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Reminiscences of Yellow Fever in the State of São Paulo

Adolpho Lutz
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It would be a great mistake to regard yellow fever as one of the less well-known diseases, the symptoms and pathology of which still await description. Quite the converse is true, for even the older literature would suffice to make physicians and students conversant with the subject. No doubt earlier text books on clinical pathology published in countries where the disease did not occur paid little attention to yellow fever.

However, there were always some authors who devoted a chapter to it in the section on tropical diseases, writing either from their own personal experience of it or else reviewing the observations made by others during wide-spread epidemics. The literature can be found in Hirsh’s treatise on Geographical and Historical Pathology. After tropical medicine evolved rapidly and gained its modern standing, none of the text-books could very well neglect yellow fever, the transmission of which had become a subject of fundamental importance. After its discovery there naturally arose a vast and relatively modern literature relating to its prophylaxis and the results of it.

It might seem unnecessary to take up again a subject with which everyone is now familiar. However, the reappearance of yellow fever in Rio recently may justify the publication of certain personal reminiscences of the many years during which I worked on yellow fever in São Paulo and in some ten foci which I visited, as well as of a month spent in Campinas at the height of the epidemic.

Some of my observations are original, others are either in agreement with or oppose currently accepted opinions. I also wish to report on some question as yet remaining open and which I consider of theoretical or practical importance.

It is known that yellow fever came to Rio de Janeiro in 1849. My father still knew the capital free from it. Later he had many children most of whom were exposed to it for variable but on the whole lengthy periods. My mother, who lived in Rio for thirty years, never had yellow fever, but both my father and one of my brothers came down with it twice and another brother was taken ill during the first epidemic in Santos in 1879, so that quite obviously there could be no family immunity. Nevertheless, the major part of the family was spared and in later years

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could be considered protected by a gradual process of immunity the reality of which cannot be denied although the exact time of its arrival can hardly ever be ascertained. Taking a third generation into account it might be said that the morbidity was of one in three, a surprising fact when one considers the extremely high incidence of former epidemics on first taking hold of a town or city.

I also was born in Rio but was taken to Europe before my second birthday without having been through any febrile episode before this. I only returned to Brazil after graduating in Medicine and remaining for about eight months in the capital during which I did not suffer from any disease resembling yellow fever. Between 1882 and 1889 I visited Rio several times but never stayed for long. In 1889, I was called by telegram from São Paulo to Campinas where there were no doctors left. There I found full-fledged pandemic of yellow fever and I expected daily to contract the disease, but I escaped without having had any fever at all. In the same house as I, there lived a man who had had yellow fever in New Orleans and another one who had been in Rio for many years. Both of them remained well, although there were large numbers of *Stegomyia* on the premises and several cases of yellow fever in the house and in the neighbouring ones as well.

Four or five weeks later, a good many other physicians had arrived from Rio while the epidemic was beginning to decline. I then saw some typical cases in Rio Claro, where there was an epidemic characterized by its high percentage of abortive and of light cases. I then travelled to Hawaii and remained away from Brazil for about two years. On my return, I treated several cases of yellow fever in São Paulo. After my appointment as director of the Bacteriological Institute of the State of São Paulo I visited several foci of yellow fever in my official capacity, but I did not spend many nights in them. I was in about ten localities where there was yellow fever but mostly for a short time. For this reason and because I had never had yellow fever, I did not consider myself immune until after this was put to the test of experimentation in São Paulo. The experiments were carried out on six volunteers who allowed themselves to be bitten by *Stegomyias*, all of which were infected on the same patient and kept alive during the period necessary. Three of the volunteers showed the first symptoms of yellow fever after an incubation of seventy to eighty hours. Dr. Ribas, who had studied in Rio without getting yellow fever, another volunteer who had also lived there and I did not develop yellow fever though we were bitten under exactly the same conditions as the first three. This speaks in favour of an imperceptible process of becoming immune despite the lack of overt symptoms.

