Altogether, as regards the employment of mercury, as well as that of potassium iodide, we are absolutely on an empirical standpoint. To mercury we ascribe a direct effect on the virus, to iodine the power of furthering the absorption of the products of syphilis. This view indeed is supported by clinical observation. Fournier especially is its advocate, and again and again emphasizes the doctrine that the course of syphilis, as a rule, depends on the treatment instituted; that the production of late gummous symptoms is due to inadequate mercurial treatment; that syphilis as a chronic disease requires a chronic treatment.

Quite different, however, is the course of a third group of eruptions which otherwise are included sometimes among the early (or secondary), sometimes among the late (gummous) forms, but which, according to their course and character, can be erected into a special class. I mean the processes progressing with so-called "suppuration," such as develop especially on the skin in the shape of pustular, bullous, and ulcerous forms, in the intestines as "abscesses." We seek their cause in an especially large quantity of bacteria at once overwhelming the organism, hence their destructive local effect, as well as their consequences which threaten the integrity of the system as a whole. On the other hand, not rarely an existing disease (tuberculosis, etc.) is the cause of the acute necrotic disintegration of the syphilitic products. The local processes have this in common with the gummous processes, that they, if left to themselves, are followed by permanent losses of substance; they differ from them and approach the papular forms by their very rapid course, new-formation and decay being effected in a very short space of time, and finally in that there is almost no treatment which can prevent the disintegration. (Mercury is powerless against so large a quantity of bacteria and otherwise injures the organism already attacked by the syphilitic virus.) From all this—aside from the not uncommon implication of the entire organism—it follows as a natural sequence that these syphilides possess a characteristic malignancy, and that we are justified in separating this group both from the papular and the gummous neoplasms. But it must be remembered at the same time that every papule and gumma, by the supervention of external accidents, may "suppurate," *i. e.*, necrose more rapidly than is usually the case.

Here again the question arises: In what manner does the virus act? Does it produce only a very acute inflammation which at once prevents any attempt at organization, or does it effect, besides this inflamation, direct necrosis of tissue? A decided answer cannot be given, even if we were to ascribe a part to the "specific tissue alterations." The actual facts are, a rapidly progressing infiltration with inflammatory cells fills the tissue, and this infiltration perishes together with the basis substance. At the periphery the course is slower; here syphilitic new-formation takes place which may be preserved from the destruction going on at the centre, by appropriate measures.

In other cases—I have in mind here the bullous syphilide in hereditary lues—the intensity of the virulence manifests itself by the dissolution of the coherence existing between the papilla and the epithelial layer. From above and below there project into the bulla the conical processes of the two otherwise interlocked layers. The form of hemorrhagic syphilide will likewise hardly find a better interpretation than by a special violence in the activity of the virus on the vessel walls.

Under this head belong finally the acute abscess formations in internal organs (*e. g.*, of the thymus gland), the joints, the bones in hereditary syphilis. Incidentally they also teach us the unity of all syphilitic neoplastic processes which differ only in their terminations, and then in their extreme forms permit of a strict classification, while the

majority of the formations represent intermediate and transitional steps, and appear to belong now more to the one, now to the other type.

However, we know two clinical forms of particularly malignant syphilis; one in the true hereditary form transmitted by semen and ovum, the other in the so-called "galloping" syphilis in acquired disease. The latter is characterized by the rapid development—beginning a few months after infection—of destructive (pustular and ulcerating) efflorescences which, in rapid succession and often in very great numbers, uninfluenced by our otherwise effective treatment, frequently enough jeopardize the life of the patient.

This clinical form of "galloping" syphilis has specially received the name of "malignant syphilis" and therefore is not to be confounded with "grave" syphilis (as, for instance, syphilis of the brain, etc.) It may also be emphasized here that it is erroneous, in this galloping syphilis, to speak of "gummous" processes. Precisely the essential characteristic of gummata, the insidious development and the slow, indolent course, is lacking.

Furthermore, hereditary syphilis is certainly the highest degree of infection that could be imagined, which will be evident at first sight from the insignificant number of syphilitic fœtuses who maintain life.

