to repeat the above examinations this year, and to examine these other varieties.

The practical results of the above investigations are, that for the production of either syrup or sugar from the sorghums, the cane should be worked when fully ripe, as evidenced by the seeds having become hard and dry, the lower blades of the stalks drying and falling away, and the appearance of off-shoots from the upper points of the stalks. At this period, not only is the total amount of sugars, both sucrose and glucose, at its maximum, thus giving the largest yield of syrup, but the relative proportions of crystallizable sugar to uncrystallizable, is also at its maximum, thus giving the largest yield of sugar.

X.—On Virulent Diseases, and Especially on the Disease Commonly Called Chicken Cholera.

By M. Pasteur.

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Virulent diseases may be ranked among the greatest of the evils that afflict living beings. To prove this, we have merely to name measles, scarlatina, variola, syphilis, glanders, the carbuncular disease, yellow fever, typhus and the cattle plague. This list is far from being complete ; the pathology of the most important diseases may find a place here.

When the ideas of Liebig on the nature of ferments, were in vogue, each virus was considered as a substance undergoing an internal change, which could be communicated to living organisms, turning the constituents of these into a virus of the same nature. Liebig was well aware that the first apparition of ferments, their multiplication and their power of decomposition, present the greatest analogies with the phenomena of life, but, in the introduction to his Organic Chemistry, he tells us that these analogies may be considered as deceitful illusions.

All the experiments which I have communicated to this Academy for the last twenty-three years, have demonstrated, either directly or indirectly, the inaccuracy of the opinions of Liebig. A single method has guided me in the study of microscopic organisms. This method has been essentially the cultivation of these minute beings in a pure state, that is: by eliminating the heterogenous substances, living or dead, which accompany them. By the use of this method, the most difficult questions are often solved in the easiest and most decisive manner. I will here recall one of the first applications which I made of this method (1857–1858).

Ferments, according to Liebig, are the nitrogenous substances of organisms, such as fibrine, albumen, casein, &c., in a state of decomposition, resulting from *contact* with air. There was no fermentation known, in which these nitrogenous substances were not present and active. One character of fermentations, as well as of diseases, was that they were spontaneous in their origin and development. In order to show that the hypothesis of the learned German chemist was, to use his own words, "but a deceitful illusion," I made up artificial mixtures whose only constituents were as follows: water, the mineral constituents essential to life, fermentable substances, and the germs of the ferments which act on these substances. With these mixtures, fermentation took place with a regularity and a purity, if I may use the word, which are never found in the spontaneous fermentation of nature. As every albuminoid substance had been excluded from these mixtures, the ferment appeared as a living being, which borrowed from the fermentable substance all the carbon of its successive generations, and, from the mineral constituents, the nitrogen, phosphorus, potassium, magnesium—elements, the assimilation of which is an indispensable condition to the formation of all living beings, be they great or small.

After these experiments, not only was the theory of Liebig left without any foundation, but the phenomena of fermentation presented themselves as simple phenomena of nutrition, taking place in exceptional conditions, the most extraordinary of which is the possible absence of any contact with air.

Human, as well as veterinary, medicine made use of the light which shone from these new results. Many investigators made experiments to discover if every virus or contagion was not an animated being. Dr. Davaine, in 1863, endeavored to show the functions of the *bacteridia* of carbuncular disease, which he had discovered in 1850. In 1868, Dr. Chauveau tried to show that virulence was due to the solid particles previously noticed in every virus. Dr. Klebs, in 1872, attributed traumatic virus to microscopic organisms. In 1876, Dr. Kock obtained, by artificial cultivation, the germs of *bacteridia*, which were similar in every respect to those which I had pointed out in *vibrios* (1865–1870), and the causes of several other diseases were ascribed to microscopic organisms. To-day those who are most opposed to the theory of germs, are wavering. Still the greatest obscurity prevails on the most important points.

In the great majority of virulent diseases, the virus has not as yet been isolated, and still less has it been shown, by artificial cultivation, that it is a living organism, and everything contributes to make us regard these "unknown quantities" of pathology as mysterious morbific causes. The study of the diseases which they cause, presents many extraordinary circumstances, among which the most remarkable is their non-recurrence. Human imagination can hardly venture to present a hypothetical explanation having any experimental foundation. Is it not still more surprising to find that vaccine, a virulent but mild disease, is a preventive, not only of vaccine itself, but of a more serious disease—the small pox? These facts were known from the remotest antiquity. Variolisation and vaccination have been practiced in India from immemorial times, and when Jenner demonstrated the efficacy of vaccination, the common people of the locality in which he practiced medicine, knew that cow-pox was a preservative from variola.

Vaccination appears as an isolated fact, but the non-recurrence of virulent diseases appears to be general. The organism does not go twice through measles, scarletina, typhus, the plague, variola, syphilis, &c.; at least it may be said that the immunity persists for a certain time.

Although in the presence of such mysteries, it behooves us to be humble, I dare to hope that the Academy will find that the facts which I am about to have the honor of presenting before it, throw unexpected light on the problems raised by the study of virulent diseases.