These observations are also in agreement with what was seen elsewhere, for instance in several towns in Northern Brazil. They show that this manner of acquiring immunity is frequent and can easily take place. However, it must be made clear that one light or abortive infection does not produce a prompt and complete immunization. Thus in Campinas it was quite common to observe, about eight days after an abortive attack, a repetition of the whole symptomatology. I consider these attacks as reinfections and not relapses because they only occurred when the patients remained inside the epidemic focus. As a rule, the second infection was mild, like the first, but in one case, that of a little girl, there was a third attack, after about the same interval, which proved fatal and was characterized by abundant black vomit, which is generally absent from abortive cases.
There can be no room for doubt as to the etiology of these abortive cases, which often occurred in the same family and began on the same day as other much more severe and protracted cases. The lower mortality of this epidemic, which was of 20 to 25%, was exclusively due to the high percentage of abortive cases, since the most severe and prolonged ones showed a very high death rate. The same thing occurred in Rio, where the proportion of abortive cases reached its highest peak and yet coincided with an almost general incidence.

Reiterated bouts occurred only after light cases and showed that immunity is acquired only gradually. I do not know of any second attack or of any relapse following shortly after a severe case of yellow fever and consider that such occurrences must be extremely rare.

During all the time that the epidemic lasted in Campinas, I noticed an extraordinary abundance of the striped black and white mosquitoes I was acquainted with from Rio but had never seen during the five years that I practised medicine in a place only two hours away from Campinas by railway. I had also noticed the absence of diurnal mosquitoes in several towns of the same zone, and this observation was confirmed by local residents. The large number of open cisterns used for watering gardens in Campinas contributed considerably to the plague of Stegomyias especially after the owners of the houses fled and left the water standing.

I used a mosquito-net, not only at night but also during the day when I wanted to read in peace. Of course this did not prevent me from being bitten often enough on other occasions.

Following the epidemic in Campinas, yellow fever broke out in the same year in Rio Claro and Belem do Descalvado, two places connected with Campinas by daily trains. I believe that not only the fever but also the mosquitoes were brought in from Campinas. The transportation of infected mosquitoes by trains also explains several sporadic and isolated cases which occurred among the railway personnel, including the wife of the station-master at Vallinhos, who lived in the railway-station and never went to Campinas during the whole epidemic there.

In the following years yellow fever expanded in the State of São Paulo. It spread first along the Paulista Railway; it devastated Limeira where I had practised for five years without seeing a Stegomyia, but spared Jundiahy and Araras, where the towns were at a good distance from the station. After the Paulista Railway, the Mogyana line was invaded and later also the Sorocabana. The only thing that prevented a more rapid propagation of the epidemic was the fact that the mosquitoes had also got to be brought in; it was merely the lack of these that prevented the numerous cases developing among the fugitives arriving from infected places from propagating the infection in the other towns.

About a dozen foci were gradually established along the principal railway lines, radiating from the capital, the city of São Paulo, to the interior of the state, but I know of only two foci occurring in places where there was no connection by railway or by river navigation. In these two places, the presence of Stegomyia was very unlikely and, already then, I attributed the transmission to forest mosquitoes related to it. One of these foci occurred in an Indian village on the Rio Verde and I only knew of it from hearsay. The other I investigated personally. I found that
cases of yellow fever had occurred in temporary shelters put up inside the forest and occupied by workmen who were cutting down the woods to make way for a railway from Funil to Campinas. I examined several of the shelters in which there had been cases of yellow fever but could not find a single *Stegomyia*, whether adult or larval, whilst forest-mosquitoes were not lacking. This observation is all the more interesting as recently, that is some twenty to thirty years later, the transmission of yellow fever by Brazilian and African mosquitoes other than *Stegomyia fasciata* has been proved experimentally. Here, this species remains the most important transmitter whereas the role of the others was the exception rather than the rule. The search for other species able to transmit yellow fever is undoubtedly of great interest.

If I had not had the opportunity of observing *Stegomyia* in Campinas, I would not have been able, on receiving a letter from Habana informing me of the results of the yellow fever experiments, to immediately point out the mosquito responsible for the epidemics in the interior of the state of São Paulo, the more so as the species did not occur in the capital city of São Paulo. I thought it likely that it might be the same species as that from Habana though I did not use the same name as the American Commission there. This proved to be true later and it was also discovered that the species had been given a certain number of other names. I immediately informed the Director of the Sanitary Service, who accepted my point of view as to the importance of the experiments carried out in Cuba. We then published some instructions about the matter and soon found out that in many places there was a coincidence between the epidemics of yellow fever and the abundance of the mosquitoes.