Wherein, in these two categories, are we to seek the reason of the malignant, grave course?

In the first place, as to the hereditary form, I think I must inculpate the quantity of the virus at once overwhelming the organism. The idea suggests itself to make the weak organism, incapable of resisting, responsible for the grave character of the disease. It should be considered, however, as opposed to this view, that acquired syphilis, in children but a few months old, does not by any means run a malignant course.

Besides, I know of no better way to explain the varying intensity of inherited syphilis, which decreases in malignancy in proportion to the increasing age of the parental syphilis, than by the gradually lessening quantity (partly spontaneously, partly temporarily by mercurial treatment) of the virus present in the parents and transmitted to the offspring.

Again, as to galloping syphilis, the attempt to find the cause of this unusual course in the debilitated, non-resistant quality of the body, could not be made to harmonize with clinical experience.

No support has been offered for the view that there are specific qualities of the virus (that is, qualitative differences). But we know an epoch in which syphilis exhibited only the character described as the "malignant" form, namely, its spread throughout all European countries at the end of the fifteenth century and the succeeding decades. The study of this epoch brings us nearer to the view of the qualitative differences between the virus of that time and that of to-day.

To explain this malignancy, the factor hitherto relied upon—the varying quantity of the virus—does not suffice.

However, in the discussion of this question two points of view, not mentioned above, come into consideration; namely, the immunity against a second infection acquired by one attack of the disease, and besides, the hereditary quality of the disease as well as of the immunity.

It is a fact observed also in other infectious diseases that epidemics which have for decades taken root among nations and produce comparatively benign affections, appear as malignant diseases when they attack a people for the first time. Instances are fur-

nished by the first appearance of measles on the Faroe Islands, the introduction of leprosy into the Sandwich Islands.

This explains to us the malignany of syphilis on its first appearance in Europe when contrasted with the present benign course in the majority of instances; they also give an explanation of the varying character of the disease in the several European countries.

The same conditions in respect to syphilis are said to prevail, for instance, in Spain. There syphilis takes a remarkably mild course which manifests itself especially in the very small number of hereditarily syphilitic children. The cause of this feature is attributed to the immense spread of syphilis for generations in all classes of the populace.

Does this enfeeblement of the disease rest on a gradual decrease of the malignancy of the virus; or on an increasing power of resistance?

Both are likely. It may be, too, that both conditions stand in a certain correlation.

Let us consider the latter point: the power of resistance to the infection; this would reach its highest degree in the incapability of being affected at all. Man does not possess this immunity spontaneously, but it is acquired when a person has passed through a syphilitic disease; a new infection then is as good as excluded, a fact borne out by the small number of real reinfections against the great many cured cases of syphilis. This "immunity" exists indubitably, and in syphilis we even possess, in the above-described difference between a primary induration and a syphilitic papule, an anatomical landmark of the modification of the tissues representing the immunity: in the indurated ulcer, hyperplastic connective-tissue cells which no longer occur in later forms of syphilis.

If this acquired immunity could be transmitted to posterity in its original strength, the succeeding generation would be protected against syphilis. This is not the case, any more than other acquired qualities are transmitted unmodified. But a certain degree of "modification" has been inherited, which has already led to a greater resistance toward the effect of the (originally unchanged) syphilitic virus. But if this generation is infected, there occurs at the same time a weakening of the virus. The latter is, as it were, under less favorable nutritive conditions, and hence its quality is weakened.

(So also are reinfections always more benign than the first attack, in syphilis, measles, scarlatina, etc.)

Let us picture to ourselves these processes: increase in the power of resistance and thereby weakening of the virus in the progressively less favorable soil, continued through many generations, would easily explain the diminution of the malignancy in nations thus affected.

