ON HEREDO-INFECTION IN TUBERCULOSIS

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"Another very important point to be brought to light is that of tuberculous inheritance: nothing prevents the granulation from passing to the fetus, considering its proportions which are not an obstacle to its going through the filter".

"... the notion of tuberculizable ground is likely to be replaced, if not completely, at least in most of cases, by that of tuberculosis in potential".

A. FONTES (1910)
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By heredo-infection in tuberculosis, we should understand transmission of the tuberculous virus from the mother to the fetus, through the placenta, the placental tissue remaining untouched.

Then it is the transfer of the virus from the maternal organism to the organism of the fetus, under conditions of anatomical integrity of the tissue of the placenta, that characterizes the inheritance of the semen.

Heredo-infection is consequently a particular incidence of congenital contagion, which arises whenever there is a lesion in the vessels or in the tissues of the placenta, allowing direct passing through of the infectant element.

Both cases may be comprised under the generic name of heredo-contagion.

Most different is thus, the bio-pathologic conceit here established, from the mere biologic conceit of inheritance, in which the fundamental notion of transmission to offspring interferes, by way of intime changes of the generating elements, of ancestral characters which are being kept with their specific aspect in the evolution of the brood.

The possibility of transmission of the tuberculous virus, from the mother to the fetus, during intra-uterine life, should be then studied, keeping in mind the theory of heredo-contagion, quite independent of morbid phenomenons likely to establish the possibility of direct pnssting of the virus.

In this second case, then, it will mean intra-uterine contagion owing to accidental cause; the case will be of inheritance of the semen by a pathologic condition inherent to the placenta; the virus will be found in most cases, in the fetal organism, under its visible, classical acid-fast ap-

(1) Memorial read before the 2nd Pan American Congress of Tuberculosis, held in Rio ed Janeiro from the 30th of June to 7th of July 1929.
pearance, and will be revealed, in morbid inheritance, by tuberculization of the child to be born.

In the first case, heredo-infection is provoked by osmotic exchanges of the feeding maternal and fetal fluids, blood and lymph, creating a condition, if not pathologic, at least miopragic, which may appear with varying stages, whose last modality is a specific change of the tuberculized tissues.

The special physionomy this type of infection bestow on the infected organism, under its slightest forms, is bound with the physiopathology of the tuberculizable ground, an expression which means in pathology the organic dyscrasia, specific of children from tuberculous parents.

In such cases, the infectious element cannot be made patent under its classical form of an acid-alcohol-fast rod.

The morbigenous action of the virus in nevertheless made obvious in its effects: hyperplasia of the lymphatic system, weakness of the circulatory function, nutritional changes consequent to instability of the endocrinous function, etc., etc., all morbid characters which may be confounded with those subject to being ascribed to toxical elements of durable action, and whose durability or persistence for a longer or shorter time, may cause them to determine a special morbid constitution approaching the conditions which nowadays are comprised under the word: pre-tuberculosis.

This is the meaning of the notion of inheritance of ground, which, besides, represents nothing else but tuberculous infection under a special weakened modality, which, with humoral changes, and the cellular physiopathology it determines, establishes the condition of instable allergy in the classical infection.

The notions of infection and intoxication are thus coinciding, owing to their identity of effects, which are observed not merely by functional changes, but also by appearing anatomical alterations.

Tuberculous infection demonstrates what has been told by occasion of studying the filtrable virus.

In such cases, where the presence of KOCH's bacillus cannot be made obvious, that is, of the acid-alcohol-fast form of the virus), the morbid frame shows itself, experimentally, comparable with those revealed by clinic.

In my opinion, the hypothesis of infection and intoxication, under such circumstances, not only are not adverse, but even complementary one to other. The demonstrations of the morbigenous capacity of the virus may be made, in infection, by its durability and its permanency, whereas, in intoxication, this property is transient.

It is, accordingly, in the condition of continuity of the morbigenous action, that reside the characteristic of the filtrable elements of the virus, subject to maintain a condition of chronic intoxication and to be transmitted, in experimental series, by inoculation, or in natural series, by passage through the placenta, from the mother to the fetus.

