus exanthematicus, malaria and dengue. It was possible to find relevant descriptions of these diseases in other chapters of the Hippocratic writings. These will be discussed now.

Typhus Exanthematicus

Relapsing fever has always been spread by overcrowding, famine and war. Close personal contact and lack of hygiene favored its transmission

[3] *Handbuch der Inneren Medizin*, ed. by BERGMANN-STAEHELIN, Berlin 1925, vol. I, part II, p. 1345 (clinical description of epidemics during World War I).

[4] M. MAYER, *Exotische Krankheiten*, Berlin 1929.

[5] FUCHS 2, p. 431–432 *(De Morbis II*, ch. 41: Another Fever), also KUEHN, *Hipp.*, t. 2, p. 249.

[6] WILLIAM MAC ARTHUR, *Brit. Med. Bull. XIII* (1957) No. 2, p. 146.

by the insect host. In a similar way typhus is transmitted by insects from person to person. In the second book on *Epidemics*, we find the account of an extremely virulent disease which seems to match fairly well the description of Typhus Exanthematicus. HIPPOCRATES wrote:

"About the Equinox, until the setting of the Pleiades (i.e., early in May), and during the Winter ... cases of phrenitis (i.e., fever with delirium) were most frequent ... and most of them were fatal. In summer, few cases occurred ... Right from the beginning, there was acute fever with slight rigors, sleeplessness, thirst, nausea, slight sweats about the forehead and collar bones, but in no case general (sweats). Much delirium, fears, depression, very cold extremities, toes and hands, especially the latter ... The extremities could not be warmed again, remaining livid and cold. The urine was scanty, dark and thin ... there was no hemorrhage from the nose in any case ... but only slight epistaxis. None of these cases suffered a relapse, but they died on the sixth day. The cases of phrenitis had all above symptoms, but the crisis occurred on the eleventh day."[7]

Modern accounts of Typhus match fairly well the Hippocratic description and permit a tentative diagnosis. The temperature remains usually high, but somewhat irregular until the tenth or twelfth day when more marked remissions introduce a rapid decrease of the fever. Normal temperature usually returns on the fourteenth day.[8] These short remissions of the fever may correspond to the observations of HIPPOCRATES that the exacerbations take place on the even days. The crisis often induces a severe vaso-motor collapse. Nosebleed is rare, as HIPPOCRATES wrote. Gangrene of the extremities can commonly be observed, a complication almost specific to typhus. HIPPOCRATES described it as an irreversible coldness and discoloration of the extremities. MACARTHUR writes that he has seen it very frequently.[9] He stresses that he has hardly observed it in any other epidemic diseases.

It is tempting to connect these case descriptions by HIPPOCRATES with the famous record of a plague which ravaged Athens shortly after the invasion by the Lacemdemonians. THUCYDIDES wrote in his *History of the Peloponnesian War* that an epidemic broke out a few days after the arrival of the enemy before Athens. Overcrowding had become terrible. HAESER

[7] LOEB, vol. I, p. 173–175 *(Epidemics I,* 18).
[8] R. C. CECIL, *A Textbook of Medicine,* 5th ed., Philadelphia 1941, p. 101.
[9] MACARTHUR, *op. cit.*

assumed that about 400,000 people were herded together in Athens in 10,000 small houses. THUCYDIDES described, in a manner more artistic and dramatic than clinical, many symptoms which are compatible with the diagnosis of typhus. He also stressed with great emphasis the occurrence of loss of fingers, toes and genitalia due to gangrene as mentioned above in the Hippocratic account. The extensive chapter of THUCYDIDES cannot be quoted here.[10] Interestingly, he mentioned that physicians died in greater numbers than the average population. This is very typical of typhus since physicians are especially exposed to infestation through lice or their infected excrements in the bedding of patients. It also impressed THUCYDIDES that relapses hardly occurred. The only care which the patients were able to obtain was given by convalescents. The other people, frightened away, left their friends and families unattended. Therefore, the mortality was extremely high. Death occurred mostly on the seventh or eighth day of illness. It matches the description by HIPPOCRATES that an acute aggravation of the illness took place on the seventh day.

It remains strange that HIPPOCRATES does not mention the typical rash. But accounts of epidemics of typhus have been published during this century in which at least 20% of the cases occurred without rash.

THUCYDIDES mentioned the outbreak of small ulcers and pustules on the skin of the diseased. These manifestations have given much cause for discussion. Even an unknown type of disease has been assumed to explain this feature of the epidemic. Such an hypothesis is unwarranted. In a state of malnutrition, the typical exanthema of typhus could become severely hemorrhagic and of brownish color. Such malnutrition would be connected with vitamin C-deficiency and scorbutic symptoms can be expected. In fact, the bleeding from throat and tongue, as mentioned by THUCYDIDES, would fit this picture. The unnatural fetid breath of these cases would be caused by the ulcerations and hemorrhages from the gum, a main symptom of scorbut. Even nowadays bleeding gums are often the only manifestation of scorbut during infectious diseases in the tropics (20%).[11] Such scorbutic complications lead to early fatalities. Discrepancies between the cases described by HIPPOCRATES and the account of THUCYDIDES may be due to local variations. The cases of Typhus Exanthematicus in the beleaguered

[10] THUCYDIDES, *The Peloponnesian War*, Modern Library, Coll. Ed., New York 1951, p. 110 ff.