The diminished malignancy of the entire character of the disease of to-day against that of old, therefore, could well be due to the continued transmission of the immunity. But this leads not so much to an increased power of resistance against the syphilitic virus as to a lessening of the intensity of the virus, because the latter has developed under progressively less favorable conditions from generation to generation. A diminished virulence of the virus, therefore, is the permanent result attained by syphilis transmitted through generations. The resistance acquired by the single individual toward the effect of an unmodified virus is of less importance. Thus the disease of a German who became infected in Spain is benign because, in that country, the syphilitic virus has gradually attained a greater benignancy; while the Europeans who acquire the disease, for instance, in China, suffer from it in almost the same malignant way as the Chinese. The cause of this malignancy of syphilis in China is ascribed by authors to the fact that the disease is

left entirely unheeded, receiving no treatment. This brings us to another factor to which we must concede the capacity of diminishing the virulence of the poison—the influence of therapeutics. Just as the latter is able in a single case to modify the course of the disease—so it likewise modifies in the course of generations the character of the virus, in the manner above explained.

It remains for us to consider the immunity enjoyed by those apparently healthy women who, without showing any objectively demonstrable signs of syphilis, have borne children hereditarily syphilitic from the father's side, and in the great majority of cases are exempt from infection. Experience teaches that these women may nurse their hereditarily syphilitic children without danger, while the infection of healthy wet-nurses by such children is not of rare occurrence. Have we to deal in such cases with immunity or disease of the women? Hutchinson is inclined to assume the latter, from a gradual poisoning of the maternal organism by the fœtus. This view is based on the observation of tertiary (gummous) processes occurring in later years, without any secondary or even primary symptoms having ever been present.

It is also possible to imagine immunity without disease, similar to the immunity toward variola which is acquired, not by variola, but by vaccinia.

It still remains for us to state that the above relations between mother and child may also manifest itself in the opposite direction, in this way, that the syphilis of a woman acquired after conception may render the fœtus insusceptible to later infection.

As regards the hereditary transmissibility of syphilis, it can be brought into perfect harmony with the bacterial nature of the syphilitic virus. This applies to the two modes ordinarily designated the "heredity" of syphilis; we understand by it, on the one hand, the infection of the first germ, whether by the semen of a syphilitic father or the ovule of the diseased mother, or both, *i. e.*, "genuine heredity." On the other hand, however, we apply this term also to "intra-uterine infection of the fœtus, healthy by conception, by syphilis acquired after conception by the mother"—a rare occurrence, but one nevertheless positively observed. This latter possibility appeared improbable to some authors because the "fixed" syphilitic contagium was said to be unable to pass through the septa between maternal and fœtal placenta. But since Spitz has furnished the proof that the spirilla of relapsing fever are able to pass that way, and since the same power has been demonstrated in the bacilli of anthrax, nobody will, at least *a vriori*, deny the similar property to the bacteria of the syphilis.

In proof of the transmissibility of syphilis by semen and ovum, we refer to the analogy with the corpuscular disease of the silk-worm. This disease (pebrine, gastine) is an epidemic, infectious, and hereditary affection during which are found in the blood and in all organs of the diseased caterpillar small glossy corpuscles (corpuscles of the cornalia) which have been recognized as schizomycetes. These (remarkably large) cocci, however, occur also within the ovum from which the diseased young animals are developed. Furthermore we are indebted to Pasteur for the experimental demonstration that the heredity of the corpuscles takes place also when an affected father impregnates the healthy mother, and the latter, remaining healthy, lays diseased eggs (paternal infection); also, when the mother is affected and lays diseased eggs.

Now, what has been observed with these large cocci of pebrine is at least conceivable for the organisms of syphilis!

We have already spoken of the various degrees of intensity of the syphilis occurring in fœtuses and its regular moderation (proportional to the increasing age of the disease

in the parents). But a few words must be added about the form termed tardy hereditary syphilis.

Although it has been much talked about, the fact is that there is no positively authenticated case of this tardy form on record. By tardy hereditary syphilis we understand a form appearing with the symptoms of the late stage of syphilis (gummous pharyngeal and nasal ulcerations, swellings of the bones, etc.), from five to ten or more years after birth, without having previously shown any indication of the disease. Theoretically we might explain these cases, inasmuch as they are analogous to those gummous affections which, in acquired syphilis, may follow the early forms after an interval of years, sometimes even of decades. Hence we should have to deal with hereditarily transmitted germs which have always remained latent, and besides, with that alteration of the tissue which we felt forced to presuppose in the case of gummous processes. This anomaly of tissue and its origin in tardy syphilis we could relegate back, first, to syphilis of the semen or ovule which from the beginning would have to create pathological tissues in a specific manner. Second, in the case of infection, if comparatively weak, of a fœtus of healthy conception, taking place in utero by way of the placental interchange of blood, the absence of early symptoms of a syphilis manifesting itself subsequently would seem capable of explanation. It is well known that Hutchinson has suggested a similar theory of the transmission of virus in explanation of *choc-en-retour* (*i. e.*, infection of the mother by an *a patre* syphilitic fœtus).