There occurs sometimes in poultry yards a fearful disease, commonly called chicken cholera. The victim overtaken by it, loses its strength, and stumbles about with drooping wings. Its feathers stand on end, and give it the appearance of a ball; it seems overcome by drowsiness; if we open its eyes, it seems to awake from profound sleep, and soon its eyelids close again. Generally death comes after a dumb agony, without the victim even moving from the position it has occupied during the last stages of the disease. In rare cases, it beats its wings for a few seconds. The internal disorders are of the most serious nature. This disease is caused by a microscopic organism which, according to Tundel's dictionary, was first suspected by M. Moritz, a veterinary surgeon in upper Alsatia; which was drawn more accurately, in 1878, by M. Peroncito, a veterinary surgeon in Turin; and which was found again, in 1879, by M. Toussaint, professor at the Veterinary School of Alfort, who demonstrated, by cultivation in neutralized urine, that this organism was the cause of the virulence in the blood.

In the study of microscopic parasites, the first, and most useful, condition to fulfil, is to obtain a liquid in which the infectious organism may be cultivated with ease, and without any admixture of other organisms of different species. Neutralized urine, which I have used with so much success to show that the product obtained by the cultivation of the *bacteridia* of Davaine, is identical with the virus of carbuncular disease (1877, Pasteur and Jaubert), does not fulfil the double end in view. But a liquid marvellously adapted to the life of the germ of chicken cholera, is a broth made from chicken's muscles, neutralized with potassa, and made sterile by a temperature superior to 100° C. (110° to 115°). The ease with which the microscopic organism multiplies in this liquid, seems prodigious. In a few hours, the most limpid broth becomes turbid, and is filled with an infinite multitude of small articulations of extreme tenuity, slightly thinner in the middle, and which at first sight have the appearance of isolated dots. These small articulations have no motion of their own, and they certainly belong to a very different group from that of *vibrios*. I imagine that they will be classified some day with other forms of virus, now unknown, when we cultivate these, as I hope we are on the eve of doing.

The cultivation of this microscopic organism presents some very interesting peculiarities.

In my former researches, one of the liquids which I used with the greatest success, was a decoction of beer-yeast in water, after filtering it to obtain it perfectly limpid, and after rendering it sterile by a temperature superior to 100° C. The most various microscopic organisms thrive on the food presented by this liquid, particularly after being neutralized. For instance, the *bacteridia* of carbuncular disease multiplies surprisingly in a few hours. It is a strange thing that this liquid is entirely unsuited to the life of the organism of chicken cholera, which dies in it in less than forty-eight hours. Is not this entirely analogous to what happens when a microscopic organism is entirely inocuous towards an animal on which it has been inoculated? It remains inoffensive because it does not develop in the body of the animal, and it does not reach the organs essential to life.

The sterility of the decoction of yeast, with respect to the microscopic organism of chicken cholera, affords us an excellent criterion for the purity of the cultivation of this organism in chicken broth. If the cultivation be pure, upon transferring it to a decoction of yeast, no development takes place, and the yeast solution remains limpid. If, however, other organisms are present, they are developed, and the solution becomes turbid. I will, in the next place, call your attention to a still more extraordinary peculiarity of the cultivation of the germ of chicken cholera. The inoculation of this organism on Guinea pigs is not so surely fatal as in the case of chickens. In Guinea pigs, particularly in the older animals, the only thing that can be observed is a local lesion, at the point of inoculation, which ends in an abcess, of greater or lesser volume. This abcess opens spontaneously and heals, and meanwhile the Guinea pig eats his food as usual, and seems to possess all the characteristics of health. These abcesses last sometimes for several weeks before discharging, being surrounded by a membrane full of creamy pus, in which the microscopic organism exists in infinite numbers, side by side with the globules of pus. It is the life of the inoculated organisms which causes the abcess, which is as a closed vessel, from which we may obtain the organism without endangering the life of the animal. The microscopic organism remains, mixed with pus, in a great state of purity, without losing its vitality. This may be proved by inoculating on chickens a small portion of the contents of the abcess. From the effect of these inoculations, the chickens very soon die, while the Guinea pig, which has furnished the virus, is entirely cured after a short time. This is an instance of the localized evolution of a microscopic organism, which causes the formation of pus and of a closed abcess, without, at the same time, causing internal disturbances or the death of the animal on which it exists. It is, however, always able to cause the death of other species on which it may be inoculated, and even the death of the animal on which it exists in a closed abcess, if through some fortuitous circumstances, it should pass into the blood or into the viscera. Chickens and rabbits, living in company with Guinea pigs, affected with abcesses of this kind, might, all at once, sicken and die, without any great change being observable in the health of the Guinea pigs. This could easily happen if the abcesses of the Guinea pigs discharged a small portion of their contents on the food of the chickens and rabbits.