In some cases, these filtrable elements of the tuberculous virus may reproduce the acid-alcohol-resistant form, with or without its pathologic sequence, provoking, however, always an instable allergic condition, which
may lead, either to hypersensibility, or to a greater resistance against the morbidogenous action of the virus.

Thus remains explained that a particular condition of the humoral constitution may be created, that gives the case special physionomy of pre-tubercular state, under the prevailing conceit; but this state, which finds as its pathogenic factor, the chronic intoxication caused by the virus, is maintained only by the same factor with the permanency of the infection. Accordingly, the physio-pathologic action of tuberculous venoms, is shown by the action of the substances elaborated by the virus, either it be exercised on the noble elements of the tissue, specially of the lymphatic tissue, bringing changes into its anatomical constitution, or on the hemo-poietic system, subject to similar changes, or even causing troubles in the general nutrition, for the action of these venoms is always suffered by the endocrine and neuro-vascular systems, on which repose, in the present state of knowledge, the automatism of the functions which regulate somatic life.

The relations thus established between the ground and the virus, grow daily more favorable to the outburst of the tuberculous disease, which in fact, is already existing insidiously.

The morbidogenous power of the virus counterweighed by the defence reaction, creates an allergic condition, a special state which may be compared to the particular state of the cellular irritableness, determined by the toxical tendency; it gives way to a condition of specific hypersensibility, whose exhaustion leaves plain field to the anaphylactic blow to take place. From the instable humoral equilibrium established by the cellular defence against the attack of the poisons of the virus, results the humoral condition of the pre-disposition to tuberculosis; from the peculiar cellular condition deriving from this chronic intoxication, decurs the appearance of the tuberculizable ground.

The somatic notion resulting from both factors, establishes the clinical frame of pre-tuberculosis, the true term under the anatomical and etiologic points of view, but wrong if considered physio-pathologically, for, in such morbid states, infection already exists, for which the stage, we might say, the sarcodial, ultra-microscopical, invisible (ultra-virus) or visible granular or pre-bacterian stage, must account.

Going further in the study of the filtrable forms of tuberculosis, I effected, in November 1926, the following series of experiments.

Tuberculus spumtum emulsioned in a saline solution, was filtered upon a CHAMBERLAND device L2, after a stage of three days in the dry-oven at 37°C. The perfect state of the filter was verified by means of smearings of the filtrate obtained on slanting gelose and in plain glycerine broth. The smeared media, maintained either in the dry-oven or at the laboratory's temperature remained sterile.

With such filtrate, I injected:

Sub-cutaneously (10 c.c. of the filtrate)—Guinea pig No. 1 (male).
(10 c.c. of the filtrate)—Guinea pig No. 2 (female).
Intra-peritoneally (5 c.c. of the filtrate)—Guinea pig No. 3 (male).
On the 28th February 1927, the Guinea pig No. I died, cachetic.
Autopsy showed absence of specific changes and of acid-alcohol-fast bacilli. In the lung we found infarcts and capillary hemorrhages. An examination of cuts of the liver, spleen and ganglia as also of the lesions found in the lungs did not reveal the presence of specific changes or of acid-alcohol-fast bacilli.

With the material obtained from this animal, I effected inoculations to a following series:

Guinea pig No. I — Injected sub-cutaneously with pulp of spleen.
Guinea pig No. II — idem, idem, with fragments of lung.
Guinea pig No. III — idem, idem, with fragments of epiploon.
Guinea pig No. IV — (female) — Injected with the water used for washing the lung and liver.

20. 2. 27.—The Guinea pig No. I dies from an interfering cause. The autopsy did not show specific lesions nor acid-alcohol-fast bacilli.

24. 2. 27.—Gu. pig. No. III dies.—Autopsy revealed increased epiploic ganglia. No specific lesions. In the epiploic ganglia, acid-alcohol-fast granulations were discovered. No trace of acid-alcohol-fast bacilli either in viscera or in the other ganglia.