At the time many people still believed in direct contagion and the black vomit was regarded as a sort of essence of yellow fever.

Although the transmission of yellow fever by mosquitoes was officially accepted and made known, it was not so well received as we had hoped and for this reason the authorities began to dwell on the idea of repeating the Habana experiments in São Paulo. I was consulted and answered that I would take part in the experiments under two conditions. The first was that the experiments of transmission through *Stegomyia* should be carried out on unpaid volunteers who clearly understood the risks they were running and that the Director of the Sanitary Service and I should be included among them. The second was that the mosquitoes intended for the experiments should not be used if the patients they had bitten during the first period succumbed to yellow fever subsequently. I hoped that by excluding the most potent virus, fatal cases among the volunteers would be safeguarded against as much as possible. Both of these conditions were accepted but the second caused a delay of almost a year. Most of the cases on which mosquitoes had been set ended in death; in other attempts the mosquitoes had to be infected in places distant from São Paulo and died before their bites became infectious; in still other cases they were devoured by little ants which entered their cages so as to get at the food set out for the mosquitoes.

I do not intend to redescribe these experiments. Suffice it to say that by the precautions taken the worst outcome was avoided in the three volunteers who did get yellow fever. The mosquitoes used had all bitten the same patient; the period
of incubation was also the same in all three cases, from seventy to eighty hours. The onset of the disease was explosive without any prodromal symptoms.

The period of incubation observed in these and in other experiments is probably the most usual one, though it is known to vary considerably. I will mention two observations which illustrate this point.

At a time when there was no yellow fever in the city of São Paulo, a Spanish couple took the morning train to Santos. The same day they had to be interned in the Isolation Hospital with symptoms of yellow fever and one of them died. This unusual occurrence was carefully controlled and can only be explained by superinfection. On the other hand, I saw an Indian who went to Rio as a member of a deputation from his tribe, all of whose companions got yellow fever there. He returned to São Paulo on foot (some 500 km) and came down with yellow fever in that place, eight days after leaving Rio. In the literature there are many cases of prolonged incubation and there would probably be more if it were not for the fact that the precise moment of infection can only be established in a certain proportion of the cases.

I have also made observations on the time of day at which infection takes place. There is a general belief, supported by many observations, that most infections occur at night or at least in the very early hours of the day. It has been stated that the inhabitants of Petropolis coming down to Rio only during the day never got infected. Even if there had been no exceptions, this did not apply to the inhabitants of São Paulo who went to Santos during the epidemics travelling down in the morning and returning to the highland on the afternoon train. One of my patients got yellow fever in this way and he happened to return to São Paulo on the same train as a young girl who went to Santos on that day from a distant place where there was no yellow fever. Both of them fell ill in São Paulo on the same day. In this instance the railway station in Santos, which was rather dark, could probably be indicted as the common focus of infection. The Spanish couple mentioned above must also have been infected in day-time.

On the other hand one may assert that Stegomyia does not bite in full day-light or on open streets. The conductors of the tramways plying to and fro all day through infected parts of Santos did not catch yellow fever. In our experiments the mosquitoes would mostly only bite under much subdued light. They are also easily put to flight by the movements of their intended victims. I found out at the same time that they can bite in total darkness provided that they are set very close to the animals experimented on.

Bedrooms are the best hunting-ground for Stegomyia. They like to sit on any dark clothes they may find hanging there. When many are present their buzzing is quite perceptible and even males can be seen in a peculiar flight-movement, oscillating to and fro. Mating can be observed indoors and in this particular Stegomyia differs from other mosquitoes. Nevertheless, they do attempt to enter or to leave at certain hours and can then be collected on the window-panes. They generally do not fly very far but, since they do not necessarily return to the same premises, they are able to convey the virus from house to house.