[11] *J. Amer. Med. Assoc. 168* (1958) 1570.

city were more likely to develop scorbut than those in the islands where nutrition probably was normal.

Many previous writers have considered this epidemic as bubonic plague, ergotism or other diseases. The analysis does not bear out these opinions. MacArthur also makes the assumption that this epidemic was typhus.[12] It appears therefore, justified to identify the so-called plague of Athens and the previously quoted description of HIPPOCRATES as accounts of the same epidemic.

There is no proof for the story that HIPPOCRATES was called to Athens during this great epidemic. No indication is given in the Hippocratic texts as to where he made these observations which we tried to correlate to the description by THUCYDIDES. GALEN mentioned the services of HIPPOCRATES during the great plague of Athens. He considered the description of the plague by the historian as a layman's job whereas HIPPOCRATES' description of the same disease appeared to be more accurate. This explains to GALEN the discrepancies of both accounts.[13] According to THUCYDIDES, the plague invaded the Greek mainland several times in subsequent years. The Athenian epidemic had its origin in Ethiopia and Egypt. From there, it spread through Northern Africa and the Aegean islands, before it reached the Greek mainland. HIPPOCRATES would have been able, in any case, to observe the epidemic even if he had not been present in Athens.

Interesting also is the observation of THUCYDIDES that the epidemic affected birds and domestic animals. We know that Typhus Exanthematicus can be transmitted experimentally to rats and rabbits. The Athenian plague was apparently also complicated by a type of dysentery. This would not, however, be essential for the diagnosis. Intestinal superinfection has been observed in many instances of typhus.

This leads us to the discussion of another superinfection of common epidemic diseases, as described in the Hippocratic text.

[12] MACARTHUR, *op. cit.* Also: F. v. BORMANN, Attische Seuche 430–426 B. C., *Z. Hygiene u. Infektionskrankheiten 136* (1953) 67–84.

[13] *The Genuine Works of Hippocrates*, translated from the Greek with a preliminary discourse and annotations by F. ADAMS, London, The Sydenham Soc., vol. I, p. 13, ref. to GALEN, *De Difficult. Respir. II*, 7.

Parotitis

Inflammation of the parotids in connection with epidemic and infectious diseases must have been a common occurrence in antiquity. HIPPOCRATES frequently mentioned it. We read in the chapter which follows the description of recurrent fever: "Painful swellings near the ears in some cases, neither subsided nor suppurated when the fever ceased with a crisis. The swellings were cured by bilious diarrhea or dysentery (not to be construed as a definition of a specific infectious disease as it is nowadays) or a sediment of thick urine."[14] The connection of these complications with the recession of parotitis is hard to understand. But it does not appear right to quote only such parts of the passages which fit our ideas. In another instance Hippocrates spoke of the complication of fevers by "swelling about the ears that grew smaller and signified nothing."[15] Also, in his book *On Crisis*, HIPPOCRATES related that during certain diseases the parotids swelled up without suppurating. The parotid is not specifically mentioned but again circumscribed as 'the area along side the ear.' If the swelling persisted during the time of the crisis a relapse of the underlying disease was considered imminent. These and other passages in the Hippocratic writings refer to secondary parotitis. Mumps were well known to HIPPOCRATES as a separate disease. His classical description of mumps even mentioned the complication by orchitis.[16] The writer of this chapter also used the same expression as mentioned above ('alongside the ear') in his description of mumps. The existence of the parotid gland, was probably still unknown.

Nowadays parotitis as a complication of internal diseases is not uncommon. Poor nutrition favors its appearance. Painless swelling of the parotids has been observed among the poor and malnourished peasants of the Nile Valley. Two-thirds of these were suffering from Pellegra, a fact which gives us a measure of their debility.[17] Parotitis also has been found in non-pellagrous malnourished Africans,[18] in Germany after the last war in prisoner-of-war camps, and even among American Indians in 1955[19] as a sign of malnutrition. Undoubtedly, longstanding alimentary deficiencies compli-

[14] LOEB, vol. I, p. 177 *(Epidemics I,* 20).
[15] LOEB, vol. I, p. 161 *(Epidemics I,* 9).
[16] LOEB, vol. I, p. 149 *(Epidemics I,* 1).
[17] I. B. BRICK, *Ann. Int. Med. 49* (1958) 1005–1008.
[18] *The Lancet 1958* (Nov. 8.) 1005–1008.
[19] BRICK, *op. cit.*

cated many acute infectious diseases in antiquity. Measured by our standards, the duration of most infectious diseases in ancient times was very extended, thus aggravating the deficiency states. The dehydration of extended fevers causing parotitis correlates well with modern observations that parotitis occurs as a complication of the vigorously pursued diuresis (by modern drugs as diuril or mercurials).[20] Dehydration after surgery in debilitated, mostly older people has recently been found as the cause of staphylococcus parotitis.[21]