The material from this animal (epipoic ganglia) was used to inject a Gu. pig IIIA (male).

On 28. 2. 27. Gu. pig II dies. Examination gave results quite identical to that observed in Gu. pig I.

The Guinea pig IIIA (male) which had been inoculated on the 24. 2.
27 with material proceeding from Gu. pig III, showed, after 8 days, an abscess at the inoculation spot, which bursting out, turned to an ulceration with the appearance of a chancre. Preparations made with rubbings of the rands of this chancre, revealed the presence of acid-alcohol-fast bacilli.

The inguinal ganglion, satellite of the ulceration, showed increase in volume. After one month, the ulceration was cicatrized.

28. 4. 28, this Guinea pig died. The autopsy showed no tuberculous lesions. Pulmonar infarcts; presence of acid-alcohol-fast bacilli, of granular shape in the tracheo-bronchial ganglia.

The ganglion, satellite of the chancre, was extirpated. Examination of cut and rubbings did not show cheesy degeneration nor acid-alcohol-fast bacilli.

The remainder of the material was injected under the skin of another Guinea pig.

This latter died 5 days later, without any lesion or without apparent cause; smearings made with the blood of the heart remained sterile.

The same ganglion of this animal was transplanted to another one, by the same technique.

This animal died after 3 days, and like the former Guinea pig, did not show any apparent lesion nor germs in the heart blood.

Guinea pig IV (female), injected on the 18. 2. 27 and which lived together with the male III, from the 24. 2. 27, brought forth on the 29. 9.
27 a young one, which died after 5 days. Autopsy revealed a zone of cheesy degeneration and necrosis in the liver, hemorrhages and infarcts in the lungs and increased volume of epiploic ganglia. No acid-alcohol-fast bacilli.
A small piece of an epiploic ganglion was inoculated sub-cutaneously to another Guinea pig. After 12 days, this latter showed a chancre beginning to form, through ulceration of the injected spot. The formed chancre kept open for one month. No acid-alcohol-fast bacilli were found within this lesion. The chancre cicatrized, and the animal is still alive, without the aspect of tuberculous, but rather exceeding fat (actual weight 980 grams).

On the 8. 12. 27, two more young ones were born, which died in May of 1928, without tuberculous lesions and without bacilli, but showing very marked inguinal polyadenia.

The Guinea pigs 2 (female) and 3 (male) procreated also. The first young one was born on the 14. 9. 27 and died after 15 days. The autopsy revealed pulmonar infarcts, capillary hemorrhages in the lungs and a necrotic zone in the liver. No acid-alcohol-fast bacilli.

On the 8. 2. 27, two more young ones were born, of a normal appearance, but with the ganglia increased. One died on the 8. 5. 28, the other one on the 14. 5. 28. Both showed neither tuberculous lesions nor bacilli.

The following synoptic table will give a more approaching idea of the recurring of the process and the observations about the experimental series as described hereabove:

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Foreign experiments generally confirm the conclusions I was led to, which will be exposed in a further part of the present work.

Since the fundamental communications of CALMETTE, VALTIS, NEGRE, BOQUET (2), F. ARLOING and DUFORT (3) numerous works, published in the course of these last few years, have confirmed the possibility of the tuberculous virus passing through the mother's placenta and causing infection to the fetus.

CALMETTE, VALTIS and LACOMME (4), SERGENT, DURAND and BENDA (5), COUVELAIRE (6) in France, MOENKEBERG, ONETTO and VERGARA (7) in Chile, NISHIMOTO (8) in Japan, NASSO (9) in Italy, VAN BENEDEN (10) in Belgium, LYDIA RABINOWITSCH (11) in Germany, all of them bringing an ample contribution of documents to the bio-pathologic phenomenon of the heredo-contagion in tuberculosis. And from the experiments afforded, results that contagion is caused without any dependence on lesion of the placenta, thus being fully justified the meaning of the expression Inheritance of semen, biologically speaking.