During the epidemics that occurred in the interior of the state of São Paulo, twice the first case occurred in a bakery.
The merit of demonstrating the transmission of the virus of yellow fever by mosquitoes is entirely due to the Commission in Habana. Former observers like Beauperthuy and Finlay deserve credit for having suggested the right solution at a time when there were no similar facts known. Finlay's experiments were not demonstrative, nor could they have been, because he naturally lacked knowledge of two important factors, namely, that the virus disappears from the circulation in the second period of the illness and that a lengthy period of incubation in the mosquito is required for it to become infectious. At the turn of the century the insight gained into the transmission of filariosis and of malaria by mosquitoes made it no longer visionary to believe in the transmission of yellow fever by then; nor could the study of mosquitoes (which on account of malaria I began soon after) be regarded as idle curiosity devoid of practical utility. All the same, the American Commission only thought of Finlay's theory after, like many other investigators, they found out that bacteriological examination could give them no results. This is the way in which one discovery leads to another which could not have been made readily without the preceding one.

At this period bacteriology stood in the fore-front of endeavour and it was only natural that research should have been concentrated on the discovery of a new germ. I myself lost a great deal of time and energy in this attempt. Obviously the first objects to be examined were the black vomit and the constantly affected organs, i. e. the liver and the kidneys. Spirochaetes and protozoa were also diligently looked for in blood taken during life. Most of the examinations were made at very advanced stages of the disease, or on cadavers, but I limited my conclusions to post-mortems made soon after death and took about sixty fatal cases with typical lesions into account. I worked out a technique which furnished me with stained sections of the most important organs in about two hours. I confirmed that neither in the preparations nor in the smears were there any germs to be found which might be connected with the lesions observed. In the cultures there generally grew only germs with nothing distinctive about them and I soon concluded that the blood-stream might be invaded by them before death, a fact which explains the early signs of decomposition of the cadaver. The invading germs were mostly coliform and gave diverse reactions in culture media. They probably came mostly from the intestine. Sanarelli's bacillus also belongs to this group. In contrast with many others it was obtained by an adequate technique and this accounts for the credit it received at first. It was, however, only rarely to be found and moreover the serum prepared from it proved to be of no avail. Shortly before the discovery of the transmission of yellow fever by mosquitoes indicated a different kind of etiology for the disease, Sanarelli's bacillus was identified with that found in hog-cholera.

In the modern history of yellow fever in Brazil, 1889 was the most disastrous year. During the hot season for three months it hardly rained and the temperature rose to unprecedented heights. In Rio and in Santos there were cases of high pyrexia which proved rapidly fatal and appeared in epidemic proportions. They had not occurred before and were classified as pernicious accesses or, more rarely, as fulminating yellow fever. It was only after much discussion that they were recognized as heat-strokes.
The same summer yellow fever appeared in Santos and in Campinas. In Santos, where there had been no yellow fever for ten years, the epidemic was very severe. The German Club lost twenty five percent of its members in a fortnight from yellow fever and from heat strokes. The yellow fever in Campinas was imported from Rio and the second case occurred in a street parallel to that of the first case. The gardens of the houses on those streets were placed back to back but there was no passage between them.

Several years before, there had been some cases in Campinas which were classified as yellow fever by competent observers. This diagnosis was, however, brushed aside or refuted on the plea that yellow fever could not climb the Maritime Range. The people living in the interior believed that they were thus protected until the facts proved that they were mistaken.

In spite of the rapid increase in the epidemic, the daily press went on debating whether there was yellow fever in Campinas or not. On a day in which forty deaths occurred I read in a newspaper from Rio that there really was no yellow fever in Campinas.

After a time it was estimated that about three fourths of the population, which comprised 20,000, had left the town; those who remained were mostly men who had jobs. Many persons returned too soon and caught yellow fever. Practically all those who lived inside the town and were not immune were infected. Total mortality was calculated at 2,000 including those who left and died elsewhere.