Dengue

When HIPPOCRATES was in Perinthos, a city of Northern Asia Minor, he observed during the summer a widespread febrile epidemic disease.[22] This appears to have been an occurrence of Dengue. According to modern descriptions, Dengue is an endemic, insectborne disease of the Near East which often assumes epidemic character, predominantly in the summer. Severe diarrhea and epistaxis are characteristic of the beginning. Temporary relief from the fever occurs on the second or third day. An exanthema usually starts on the fifth day in the form of small elevated granules which do *not* itch and subsides with the fever on the ninth day. The appearance of this exanthema might show great variations.

HIPPOCRATES made the following observation which appears to match this description. The patients which he observed during an epidemic had indigestion with colorless, thin watery, sometimes foamy stools, but did not vomit. Respiration was fast (i.e., a sign of high fever), epistaxis occurred. Liver and spleen appeared not enlarged. Sweats which he observed in the early phase may correspond to the temporary relief of the fever on the second or third day, as mentioned above. An eruption broke out between the seventh and ninth day which appeared similar to small millet grains or flea bites, but did *not* itch. The rash lasted until the crisis occurred. Most patients recovered after about two weeks when sweats led to the crisis and recovery. Relapses were rare. Parotitis was frequent.

The similarities between the Hippocratic text and the modern descriptions are suggestive that the epidemic in Perinthos may have been Dengue

[20] *New England. Med. J. 260* (1959) 1079.
[21] *New England Med. J. 259* (1958) 1249.
[22] FUCHS 2, p. 172–173 *(Epidemics II,* 3, I).

fever. It remains strange that HIPPOCRATES observed the typical, almost diagnostic rash, only in women. We do not know of any epidemic in which a rash appears only in female patients. HIPPOCRATES also did not mention the severe pain in joints and muscles so characteristic of the disease. But one should be reluctant to assume another hypothetical or unknown disease to explain such possible omissions in the text.

Undulant Fever

HIPPOCRATES observed during a summer and autumn, probably again in Thasos, many continuous, but not violent fevers. He wrote that these patients had been ailing for a considerable time, without suffering great distress in any particular manner. Their bowels were not disturbed; appetite was not lacking. It was quite possible even to give them food. They did not exhibit shivering fevers, but had only light sweats. The attacks of fever were variable and irregular. The earliest crisis appeared about the twentieth day, in most cases about the fortieth, though in many it came around the eightieth day. In some cases, this illness terminated after an irregular course, without a typical crisis. In the majority of the cases the fevers relapsed after brief intervals or became so protracted that they lasted even through the winter. The fevers did not prove fatal unless people were previously affected with consumption. Most patients withstood it well.[23]

HIPPOCRATES almost suggests in the description of this epidemic the designation 'undulant': "In the majority of these cases, the fever relapsed after a brief interval, and after the relapse a crisis occurred at the end of the same period as before."[24]

Modern observations confirm that the first period of fever usually subsides after two or three weeks (i.e., the 20 days of HIPPOCRATES) and that relapses are frequent, but not as severe as the first attack. The prognosis is usually favorable. Again we are tempted to correlate a well-known epidemic disease with some degree of certainty with one described by HIPPOCRATES because of the course of the fever. HIPPOCRATES, like other physicians of antiquity, did not give specific names to most diseases although they were well able to identify many infections as separate entities. Centuries later numerous names were given to some of these diseases. Much

[23] LOEB, vol. I, pp. 151–153 *(Epidemics I,* 3).
[24] *Ibid.*

confusion arose from this habit. Before the cause of undulant fever was recognized by BRUCE in 1886, accounts of this disease designated them with terms which remind us of the Hippocratic style: as bilious remittent fever of the Mediterraneum, Cretan Fever, Neapolitan Fever, and other names according to the prevailing location of epidemic or observer. Others choose their titles by symptoms: febris sudoralis, or gastric or bilious remittent fever, Mediterraneum phthisis (a real Hippocratic expression), or simply: remittent or continued fever.[25]

We have to give credit to HIPPOCRATES in that he refrained from giving futile denominations to diseases whose causes were not understood. There is more wisdom than one would first assume in the advice of the ancients "to understand the symptoms, but to disregard names."