Clinical observation brings also a wide documentation to the said phenomenon.

ARLOING and DUFORT (3) in 1926, report the following case to the Paris Academy of Medicine:

Early birth on the 7th month, from tuberculous mother with advanced pulmonar lesions, on the 31st October 1925. Fetus weighs 1,310 gram; placenta weighs 310 gs.

Immediately after the birth, the baby is taken off from mother and brought up in the couveuse.

Somatic examination of the baby reveals nothing. Temperature oscillates between 34°2 and 35°C. On 9th November, temperature reaches at 37° and keeps unchanged until the last days of life.
GUINEA PIGS INOCULATED WITH AN EMULSION OF TUBERCULOUS SPUTUM HAVING BEEN KEPT FOR THREE DAYS IN THE DRY OVEN AT 37°C, AND FILTERED ON CHAMBERLAND BOUGIE N. L2 (19, 11, 26).

<table>
<thead>
<tr>
<th>Guinea Pigs</th>
<th>Male</th>
<th>Female</th>
<th>2. Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Birth</td>
<td>10 c.c. of filtrate</td>
<td>EC. of acid-fast bacilli</td>
<td>2. Alive</td>
</tr>
<tr>
<td>Second Birth</td>
<td>5 c.c. of filtrate</td>
<td>10 c.c. of acid-fast bacilli</td>
<td>2. Alive</td>
</tr>
</tbody>
</table>

On the 10th day, Gu. pig B, male, was killed, and found to have numerous small hemorrhages in the liver. On the 12th day, Gu. pig D, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 14th day, Gu. pig E, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 16th day, Gu. pig F, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 18th day, Gu. pig G, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 20th day, Gu. pig H, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 22nd day, Gu. pig I, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 24th day, Gu. pig J, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 26th day, Gu. pig K, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 28th day, Gu. pig L, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 30th day, Gu. pig M, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 32nd day, Gu. pig N, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 34th day, Gu. pig O, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 36th day, Gu. pig P, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 38th day, Gu. pig Q, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 40th day, Gu. pig R, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 42nd day, Gu. pig S, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 44th day, Gu. pig T, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 46th day, Gu. pig U, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 48th day, Gu. pig V, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 50th day, Gu. pig W, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 52nd day, Gu. pig X, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 54th day, Gu. pig Y, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 56th day, Gu. pig Z, male, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli.

On the 15th day, Gu. pig A, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 17th day, Gu. pig B, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 19th day, Gu. pig C, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 21st day, Gu. pig D, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 23rd day, Gu. pig E, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 25th day, Gu. pig F, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 27th day, Gu. pig G, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 29th day, Gu. pig H, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 31st day, Gu. pig I, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 33rd day, Gu. pig J, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 35th day, Gu. pig K, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 37th day, Gu. pig L, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 39th day, Gu. pig M, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 41st day, Gu. pig N, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 43rd day, Gu. pig O, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 45th day, Gu. pig P, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 47th day, Gu. pig Q, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 49th day, Gu. pig R, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 51st day, Gu. pig S, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 53rd day, Gu. pig T, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 55th day, Gu. pig U, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 57th day, Gu. pig V, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 59th day, Gu. pig W, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 61st day, Gu. pig X, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 63rd day, Gu. pig Y, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli. On the 65th day, Gu. pig Z, female, was killed, and found to have a large, central, necrotic area in the liver, with a large number of acid-fast bacilli.
The baby dies on the 25th December. These are the weights recorded during the period of life:

Weight when born — 31st October: 1,310 gram
12th November: 1,300
22nd November: 1,400
3rd December: 1,490
9th December: 1,440
20th December: 1,170

During the last 5 days of life, the decrease of weight was rapid, without appearing any special morbid phenomenon that could account as well for the loss of weight as for the causa mortis.

Autopsy revealed nothing abnormal, except a slight hypertrophy of the mesenterial ganglia.