I shall now add a few words on the diagnosis of yellow fever. It undoubtedly can and must be made during the illness. It is absurd to withhold prophylaxis until the patient dies so as to make a posthumous diagnosis by examining his viscera. This would be equivalent to waiting for cultures of the Klebs-Loeffler bacillus to develop before applying serum and taking other urgent steps in treating diphtheria. The common sense and past experience of the lay-public often diagnosed yellow fever long before it was officially acknowledged. And yet, it is the physician in charge of the patient who ought to be the first to suspect and to diagnose yellow fever. He should keep the possibility in mind and follow the case carefully from the beginning; if he happens not to be familiar with the disease he must study it as quickly as possible or consult a more experienced colleague. The use of a mosquito-net is the most urgent and important step; at the same time enquiry must be made as to the occurrence of Stegomyia. Even if at the beginning of a case, yellow fever may be just a possibility, or a probability, the course of the illness should bring certainty unless it is an extremely mild or abortive case. It is inexcusable that a serious or fatal case should be undiagnosed, on the pretext that clinical diagnosis cannot be made before the crisis or death. The lack of former observations may render the problem more difficult but it is not insoluble. Still less than an isolated case is it permissible for an epidemic to go unrecognized.

I do not consider the diagnosis of yellow fever difficult and after my experience in Campinas I never saw a case, even an incipient one, without thinking of the possibility or even the probability of yellow fever and without being certain by the fourth day at the latest.

Even in light and ambulant cases slight jaundice and albuminuria can be demonstrated from the fourth to the sixth day. This retrospective diagnosis is of
great importance in patients arriving from a place where there is a suspicious disease. *Herpes labialis* sometimes appears even in light cases and can still be recognized after several days so that it may occasionally attract attention and help in establishing retrospective diagnosis.

My clinical observations were made on patients from various foci in the interior of the state of São Paulo or coming from Santos. There were only two years in which I saw autochthonous cases in the city of São Paulo and they were quite circumscribed epidemic foci. All these cases were affiliated to the virus from Rio, which in 1889 was imported more or less at the same time into Campinas and into Santos. It may be for this reason that the cases in the interior of the state and in the capital generally followed the same type. The relatively low mortality was probably due to the large number of abortive cases. It seems to me that in Santos mortality was on the whole higher because there were more severe and superacute infections. As for the cases which have occurred recently in Rio de Janeiro, I saw little of them and no detailed observation of their clinical aspects has been published. I have the impression, nevertheless, that these cases, whose virus was reimported some twenty years later showed a somewhat different type.

As for the cases described in the literature they do not seem entirely typical either so that at times one wonders if the authors were really describing the same disease. It is admissible, however, that the general type may undergo modifications, as suggested by some authors, the more so as the disease experimentally produced in monkeys nowadays is very different from that seen in human beings.

In my descriptions I shall limit myself to the cases I observed from the beginning, leaving aside those that entered the isolation Hospital at a more advanced stage. Of these I saw many more because the Bacteriological Institute was on the same ground as the Isolation Hospital.

In my personal experience most of the cases which can be considered typical do not show any podromic phase. Neither of the three experimental cases complained before of the sudden onset of fever, which began with a chill and cold shivers, accompanied by a very rapid rise of the temperature to 40ºC, or more, a congested face and blood-shot eyes. At the same time there develops an intense ache in the forehead, the interorbital region and in the sacrum and the legs. These symptoms, never absent in my cases, immediately arouse suspicion of yellow fever. Part or all of them obviously occur also in other diseases, for instance, in sunstroke, malaria, small-pox, dengue or influenza, but differential diagnosis from most of them can generally be made by the local sanitary conditions, the absence of hematozoa in the blood-film and by other considerations. In any case, the patients must be immediately put to bed and are generally quite willing because they feel acutely ill. Mosquito-nets or their equivalent must be resorted to immediately and are also useful in dengue and malaria. From now on the temperature must be carefully checked and recorded, preferably on a temperature chart. Urine analysis must be made, not with a view to finding protein, but rather so as to exclude a preexisting albuminuria. A very slight jaundice, such as sometimes found in apparently healthy persons must also be looked for so as to be excluded. Prognosis now depends on the duration of the fever. Should it fall within the first twenty-four hours, as it often does, the case is presumably an abortive one, since a pseudo-crisis in an intermittent
one is a quite exceptional occurrence. If a fever does not last beyond forty-eight hours prognosis is still favourable but examination from the fourth day on should confirm diagnosis by the presence of a very light degree of jaundice and albuminuria. If fever lasts longer, prognosis becomes steadily worse. Three whole days of fever rarely permit a final recovery.