The history of undulant fever presents the typical process of *evolution of a clinical concept:* First its development from a single or unusual observation to the recognition of a new disease entity. Secondly the recognition of the anatomical seat of its predominant pathology; and thirdly, the discovery of its essential causative agent. It took a very long time until undulant fever was understood as a specific disease. Names as 'Mediterranean Fever' and 'Septicemia of Malta' represent only a tentative identification of this malady. It is worth mentioning that the names just mentioned were taken from the title of a paper written in 1908 and from CECILS textbook[25,26] although they sound as if they were coined by HIPPOCRATES or SYDENHAM. Ten years later, in 1918, the picture suddenly changed, when EVANS recognized the identity of Bangs organism (discovered in 1897) with the micrococcus melitensis (isolated by BRUCE in 1886). It then became obvious that these apparently separate syndromes represented only one disease. This achievement fulfilled a general postulate already set up by HIPPOCRATES. He was aware that the cause of a disease should not be assigned to an occasional or unusual event near the day on which the disturbance arose since this would keep us ignorant of the real truth. He insisted on investigating the alterations of the humors and the changes of their functions (in Greek: dynameis), of their intensity and strength, to use his expressions. He even asked for examination of those structures of the body whose appearance and consistency had been altered by the disease.[27]

[25] J. W. H. EYRE, *The Lancet 1908* (June 13). 1677–1678.
[26] CECIL, *op. cit.*, p. 282.
[27] LOEB, vol. I, p. 57 *(Ancient Medicine XXI).*

The writings of SYDENHAM (1624 to 1672), who revived the Hippocratic method of clinical observation, reflect a great resignation of ever finding the real cause of most epidemic diseases: "A search into efficient, or material causes is doubtless one of the most idle and impertinent uses we can make of the powers of our understanding; for as they lie far beyond the reach of our senses, we cannot but fail in the attempt." Recommending a purely empirical, clinical attitude in diagnosis and therapy, he continued: "Would it not be acting more prudently ... rather to apply ourselves to mark their effects and operations, so as to draw from thence a set of directions which ... if judiciously applied ... serve to conduct us with safety and security in most occasions?"[28] Until the advent of antibiotic we did not advance much farther, especially not in the case of undulant fever.

Splenomegaly (Malaria or Bilharzia)

The spread of malaria through Greece and its colonies, especially Sicily, during the 5th century B.C., has been described by competent authors.[29] In this paper, we will discuss only the problem of excessive splenomegaly, a frequently encountered syndrome in areas of endemic malaria. It has been assumed that malaria had spread northward from its original abode, most likely located in the Nile Valley. It is known that EMPEDOCLES drained the swamps in the surroundings of Agrigentum, a city of Southern Sicily, in order to free this important harbor from an endemic fever. This event took place during the lifetime of HIPPOCRATES, about 450 B.C.

Identification of acute malaria from Hippocratic texts is based on frequently mentioned descriptions of fevers which appear to be characteristic of this disease. Chronic untreated cases of malaria may be free of fever and often represented only by splenomegaly with anemia. The occurrence of this syndrome in districts located near brackish water was frequently observed by the ancient physicians. Lack of familiarity with the specific causes made them confuse malarial splenomegaly with another type also connected with the life in swamps, canals or inundated areas. This is Bilharzia, a type of Schistosomiasis, known to have been endemic in Egypt from ancient times since the parasite was recovered from mummies.[30]

[28] *The Entire Works of Dr. Sydenham,* by J. SWAN, London 1763, p. 49, Note O (Chapter V: Of the Internal Fevers of the Years 1661–1664).

[29] See Bibliography in G. SARTON, *A History of Science,* Cambridge 1952. vol. I, p. 341, n. 46.

[30] F. JONKHEERE, *Une Maladie Egyptienne,* Bruxelles 1944.

In Egypt, the water of the irrigation canals has always been used for bathing and drinking. The parasite can enter the host either through the intestinal mucosa or the intact skin, even after very short contacts. Although the Near-Eastern type of Schistosomiasis affects predominantly the urinary tract with excessive formations of incrustations and stones in the bladder, considerable enlargement of the spleen as the only symptoms is not uncommon. Unfortunately, HIPPOCRATES does not indicate where he observed this syndrome. It appears fairly certain that he came to Lybia on one of his far flung trips but we have no evidence that he had been in Egypt. In view of the close trade connections with Greek settlements in northern Egypt it is quite likely that he may have seen patients arriving from that infested area.

It is of course impossible to decide from the ancient texts if the following passages in the book *Airs, Waters and Places* represent a description of splenomegaly due to chronic malaria or Bilharzia or any other cause. A modern observer would refuse to decide this clinical problem without the aid of a laboratory. HIPPOCRATES wrote: "Such waters as are marshy, standing and stagnant must in summer be hot, thick and stinking, because there is no outflow, and as fresh rainwater is always flowing in and the sun heats them they must be of bad color, unhealthy and bilious. Those who drink it have always large smooth spleens, and hard thin abdomens, while their shoulders, collarbones and faces are emaciated. The fact is that their flesh dissolves to feed the spleen, so that they are lean. This malady is endemic both in summer and winter. In addition, the dropsies that occur are very numerous and very fatal. For in summer, there are epidemics of dysentery, diarrhea and long quartan fever ... babies are big and swollen ... and become emaciated and miserable ... men are subject to enlarged veins and ulcers of the legs ... Such waters, I hold, are absolutely bad."[31]

It is difficult to escape the impression that he was speaking of Egypt and therefore, of Bilharzia since he specifically connected the occurrence of "stones, kidney disease, stranguria (i.e., the difficult passage of urine) and swelling of the inguinal region" with the drinking of water from very many sources. He spoke of especially "large rivers into which other rivers flow, or lakes fed by many streams of various sorts." He intimated the

[31] LOEB, vol. I, p. 85. The translation of the word 'gastēr' has been changed to 'abdomen' for clinical considerations (see LIDDELL-SCOTT, *Greek-English Lexicon:* gastēr: paunch, belly) also the word 'memuomenos' to 'smooth' (ref. spleen).