With fragments of the viscera, several inoculations were effected on Guinea pigs, which all kept in good condition of health. Rubblings from the mesenterial ganglia revealed presence of acid-alcohol-fast bacilli. The inoculation of the filtrate of an emulsion of these ganglia to Guinea pigs, determined the death of the inoculated animals by cachexy, their ganglia showing acid-alcohol-fast bacilli.

CALMETTE, VALTIS and LACOMME’s (12) observations enabled these celebrated investigators to draw the following conclusions:

“In the course of certain severe tuberculous affections, the passage of the tuberculous virus from the mother to the fetus, during pregnancy, may appear with less exception as was thought up to now: The transplacental tuberculous infection, is most often ascribable to elements microscopically invisible, but filtrable through earthen bougies”.

Later on, CALMETTE and his co-workers, inform again the Academy of Sciences (12) of their conclusions as follows:

“This transplacental infection presents very peculiar and varied characters, of the infection obtained by direct transmission of the normal forms of the KOCH’s bacillus, so that this may lead to distinguishing the proper bacillar inheritance, this being rare, from the transplacental infection by the ultra virus, which on the contrary, is most frequent, and when not determining the rapid death of the fetus, of the new-born child, by progressive disassimilation, does not appear to bring serious consequences for the health of the sucklings, since they are kept from bacillar infections in their family circle”.

Similar conclusions, even developed, have been communicated by CALMETTE (13) to the 8th Conférence Internationale de Tuberculose.

The pathogenic action of the filtrable elements of the tuberculous virus is then exhaustively demonstrated. And the possible passing of these elements through the placenta furnishes us with a key to the complicated riddle about morbid inheritance in tuberculosis.

Still here clinic confirms experimental observation. A great similarity may be found between the morbid frames determined by experimental
inoculation of such elements, and that which represents the former notion of pre-tuberculosis, of lymphatic temperament, of predisposed ground.

Since my first works in 1910 (1) up to those of VAUDREMER in 1921 (14), of VAUDREMER and his co-workers, (15, 16, 17 and 18) in the following years, until the newest ones of the already named authors, one must recognize that the infection determined by the filtrable elements of the virus, is different from the classical tuberculous infection, whose character is chiefly a dystrophic clinical frame, alias the commonest, and causing cachexy, and that, in 8 to 10 o/o of injected animals, according to MALARTRE (19), or a percentage of 3, according to CALMETTE (13) such infection evolves toward the classical form.

ARLOING, DUFOURT and MALARTRE (19) have given a clear exposition of the characters of these forms, and classify them in nodular type, the rarest, cachectic type, the commonest, and an ephemeral curable type, this latter only able to be detected, owing to the transient allergic reaction, revealed by the tuberculin test.

Thus a new field to experiments is open for investigating and determine a relative immunisation of children from tuberculous parents, which would mean a greater resistance to evolution, not only of the virus as also of the disease, creating scrofulous or chronicical conditions of the classical forms of the infection.

From the experiences of BOQUET, NEGRE and VALTIS (20) of MAC JUNKIN (21) PARAF (22), of ARLOING, THEVENOT, DUFOURT and MALARTRE (22), we are authorized to conclude to the fact of a certain grade of resistance being bestowed upon the organism of the Guinea pig by the inoculation of the filtrable elements of the virus, to a later virulent infection by the acid-alcohol-fast form.

To support this explanation, there are besides VAN BENEDEN's experiment (24), who obtained in a Guinea pig the phenomenon of KOCH, in consequence of two inoculations of tuberculous extra virus, obtained in two different stuffs (filtrate of pleuretic outspill, filtrate of spuitum) and those of VALTIS, SAENZ and MONALDI (25), which also are a confirmation of DEBRE, LELONG and BONNET's (26).

Then, it can be foreseen that: vaccination of children from tuberculous parents, may be effective, under still undetermined conditions of vaccination dose renewed in transient or curable forms of the transplancetal infection, by the filtrable elements of the virus.

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In October 1927, I had an opportunity to report to the First Pan-American Congress of Tuberculosis, held in Cordoba, the first conclusions of the series of experiments, which I detailedly exposed in the first part of the present work.