I saw only two cases in which the fever of the first period was intermittent. Both fell in São Paulo but one came from Campinas and the other from Santos and special circumstances made the diagnosis of yellow fever easier. This possibility, though extremely unusual, must be kept in mind. These pseudocrisis do not ensure favourable prognosis for both my cases proved to be fatal.

As a rule the virus disappears from the blood-stream towards the end of the third day, as one may deduce from the more or less complete remission of the symptoms which then occurs. The patient and his family have the illusion that this is the end of the illness, whereas the experienced physician looks ahead to imminent danger. After a day or half a day of remission, the temperature may go up again and proceed as an irregular fever.

This, however, no longer has the significance it had, which is now taken over by the condition of the kidney function. The greatest danger is now anuria. This is preceded by a rapid increase of albumin from the fourth day on and is accompanied by progressive reduction in the quantity of urine. Complete anuria, when even catheterization of the bladder fails to bring forth any urine, is hopeless. Death under conditions of uraemia ensues mostly on the fifth to sixth days and only seldom before or after them. If complete anuria is not reached, the output of urine increases again rather rapidly, and already on the next day, after the most critical hours, an actual pelyuria may take place with an enormous amount of cylinders in the urine. Albuminuria does not, however, really decline as fast as it would seem because the albumia is now dispersed in a much greater quantity of liquid. In favourable cases it soon ceases. Unlike scarlet fever, the conditions never lead to generalised oedema nor does nephritis follow it. Physicians that are familiar with the impressive amount of cylinders found in the urine of uraemic patients cannot doubt that the suppression of the secretion is due mainly to mechanic causes and that the damage to the kidney cells is not so deep-seated as one might conclude from examining microscopic slides, which often portray post-mortem changes when death followed uraemia and prolonged agony.

Should the patient escape the dangers of anuria his life is still threatened in consequence of other disorders connected with the toxic state induced from the beginning and generally manifested by icterus and a tendency to hemorrhage. These disturbances may be quite transitory or more persistent. In the latter case, if death does not supervene at the end of the first week or in the beginning of the second one, the disease goes over into a chronic phase generally unaccompanied by fever, which can last for some weeks and end either in death or by recovery. In this state, which I observed in about ten per cent of the severe cases, jaundice, which at first is mild, increases steadily and may develop into complete cholomia in which the faeces become unpigmented, the urine gives Gmelin’s reaction and the appearance of the patient fully justifies the name of yellow fever. In this stage albuminuria and the tendency to hemorrhage may continue but it is the condition
of the liver that deserves most attention. Percussion shows a gradual reduction of the dulness which may disappear altogether in four weeks. If the patient dies the post-mortem will show the liver so far retracted that only its sharp anterior border touches the epigastrium whilst the weight has fallen from 1500-1800g to 700-800g. If the patient survives dulness returns to normal in a few weeks. I have shown patients who were up and about and apparently normal but in whom dulness over the liver could not be demonstrated.

Acute atrophy of the liver in yellow fever was not unknown to the older authors but seems to have been somewhat neglected of late. I cannot recollect reading any report on complete recovery. These observations deserve a greater interest because they prove both the destruction and the capacity for regeneration of human liver-cells in a most impressive manner.

Icterus also deserves mention. Like the other characteristic signs of yellow fever, it does not develop immediately so much so that pronounced jaundice at the onset of a pyrexia speaks against rather than in favour of yellow fever. The physician who is looking for the first signs of jaundice must examine the patients in very good daylight and make the patient rotate the eye-balls so that the part on the sclerotic generally covered becomes visible. This is necessary because the incipient faint yellow tinge is destroyed by light in the area generally exposed. At first icterus is slight even when the serum of the patient's blood shows a clear yellow tinge. The colour of the sclerotic is citron-yellow with a slightly greenish tinge but it is never orange-colored in the first period. Despite the statements of several authors, the urine does not give Gmelin's reaction. Shortly before death jaundice may still be slight but it becomes more distinct in the cadaver. As mentioned before, intense jaundice similar to that seen in a different disease without fever is a very late symptom in yellow fever.