Nile when he spoke of the use of foreign waters which came from extremely far distances. Interestingly, he mentioned an observation typical for the Nile Valley "that such waters leave a sediment of mud and sand, and that their drinking causes the diseases mentioned before."[32] Thus HIPPOCRATES recognized the connection of splenomegaly with the presence of stagnant water and, also made the mode of infestation understood. This proves again his astounding clinical acumen. Nowadays, on purely clinical evidence, a differentiation between malarial and parasitical types of splenomegaly is hardly possible. But HIPPOCRATES could not even presume a parasitical etiology.

These difficulties connected with the purely clinical symptomatic description of splenomegaly by HIPPOCRATES remind us of similar problems which turned up in the definition of *Banti's disease.* This ailment represents splenomegaly with anemia, complicated in the final stage by ascites. Only during the past decades a nosologic classification and understanding of many splenomegalies with ascites and anemia has been achieved. Yet a group of such cases has remained, which we still diagnose as Banti's disease. They are only a syndrome, their cause remaining unknown. The discussion of clinical cases of splenomegaly illustrates again the previously mentioned fundamental clinical problem. Historically, we find first the description of the syndrome. This was how HIPPOCRATES as well as BANTI proceeded.[33] The latter had the impression that behind the syndrome, called after him, several diseases were hidden. They could even not be differentiated by their microscopical picture. In his paper on *Splenomegaly with Cirrhosis of the Liver,* published in 1894, he admitted that he could not find the causes in order to explain his observations. He wrote: "It is impossible either to affirm or to deny the identity of two diseases on the grounds of their symptoms or their anatomical changes. Do not, for instance, miliary tuberculosis and typhoid fever sometimes present an absolutely identical symptomatology? May not both the staphylococcus aureus and the Eberth bacillus produce an abscess?" And further: "In order to differentiate or to identify two morbid conditions with strict regard to scientific principles, we must know the determining causes of both, and of these, we know nothing either in respect of splenic anemia or sple-

[32] LOEB, vol. I, p. 95.

[33] G. BANTI, Splenomegaly with Cirrhosis of the Liver, *Med. Classics 1* (1937) 907–913 (published in 1894).

nomegaly with cirrhosis ... But in spite of the fact that we cannot exclude the possibility of infectious origin, I am inclined to believe that, since there are no other causes evident, such an assumption would seem quite reasonable." Since BANTI did not find the causal factor, he could not proceed beyond the description of the syndrome. Clinically splenomegalies of malaria, Bilharzia or other causes have many important clinical aspects in common regardless of their different etiologies. Therefore, the description of HIPPOCRATES appears as a similar valuable and correct contribution to clinical medicine, illuminating for the first time the existence of an important syndrome. There is, of course, besides this similarity no connection between the writings of BANTI and HIPPOCRATES. This resemblance becomes even more striking. When BANTI wrote that "the morbid causes exert at once their action on the spleen ... penetrate into the blood and thus determine progessive anemia", it is not very different from the previously quoted Hippocratic text "that their flesh dissolves to feed the spleen."[34] And when BANTI speaks of altered biochemical processes due to toxic substances, he does not give more information than HIPPOCRATES' suggestion of altered humors. Both BANTI and HIPPOCRATES remained in the dark about the real cause of the syndromes which they described so lucidly. It was not primitive thinking which obscured the further development of the Hippocratic concepts of this disease. Only the lack of anatomical and microscopical techniques prevented deeper understanding and classification. HIPPOCRATES already had stressed the knowledge of anatomical facts as the basis of correct thinking. Considering the study of the human body as a part of natural science, he told his disciples that "a physician should be at great pains to know about natural science, if he is going to perform aught of his duty."[35] His advice was not fruitless when one remembers the considerable number of anatomical treatises in the Hippocratic collection and, later, in the writings of ARISTOTLE.

If we speak of anatomical understanding by the ancient physicians, it refers only to their consideration of an organ as the predominant seat of the disease. Any further understanding of the disturbed structure or function of such organs was impossible in Hippocratic times. Yet the ancients attempted to explain the affliction of a particular organ by a disturbance

[34] G. BANTI, Splenomegaly with Cirrhosis of the Liver, *Med. Classics 1* (1937) 913–927 (published in 1898).