My opinion is that the experimental facts I observed may be explained as ascribable to the action of the filtrable elements of the tuberculous virus, the same exercising their morbigenous power, provoking the death of the first Guinea pig by cachexy. Inoculated anew to a second animal, the virus determined the formation of a chancre at the inoculation spot
(which contradicts the general observation upon the pathogenic action of the virus), with the regeneration of acid-alcohol-fast forms.

The acid-alcohol-fast forms were re-absorbed, but the satellite ganglion, transported to another Guinea pig, caused, by two consequent passages, the death of the animal after 5 days.

On the other part, the morbigenous power of the virus showed itself, once in a first passage, another time in a second passage in the maternal organism, and after a third passage in the organism of the fetus, in which always identical lesions were visible: pulmonary infarcts, pulmonary capillary hemorrhages, necrosis and cheesy degeneration of liver, polyadenia and cachexy.

In one case, by a fourth passage, a typical change was formed, which cicatrized after one month. In no incidence was the virulent element found under the shape of acid-alcohol-fast bacillus.

Everything, in this experimentation happened as if some latent infection were ruinng little by little the organic resistance, through lasting functional troubles, which led to the formation of lesions which were easily verified.

This dyscrasic condition was transmissible from the mother to the fetus, thus giving a new confirmation of the notion of morbid inheritance. Still an interesting fact results also from the experimental series above referred to, that of having been the tuberculous virus, characterized by the acid-alcohol-fast form, discovered only in such cases, where the infection by the filtrable elements was got at by direct inoculation of the virus.

In cases, where the biologic phenomenon of inheritance interfered, this latter was made patent only by morbigenous power, with the decurring functional and anatomic troubles, without being possible to bring into evidence the figurative etiologic element.

This observation demonstrates that even in cases where the passage of the figurative element of the tuberculous virus (acid-alcohol-fast bacillus) from the mother to the fetus does not effect itself, the morbid inheritance is made obvious.

We shall thus have established the notion of pathenergogen, that is to say, of the morbigenous energy pertaining to heterologous stuff, and which in the present case is to be dissociated from the notion of ultra virus, this latter being considered as a metacyclic stage of germination of the tuberculous virus, or of the granular form of this virus, which to gather represent an integralizing, biogenic stage in the vital cycle of the KOCH's bacillus.

I consider as the responsible for morbid inheritance in tubercular infection, the morbigenous element accompanying the tuberculous virus, which is not cultivable in vitro, nor morphically revealable in vivo, but is likely to be transmitted in experimental series by direct inoculation, or by natural passing through the placenta, is dproved to exist only by its effects and is also characterized by continuation of these same properties. This is what I called: pathenergogen.
CONCLUSIONS

The morbid inheritance from mother to fetus, takes place, in the tubercular infection, by the placenta, allowing in certain most unfrequent cases, the evolution of the etiologic agent up to the known classical form, represented by the acid-alcohol-fast rod; transmitting the potentiality of evolution of this factor, made patent through subsequent passages to sensible organisms, in less rare cases, and bestowing, in much more numerous cases, an atypical tuberculous illness, whose symptoms are changes in the lymphatic system, such as micro-polyadenia, hyperplasia of the ganglia, through infarcts and capillary hemorrhages, necrotic changes in tissues and viscera, and through a deep perturbation of the feeding metabolism which may attain to the extreme degree of causing death.

The functional changes and perturbations, which are characteristics of the atypical tuberculous disease, have been observed by all investigators who have undertaken the problem, even by those who have been led to deny the existence of the filtrable form of the virus, and who considered these symptoms as being the results of a toxical action.

This explanation cannot hold in the case, owing to the fact of these lesions being transmissible by consecutive inoculations, and of they appearing repeatedly, even when the pathogenic element is supplied by an organism to which it was passed through the placenta, as a maternal inheritance (FONTES) (27).

In tuberculous infection, then, there happens heredo-contagion together with the decurrent morbid inheritance.

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