But in none of the cases of so-called tardy syphilis thus far reported can preceding disease (without early forms) be positively excluded. There is always an absence of non-syphilitic history attested by accurate medical observations. For of course little reliance is to be placed on the statements of the patients or their relatives that the children have always been healthy. Another source of error lies in disregarding the exceedingly frequent occurrence of syphilis acquired in the first years of life. I content myself with enumerating briefly the most frequent modes of infection : infection during the passage through the parturient canal; from the midwife; from the wet-nurse; from domestics; from relatives by means of kissing, sleeping in the same bed, etc.; during vaccination; during ritual circumcision; by attempted rape, etc.

If we add to all this the comparatively great benignancy of infantile, acquired syphilis, especially under proper treatment, we shall not be surprised that tertiary symptoms are interpreted as tardy hereditary syphilis, because the infection could no longer be traced.

Surveying again the entire picture of syphilis from our standpoint, we obtain the following theses :

I. *Infection.* The bacteria enter the organism at any part of the surface of the body where the lack of epidermis or epithelium permits penetration into the plasmatic channels.

The virus remains then at the point of infection, but some germs at once enter the circulation and rest in the lymphatic glands appertaining to the point of infection.

II. Then follows the stage of the first incubation, during which nothing can be noticed of the presence and effect of the bacteria; but in that time increase of the bacteria certainly takes place at the point of infection and the neighboring lymphatic glands; finally, formation of the primary affection and swelling of the primary lymphatic glands.

III. Saturation of the organism by the bacteria multiplying in the primary affection and in the lymphatic glands.

IV. Gradual disease of the several systems: glands, skin, mucous membrane, etc. The glands become the depositories of the bacteria and harbor them in the so-called latent periods.

V. Either spontaneously or by energetic, persistent treatment these germs are finally destroyed, or else the germs are preserved, and,

VI. Relapses follow the intervals of latency, larger quantities of the bacteria again gaining access to the circulation.

VII. The nearer to the date of infection, the larger is the number of the bacteria present in the body. Hence in later periods :

1. Gradual decrease in infectiousness.
2. Gradual decrease in the capacity of hereditary transmission.
3. Rarer and but isolated occurrence of foci of disease.

VIII. At the same time there has been gradually developed, perhaps by chemical by-products of the bacteria, a modification of the tissues which in later stages forms the basis for the gummous forms.

IX. Mercury is a direct poison for the bacteria of syphilis and, if used in sufficient quantity and for a long time, is capable of preventing the development of the gummous stage. Potassium iodide furthers the absorption of the neoplasms; those of the early stage in a slighter degree, most strikingly those of the gummous stage.

Respecting the varying malignancy of the disease, aside from constitutional anomalies originally present, there enter into the consideration :

1. Chiefly the QUANTITY of the virus at once overwhelming the organism; hence the dependence of the course on the energy of the treatment (see IX.).

2. Possibly also a changing quality[1] of the virus, which might have suffered a weak-

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[1] In reference to the changing quality, *i. e.*, the variable malignancy of one and the same fungus, we have only lately again acquired more positive information. Pasteur, Toussaint, and Chauveau had previously found that it was possible, by specially arranging the experiments, particularly by increasing the temperature of incubation, to deprive the fungi of anthrax more and more of their virulence, so that after some weeks they finally became altogether harmless. Withal, the morphological qualities and propagative powers remain unchanged. Fungi thus modified even transmit their respective degrees of virulence to their descendants. Koch ("Ueber die Milzbrandimpfung. Eine Entgegnung auf den von Pasteur in Genf gehaltenen Vortrag," 1881) has recently confirmed these experiments, and therefore, in the doctrine of infection, we must henceforth take into account a changing virulence of morphologically identical bacteria, depending on external conditions.