[35] LOEB, vol. I, p. 53.

of its composition, by a faulty mixture of the hypothetical constituent humors. As causes of this alteration, they assumed the influence of extraneous factors such as climate, water, air, weather, locality, the composition or spoilage of food and other causes. The same explanations were also applied to the attempted understanding of epidemic diseases. The ancients did not consider an infectious mode of transmission in the modern sense. We associate the word epidemic with the idea of micro-organisms, whereas the Greeks understood the word epidemic to mean only that this particular ailment 'stayed in one place' was 'staying among the people' ('epi' meaning 'in' and 'demos': the people). That this was the ancient meaning follows from the fact that many chapters of the seven books on *Epidemics* are devoted to discussion of various internal diseases, which we would never include in the class of 'epidemic diseases'.

Yet, even in the modern New Century Dictionary, the word 'epidemic' is defined in the same sense, as a disease only temporarily prevalent in a locality. Its author does not connect the term with the idea of infection. Similarly in the previously quoted *Handbuch der Inneren Medizin,* the contemporary author even spoke of epidemics of scorbut amongst prisoners or entire populations. In fact, this word as so many others, is commonly used by us in an incorrect manner. What HIPPOCRATES called epidemic diseases were just frequently encountered ailments. Most of these were actually infectious or most likely of infectious origin in the light of modern knowledge. This is especially true for the first and third books on *Epidemics,* the only of the seven treatises of this title definitely attributed to HIPPOCRATES himself. An historical analysis of the Hippocratic concept of infection will lead us to the understanding of the ideas, different from ours, which the Greeks connected with those diseases which we now consider communicable.

The Ancient Concept of 'Infection'

The word infection has been derived from the Latin word 'inficere', which has the meaning of dying, tainting, and only much later of contaminating.[36] In its medical use, it expressed a kind of putrescence associated with bad odors. The Greek word 'miasma' equally denotes tainting and defiling. Its

[36] O. TEMKIN, *An Historical Analysis of the Concept of Infection,* Studies in Intell. History, John Hopkins Press, 1953, pp. 123–147.

later use suggests unwholesome or bad air. Translated into Italian, this is mal-aria, or shortened 'malaria'. Nowadays this old expression designates the cause of an infectious disease due to plasmodium, carried in the body of the mosquito travelling from the swamps through the surrounding air. No better example could be found to illustrate the faulty use of ancient names for the designation of diseases in this age of science. Names remain like superstitions. Their original meaning gets lost; the word coined for a specific purpose is used thoughtlessly or assumes an entirely new meaning. We must now carefully inquire into the different ideas which the ancients connected with a word, which expresses to us only the influence of bacterial or viral contamination.

The concept of miasma and defiling arose from the ancient belief that devine influence or the revenge of the gods brought about sickness. The most famous examples are the plagues of Egypt at the time of the exodus of the Jews and the pestilence which afflicted the Greeks at the shores of the Trojan plain when they had insulted Apollo's priest. Such divine interference in bodily manifestations has been denied and definitely refuted by HIPPOCRATES who was searching for natural causes or explanations in connection with the arising new science. In order not to antagonize the religious feelings of his contemporaries, he declared all diseases as equally devine. Nobody wanted to deny that nature with all its goods and ills was the creation of the gods.[37] The main characteristic of his writings is the attempt to objectivity and denial of superstitious beliefs. One can only appreciate this fully against his historical background: the crude Egyptian medicine and the superstitious lore and customs of his own people. Ancient beliefs, dating before HIPPOCRATES, relying on amulets and votive offerings, are still in use today amongst the uneducated people of the same area. It is rather unlikely that the medical aspect and the superstitious meaning of the idea of contagion were strictly separated even in the medical writings of the Hippocratic times. This lack of clear thinking delayed the separation of scientific observations from their explanation as due to supernatural influences. On reading the much later papers on contagion by FRACASTORO (1482 to 1553) and MEAD (1673 to 1754), one wonders why the sharp logical thought of the ancients was not able to come to a similar distinction between observations and wishful interpretation. This is particularly strange, since the facts observed by the Renaissance physicians must have been very

[37] LOEB, Vol. II, p. 151.

similar to those made by the ancients, as for instance, the transmission of infectious diseases by imported merchandise and the like.

It has been said the Greek idea of contamination arose from the Egyptian observation of worms as a cause of infectious or other diseases and that the Egyptians even may have observed the parasite of the endemic hematuria caused by Schistosomum. But SAUNDERS writes[38] that the ancient Egyptians assumed that disease gave rise to formation of worms in putrified matter and that they did not recognise the parasites as cause of diseases. This supersedes the opinion of other writers that the Egyptians saw in the worms the etiological factor.[39] Therefore elimination of stagnant residues and foul gases was considered as contributory to the termination of diseases,[40] especially in abdominal ailments. It is rather likely that the Egyptians did not give much thought to the possibility that these 'exhalations' could convey a contagion to other people.[41] Relying on their idea of obnoxious residues in the body due to remnants of food or stagnating bodily humors ("perittoma") they favored the venesection. Thus, the age old concept of excess residue led to the invention of blood letting and enemas. The two procedures were considered equivalent.[42] Even nowadays monthly strong purging is a widespread custom in Egypt and is done in the hope of keeping illness away.