Hemorrhages are characteristic for severe cases with a prolonged initial period of fever. In abortive cases there are no hemorrhages but they are so constant in severe cases that complete absence of hemorrhages in the body at post-mortem suggests an error of diagnosis. The most common site of hemorrhage is the stomach where the blood seeping out slowly is acted on by the gastric juices so that it takes on the appearance of coffee-grounds. Vomiting is very common at this phase and the black color of the vomit is so impressive that it has been used as a name for the disease in several languages. When there is no vomiting, the black masses are generally recovered at the post-mortem. Rests of black vomit in the stomach are one of the most characteristic macroscopic findings in yellow fever and are rarely absent. The same process of seeping out of blood often occurs on parts of the mucous membrane of the nose, mouth and uterus and in the latter it is similar in aspect to menses. The mucous membrane of the lower part of the small intestine is also often the seat of hemorrhages. Small petechiae on serous membranes are so commonplace that they can hardly be regarded as diagnostic in post-mortem of yellow fever.

Non-traumatic hemorrhages in the skin, the muscles and other organs are less frequent. It is just the most affected organs, i. e., the liver and the kidneys, which generally remain free from them. I saw only a few cases in which the bad general condition of the patient was associated with hemorrhagic and hemophilic diathesis. In one of these cases blood seeped out of two sebaceous glands on the back of the
nose and would hardly coagulate. In quite hopeless cases profuse bleeding may occur in the stomach, the intestines and in enclosed foci of hemorrhage, but death can hardly be attributed solely to the loss of blood.

I see no reason for classifying such cases, in which one symptom apparently predominates, as especial forms because it is just the combination or succession of different symptoms, all of them resulting from the same intoxication which characterizes the disease. The fluidity of the blood is noticeable during post-mortems even when the evidences of hemorrhage are few. It also explains the very strongly developed lividity of the dead body.

In white patients I have always found black vomit ominous. Cases are quoted in which patients recovered after it. I have seen such cases myself but when this symptom is very marked recovery becomes quite a rare exception. In Negroes, who on an average stand yellow fever better than whites, I have seen black vomit without a very severe general state.

Sensitivity in the region of the stomach together with a feeling of anxiety and continuous vomiting may occur already at the beginning of the illness. It would seem to indicate a special localization of the virus and makes a bad impression. In these cases an injection of morphine may be very helpful. In other patients vomiting begins later and the vomit soon becomes black. If singultus then supervenes, the outlook is very grave.

The course of the disease which I have just described may be considered as typical and it corresponds to the great majority of the cases seen. Superacute cases with fulminating symptoms are observed more often at the beginning of epidemics and in places with a constantly hot climate for instance in the coastal lowland. In these cases there is no remission and the symptoms of toxicity appear very early. I remember one case seen in Santos in which boiling the urine resulted in complete coagulation already on the first day. This is however a very rare occurrence; so is death on the second or on the third day, which I have never witnessed. Fatal ending even on the fourth day I consider as also quite exceptional. The early appearance of toxic signs seems to indicate that the production of toxins began very early, even before fever indicated the invasion of the blood-stream.