Besides the temperature, there is certainly a whole series of other factors (*e. g.*, acquired and inherited immunity) which modify the development and the qualities of bacteria. It has long been known that not every animal species is receptive of any and every disease; we have even learned that closely related animals, such as field and domestic mice, or various races of sheep, react differently on the same virus, and hence it will appear plausible that different human races show similar variations, or even that within the same race the receptivity of the several individuals for the disease-producers is not always the same. The history of leprosy, of yellow fever, scarlatina, typhoid fever, etc., abundantly illustrate what has been set forth above. In fact, this circumstance is nothing else but what we continually observe in the cultivation of bacteria, viz., that even the most insignificant alterations of the experimental conditions may influence or retard the development of the organisms. (Comp. the very commendable essay by Lichtheim, "Ueber den gegenwärtigen Standpunkt der Pilzlehre mit Rücksicht auf die Infectionskrankheiten," in *Aerztl. Vereinsblatt*, March, 1883, pp. 53 et seq.)

ening by the immunity due to previous disease and further hereditary transmission of this immunity in the course of many generations.

IV. GLANDERS.

For the description of "glanders" malleus I refer to the paper by Bollinger in Vol. III. of this Handbook. A detailed discussion appeared superfluous, because Bollinger shares our conviction, culminating in this, that in glanders we have to deal with fixed, *i. e.*, organized contagia, and because, since the publication of his essay, our knowledge of the nature of the contagium has, unfortunately, not been widened.

POSTSCRIPT.

I abstract from the *Deutsche Medicinische Wochenschrift* a "preliminary communication on the labors of the Imperial Board of Health by Dr. Struck, which have led to the discovery of the bacillus of glanders:"

In the first place, a certain form of bacteria was searched for in the specific products of glanders, the so-called farcy buds, by staining sections of tissue from the lungs, spleen, liver, and nasal septum of a horse killed on account of glanders. In specimens stained with a concentrated aqueous solution of methyl-blue, afterwards treated with greatly diluted acetic acid, dehydrated in alcohol, and embedded in oil of cedar, there were found now and then slender rods having about the size of the bacilli of tuberculosis; no other forms of bacteria were present in the specific products. In order to determine whether these bacilli stood in causal relation to glanders, cultivation was resorted to.

On the 14th of September, according to what Koch has taught with reference to the cultivation of the bacilli of tuberculosis, a number of sterilized reagent-glasses containing horse or sheep blood serum were charged with particles carefully selected from glanders tubercles from the lungs and spleen of a horse killed because of glanders. In the first two days no changes were noticed. But on the third day there were noticed in the majority of the glasses numerous small translucent little drops which had formed scattered on the surface of the serum. These contained, as shown by staining them on the covering glass, countless fine bacilli of the above-mentioned size. Inasmuch as the drop existed uniformly in nearly all of the culture vessels, and only this one species of bacteria had developed in them, the experimenters were inclined to test these bacilli immediately in reference to their original relations to glanders by reinoculation into animals receptive of the disease.

But in order to meet the objection, if the transmission should be successful, that the inoculating material perhaps still contained particles of the original charge of glanders material, the cultivations were continued for a month through four generations.

From the resulting fourth cultivation, containing nothing but the above-described fine bacilli, a small quantity was abstracted on October 14th, and inoculated into the pituitary membrane and into both shoulders of an old, otherwise apparently healthy horse. After forty-eight hours the animal began to be very feverish; at the points of inoculation deep ulcers developed, from which knotty cords of lymphatic vessels extended to the swollen glands of the throat and shoulders, so that about a week after inoculation the horse presented the pronounced clinical picture of glanders. After about one month, the ulcers began to cicatrize, the glandular swelling decreased, the animal appeared also to have improved so that it became doubtful whether the symptoms after inoculation should be actually interpreted as glanderous. On November 25th the animal was killed, and the post-mortem yielded a most surprising result. On the nasal septum as well as on the points of transition from the nasal into the pharyngeal cavity there were numerous white, in part stellate nodes; in the lungs, old fibrous, likewise calcified nodes, but, besides, some quite fresh gray nodes with a red areola, and at the root of the lung a glanderous growth about the size of an apple.