We know that the Hippocratic physicians knew about the existence of tape worms and ascaris. But the few revelant passages in the texts do not bear out that they considered these as cause or offspring of these ailments.[43] Apparently, this problem did not interest them greatly.

The great variety of infectious diseases which HIPPOCRATES was albe to distinguish is astonishing. According to the opinion of the physicians of this period, the most important mode of transmission of these and even of other diseases, was by distance, through air and by breathing. This has clearly been expressed in the Hippocratic writings. We read: "that illness is often caused if the air (pneuma) has become deteriorated by some miasma ... If the pneuma is contaminated by exhalations (miasmata) which are

[38] Personal communication by Dr. J. B. DE C. M. SAUNDERS, University of California.

[39] M. NEUBURGER, *Geschichte der Medizin*, vol. I, Stuttgart 1906.

[40] R. O. STEUER and J. B. DE C. M. SAUNDERS, *Ancient Egyptian and Cnidian Medicine*, University of California Press, 1959, pp. 8 and 79.

[41] *Ibid.*, p. 62.

[42] *Ibid.*, p. 6.

[43] NEUBURGER, *op. cit.*

damaging to human nature, people become ill."[44,45] The further text suggests the possibility that these physicians had even noticed the occurrence of airborne infections of man and beast and that this may not have been only a guess based on mythical or mystical analogies. "When the air has become ill adapted to some other species of animal then they fall sick."[46] In the treatise *On the Nature of Man* HIPPOCRATES or one of his disciples[47] wrote: "When an epidemic of one disease is prevalent, it is obvious that the cause is not the regimen but what we inhale and that this is obviously charged with some unhealthy discharge (apocrisis)."[48]

GALEN, who earned great contempt for fleeing from Rome during an epidemic, wrote that the great plague in Athens may have been caused by some air borne agent: "It may be the case that owing to the continuity of the air, some putrid miasma flows from Ethiopia and is the cause of fever in those whose bodies are susceptible of being affected by it."[49] He overlooked the fact that it broke out in the crowded quarters of the Athenians whereas the Lacedemonians escaped because they abandoned the siege of Athens immediately after they had heard of the epidemic inside the fortified walls of city and harbor.

We are unable to discern from the writings of HIPPOCRATES if he considered the contagion carried by the air as a physical or an animated principle. Even this distinction may be wrong since many of the contemporary philosophers considered the animating forces of the soul as a physical principle: a very fine element, like the other four elements. Even modern bacteria and viruses are not inanimate physical principles *sensu strictiori*. The author of the book *Problemata* which has wrongly been attributed to ARISTOTLE, but is to be found in the editions of his collected works, wrote that people who come into contact with patients suffering from scurvy, scabies and impetigo inhale such air and become diseased because the inspired air is corrupted.[50] Scurvy apparently was considered, even as late as the 17th century, as an infec-

[44] FUCHS 1, p. 444 (Breaths. ch. VI).

[45] LOEB, vol. II, p. 235.

[46] *Ibid.* as 44 and 45.

[47] A. CASTIGLIONI, *A History of Medicine*, New York 1947, 2nd ed., translated by E. B. KRUMHAAR, p. 153.

[48] FUCHS 1, p. 202 (Nature of Man, ch. X); KUEHN, t. 1, p. 361.

[49] Quoted from SAUNDERS, *op. cit.*, p. 63.

[50] *The Works of Aristotle*, translated ed. by W. D. ROSS, Vol. VII: *Problemeta* (by E. S. FORSTER), Oxford 1927 (will be quoted as 'problemata'), here: 887 A 31.

tious disease, possibly because of the sudden outbreak amongst large groups of people and its complication by ulceration, bleeding and secondary infections of the gums.

ARISTOTLE, shortly after HIPPOCRATES, considered such cases as infectious because they produce a heavy discharge from the affected surfaces.[51] Thus, he actually did not speak of air as the only medium of transmission. But he did not clearly differentiate between infectious and, as we call them, internal diseases. He ponders: "Why is that those who come in contact with phthisis or ophthalmia or scurvy become affected by them, but there is no contagion from dropsy or fever of apoplexy and the rest."[52] He concluded that in ophthalmia the eye assimilates, or absorbs to itself, what it sees. He simply suggests herewith that the assumed emanation which carried the visual image from the external object into the eye[53] and which is of the finest corpuscular nature, may also carry the contaminating agent.— He states that the contagious product of cases of phthisis may be contained in the breath: "The breath of these patients getting weak and labored, becomes corrupted as in plagues. Whoever comes into contact with those suffering inhales their corrupted breath and so, himself, contracts the disease." In his deductive approach, ARISTOTLE missed the correct conclusion from observations of transmission of diseases by personal contact although he actually came near the solution of the problem. ARISTOTLE was more concerned with classifying his observations in a prearranged system of concepts than being guided by experience, at least in the medical field. This becomes dramatically obvious in the following passage: "Why is it that those who come into contact with certain disease become affected by them, but no one ever becomes healthy by contact with health? This is because disease is a state of movement while health is a state of rest."[54] Thus, preconceived ideas and words, assuming the meaning of philosophical concepts and fallacious truths, precluded simple and straightforward interpretation, even for such a keen observer as ARISTOTLE. Even later in antiquity, the infectious character of diseases was actually never recognized, or even known,[55] although it was often suspected.