A few words might be added on the treatment of yellow fever. In 1889, the lay public and some members of the medical profession believed that treatment with quinine should be preceded by an emetic. The triad was completed by prescribing a laxative and a diaphoretic at the beginning of any acute febrile disease. I never subscribed to this practise and considered its inefficacy in yellow fever already proved. However, during the epidemic in Campinas, and later in Rio, quinine was prescribed by some of the other doctors who persisted in believing that yellow fever was a form of malaria. If the patient’s stomach revolted against the treatment, hypodermic injections were resorted to. The preparations used mostly came from Italy. Sores and abscesses often occurred and sometimes amounted to a severe complication. Fortunately, these interventions, which disregarded the principle of Primum non nocere stopped when the doctors realized that even most effective antipyretics were unavailing in yellow fever. Kairin was the first one used and enjoyed an ephemeral popularity; later on, bottles of it could be seen standing on the shelves of every pharmacy.
In the first stages of yellow fever antipyretics have the only disadvantage of hindering the observation of the temperature, but I saw one effect on a convalescent from a rather severe case, which shows the need for extreme caution in the more advanced stages. The patient, who was a robust man, took a gram of antipyrin on his own account. He immediately had a very severe reaction, characterized by an acute oedema of the cheeks and a sensation of precordial constriction. When I saw him the heart beats had stopped completely. On auscultation, only occasional weak and indeterminate sounds were audible. After a period of extreme anxiety, which lasted for several minutes, a very small pulse reestablished itself with a frequency of 180 beats to the minute. The general state then improved promptly. As the patient had never had such an attack, even when he had taken antipyrin, alteration of the myocardium due to yellow fever may well have been responsible.

Therapeutic trials of remedies against yellow fever would have to be instituted promptly so as to try to prevent the proliferation of the virus and the production of toxins, as much as possible. The criterion of specific efficacy of a drug would be the rapid lowering of the temperature and the absence of the subsequent symptoms, that is a course of the disease similar to that of abortive and mild cases. The occurrence of such cases renders rather difficult the distinction between spontaneous improvement and the healing virtues of the product used. Later on, when the process of infection has come to an end with the withdrawal of toxins from the circulation, treatment must be strictly detoxicating. In this stage also, the qualities of a product could only be surmised by the increase in the percentage of favourable outcomes. The prognosis of fully developed yellow fever depends on two factors, which are hard to evaluate, i.e. the amount of toxins produced and the resistance of the patient.

At the present time there is no certain cure available which would destroy the toxins and stop their effects. Attempts with the newer drugs do not seem to have been undertaken systematically, probably because the number of patients and observers has decreased. In São Paulo, I treated a number of cases from the beginning with Salol. The dose prescribed was 12g distributed over the first thirty six hours. It was well tolerated and diminished the pains characteristic of the first period. After that, I did not give any more Salol because I know from past experience of this drug that when this dose is reached Salol is only eliminated slowly. The results were so favourable that I would have gone on with this treatment if I had had more patients in the first stage of yellow fever. I do not remember the exact number of cases but I do recollect that among a good many only one ended in death and that several days after interruption of the treatment. These results were certainly encouraging although the possibility of a series of mild cases cannot be entirely excluded.

In the second period I used a diuretic, the good qualities of which I had also known for several years. This was tartarus boraxatus, which can be given with no fear of ill effects even in high doses and per rectum if there is gastric intolerance. Its diuretic action was evident even when anuria threatened; however, the slight increase in secretion seen in such cases did not help at all nor did it prevent the symptoms of uraemia.

When total anuria is imminent, decortication of one or of both kidneys might be resorted to, especially if there was no pronounced tendency to hemorrhage.
present. This might be combated by transfusion of blood but in this condition general intoxication is so marked and prognosis so unfavourable that great courage would be required to risk an intervention to which the death of the patient might be attributed.

As for the prophylaxis of yellow fever the general collective measures are clear enough since the mode of transmission was proved. Before that it was still based on general principles and similar to the methods resorted to against cholera and abdominal typhus.

A great deal of money was spent on disinfectants which were poured down the latrines. In Campinas, drinking water was fetched in from outside while mosquitoes were allowed to breed freely in the local supply. Some persons attempted to protect themselves against yellow fever by taking Fowler’s solution, which soon proved useless in the usual doses.

Formerly it was believed that the same prophylaxis would do for all infectious and epidemic disease. One of the greatest steps in the progress of Preventive Medicine came from the recognition that each infectious and parasitic disease requires its own form of prophylaxis, based on the biology of the parasite and/or of the transmitter. Even so, complete eradication of a disease and definite elimination of its foci is a difficult task as demonstrated for Ankylostomiasis and Malaria. The last years have shown that this also applies to Yellow Fever, which had been considered as almost extinct.

It is indispensable to keep up prophylactic measures against mosquitoes and to see a constant menace in the presence of Stegomyia, not only where there actually is yellow fever, but even where it is unknown.