Judging from this result, the animal had formerly recovered from an infection of glanders. That the recent eruptions were to be attributed to the artificial infection could not be positively asserted. But, as it furnished recent glanderous material, the latter was used in securing fresh cultivations. From these were again developed, after three days translucent droplets containing solely the above-described bacilli.

The same bacilli were found, besides, in the recent glanderous products of the dissected horse, after they had been treated with methylene blue.

Again, in the course of November, the fresh organs of a horse killed on account of glanders were examined. It was likewise possible to cultivate the same bacilliferous droplets from the glanderous nodes present in the liver of this animal. Finally, on the 1st of December, successful cultivations were made from fresh glanderous nodes of a fourth case. The result was always the same.

In the mean time the pure cultivations of the bacilli were also successfully inoculated into other species of animals that were at hand, namely, rabbits, mice, and guinea-pigs.

The rabbits reacted variously: while some animals on dissection exhibited merely local ulcers and swelling of the corresponding glands, others showed the pronounced picture of glanders. The inoculations with cultivated glanderous material into white mice, otherwise exceedingly receptive of infections of all kinds, gave negative results. Positive results, however, were obtained by the inoculation of field mice.

The results of the inoculation of guinea-pigs were surprising. Here the course of the disease varied in rapidity corresponding to the quantity of the cultivated material injected. Invariably by the third or fourth day an ulcer with greatly indurated margin developed at the point of inoculation; then the corresponding lymphatic glands began to swell to the size of a hazel-nut, or even to that of a chestnut. In many animals the process remained for weeks in this stage—probably the contagium was retained in the glands—but in others, especially those which had received a large quantity of bacteria subcutaneously, acute nodular swellings developed in the testicles, or else the ovaries or the vulva. At the same time some of the feet presented nodular swellings which latter also appeared on several parts of the skin, or else ulcerative processes developed in the nasal cavity which even led to perforation of the bone toward the outside. Finally, in some of the animals a general infection was suddenly developed which rapidly ended fatally. In such cases, especially the spleen and the lungs were interspersed with innumerable submiliary gray nodules bearing a great resemblance to miliary tubercles. These exhibited the fine bacilli found in glanderous products of the horse. All these alterations manifested their glanderous character, besides, by exhibiting the same phenomena which are observed in glanders of the horse—the metastases in the testicles of stallions, as well as the inflammations in the marrow of the bones which have their seat particularly in the ribs of horses, belong to the typical picture of glanders. The cultivations from all these organs—testicles, spleen, lungs, etc.—furnished always the same, above-described pure cultivations, which had been obtained in four different cases from the various organs of glandered horses.

Although these results rendered it exceedingly probable that the bacilli are the cause of glanders, the decisive reinoculation of pure cultures into horses was still lacking. Therefore two healthy horses were inoculated on November 28th with pure cultivated bacilli. The inoculating material for the older animal was the eighth generation cultivated for ten weeks outside of the animal body from the pure cultures obtained on the 14th of September; that for the younger animal was a cultivation which had been obtained from the testicle of a guinea-pig inoculated with the fourth generation of the culture from the 14th of September and which had died on November 8th, the cultivation having been continued through five more generations outside of the animal body. In order to obtain the most rapid infection possible, injections were made on both sides of the neck, the breast, in the flanks, and, in the younger animal, also on the dorsum of the nose. The Schneiderian membrane was not touched in order to ascertain whether secondary eruptions would develop on the intact mucous membrane. A few days later, the points of injection showed diffuse, doughy swellings on both animals. The animals were off their feed, their legs became stiff, and their coat rough. After about a week, cords like strings of beads could be felt extending along the skin to the corresponding glands, in both animals. The swellings had broken and secreted a turbid yellowish-green fluid. On the twelfth day, besides the former symptoms, there was observed on the young horse an ulcer in the skin of the forehead, about the size of a silver quarter, which had penetrated to the frontal