[51] *Problemeta*, 887 A 36. [52] *Ibid.*, 887 A 22.

[53] R. SIEGEL, Theories of Vision and Color Perception of Empedocles and Democritus; Some Similarities to the Modern Approach, *Bull. Hist. Med. XXXIII* (1959) 145–159.

[54] *Problemata*, 886 B 8.

[55] E. W. GOODALL, On Infectious Diseases and Epidemiology in the Hippocratic Collection. *Proc. Royal Soc. of Med. London 27* (1934) 525–534.

HIPPOCRATES was free from similar philosophical generalisations and confined himself to observations. He wrote that an active agent of disease may be left in the body and cause further clinical symptoms: "That what remains of the disease after the crisis is usually causing a relapse."[56]

We find further indication that an active agent was considered as the extraneous cause of abscesses.[57] We read "Abscesses as the tumor of the lymphnodes (bubo in Greek) are parts which contain blastemata." 'Blastema' means something which is propagating, the offshoot of some plant. But it would go too far to translate it as 'germs' (FUCHS[1]). The possibility of water as a carrier of contagious agents also was not overlooked. Instances of definite precautions are rarely found in the literature. King Darius of Persia, on his expedition to Southern Russia, ordered that his own water supply should be taken along in golden flasks during his campaign. HIPPOCRATES recommends rainwater in order to avoid certain ailments, knowing that water was their source. SOLANGES[58] collected many passages which prove the foresight of the Hippocratics in relation to prevention of infectious diseases. HIPPOCRATES advised the washing of wounds and uterus with wine or vinegar, demanded utmost cleanliness in the physicians office, especially the cleaning of surgical tools; he suggested that these should have smooth surfaces; he ordered application of clean compresses on wounds and, again, advised boiling drinking water.

But it took a long time until these intuitive guesses could fertilise later research. The ancient animistic aspect of infection, although not mentioned any more by GALEN, did not become obsolete for another 1500 years. SYDENHAM, the father of modern clinical description, although leaning heavily on HIPPOCRATES was not yet free from an animistic aspect of the transmission of epidemic diseases:

"It must further be observed that all epidemics at their first appearance, as far as can be checked from their symptoms, seem to be more of a spirituous and subtle nature, than when they become older ... For whatever those particles are which, being intimately mixed with the air, are esteemed to produce an epidemic constitution, it is reasonable to conclude that they are possessed of a greater power of acting at their first appearance, than when their energy is weakened."[59] The concepts of infection and trans-

[56] FUCHS 1, p. 76 *(Aphorisms II,* 12).
[57] FUCHS 2, p. 25 *(Epidemics VI,* 2 II).
[58] M. SOLANGES, Thèse pour le doctorat en médecine, Paris 1894.

mission in the modern sense had to be disentangled from such and other concepts by the logical genius of FRACASTORO, MEAD and others. Even nowadays some diseases are only classified by clinical reasonings as infectious, although the contagion is yet unknown. Since the delineation of the clinical pictures necessarily has to preceed the discovery of their microbial causes, the Hippocratic approach was an absolutely correct and necessary step in the evolution of epidemiology.

Even discovery of bacteria or viruses would be useless to a clinician unless a clinical picture is found to which the microbe can be causally related. Modern research often makes the pendulum swing in the other direction. Many conditions are erronously explained by germs only because they are found in the host during times of illness.

The therapeutic activity of the ancient physicians was necessarily restricted to supportive and dietetic measures, guided by the right prognosis. "Wherefore the greater complexity of these ills requires more exact methods of treatment ... It is laborious to make knowledge so exact that only small mistakes are made here and there."[60] "If a man can, in this way, conduct with success inquiries *outside* the human body, he will always be able to select the very best treatment."[61] The lack of suitable concepts or methods made it impossible to pursue these ideas, which were to remain dormant until the invention of the microscope, of vaccination and chemotherapy. Medical science takes advantage of the newest developments of science as they come along. "There is no proof that an established starting point exists in the therapeutic arts nor is there a second start nor a middle nor an end of the road, but we approach it soon with one, soon with another concept."[62]

[59] T. SYDENHAM, *op. cit.*, p. 156, ch. 6.
[60] LOEB, Vol. I., p. 27 *(Ancient Medicine IX).*
[61] *Ibid.*, p. 63 (ch. XXIV)
[62] FUCHS 2, p. 384 *(De Morbis IX).*