An observer who witnessed these facts, and was ignorant of all the points, might well be astonished to see chickens and rabbits die in great numbers, without any apparent cause, and he would be apt to believe in some spontaneous disease. Certainly, he would not suppose that the Guinea pigs were the cause of all the trouble, when he saw them all in good health, and particularly if he knew that the Guinea pigs themselves often suffer from the same disease. Many of the mysteries in the history of contagions will some day be solved in easier ways than the one I have just mentioned. We may reject theories which are in contradiction with known facts, but we must not reject them solely because some of their applications elude our grasp. The combinations of nature are both simpler and more varied than those of human imagination.

I may easily convince you of the truth of these statements, if I add that, if a few drops from a cultivation of our microscopic organism, be placed on bread or meat given to chickens, they are sufficient to propagate the evil to their intestines, in which the little organism propagates with such remarkable rapidity, that the excrements of chickens so poisoned cause the death of those on whom they are inoculated. These facts enable us to understand the manner in which this fearful disease develops in poultry yards. Evidently, the excrements of the diseased chickens have most to do with the contagion. Nothing would be easier than to prevent the spread of the disease by isolating the chickens for only a few days; by washing the poultry yard with plenty of water, and particularly with water containing a little sulphuric acid, which kills the germ of this disease. The excrements should be carried off to a distance. After a few days, the chickens that are still alive could be brought together again with perfect safety, because this disease is so rapidly fatal that in a short time all the diseased animals would be dead.

If the cultivation of the infectious organism in chicken broth is repeated many times over, by passing from one cultivation to the next by sowing an infinitely small quantity, such as may be gathered on the point of a needle, the virulence of the germ is not weakened by the process. This is analogous to the ease with which it multiplies in the bodies of the *Gallinaceæ*. This virulence is so great, that the inoculation of a minute fraction of a drop will cause death in two or three days, and most generally in less than twenty-four hours.

Having established these preliminaries, I now come to the most important portion of this communication.

By operating certain changes in the process of cultivation, the virulence of the infectious germ may be much lessened. This is the vital part of the subject. I beg the Academy's permission to withhold a description of the processes by means of which I determine this diminution of virulence. My object is to insure independence in my studies.

The diminution of virulence is seen in cultivations by a slower development of the infectious organism, but, in reality, the two varieties of virus are identical. In the first or very infectious state, the inoculated germ may kill twenty times in twenty. In the milder state, it may twenty times in twenty give rise to illness, but not to death. These facts have an importance which is easily understood, as they allow us to form an opinion, in this particular disease, of the problem of its recidivation or non-recidivation. If we take forty chickens, and inoculate twenty of them with the very virulent virus, these twenty will die. If we inoculate the other twenty with attenuated virus, these will all be ill, but they will not die. We let the twenty chickens be entirely cured, and then if we inoculate them with the very infectious virus, they will not die. The conclusion from this is evident. The disease is its own preventive. It has the character of virulent diseases, which do not recidivate.

Let us not be astonished at the singularity of this result. All things are not here as new as they appear at first. In one important particular, however, there is a novelty which will be pointed out. Before the time of Jenner, who himself practiced this method, as I have already mentioned, there was a practice of inoculating variola to preserve from variola. In our day, sheep are inoculated with murrain to preserve them from murrain, and cattle are inoculated with peripneumonia to preserve from this fearful disease. Chicken cholera shows us an immunity of the same kind. It is an interesting fact, but it does not show any theoretical novelty. There is, however, an important novelty in the preceding observations, a novelty which gives food for reflection on the nature of virus. It consists in this, that we have here a disease whose virulent cause is a microscopic parasite, which may be cultivated outside of the animal economy. The virus of variola, the virus of vaccine, those of glanders, syphilis, the plague, &c., are unknown in their nature.

This new virus is a living organism, and the disease to which it gives rise has one thing in common with virulent diseases, properly so called, a quality heretofore unknown in virulent diseases, caused by microscopic parasites: it is, that it does not recidivate.

The existence of this disease is a connecting link between virulent diseases caused by a living virus, and other diseases, in the virus of which life has never been recognized.

I would not have it believed that the facts present the constancy and mathematical regularity which I have mentioned. To believe this would be to ignore the great variability in the constitution of animals, taken at hap hazard from among domestic animals, and also the variability in the manifestations of life in general. The very virulent virus of chicken cholera does not always kill twenty times in twenty. Sometimes this virus only kills eighteen times in twenty, but generally twenty times in twenty. We may also remark that the virus, when reduced in virulence, does not save life twenty times in twenty. Sometimes this happens only eighteen times in twenty and even sixteen times in twenty. Neither is it an *absolute* preservative by one inoculation. We may more surely prevent recidivation by two than by one inoculation.

If we compare the results above stated with what is known of vaccine and its relations to variola, we may see that the less vigorous organism which does not cause death, is analogous to a vaccine, relatively to the one that kills, for it gives rise to a disease which may be called mild, as it does not cause death, and, at the same time, it preserves from the disease in its most deadly shape. What other condition must this organism fulfil to be a true vaccine like that of cow-pox? This condition is that it should be a definite variety, and that we should not be obliged to prepare it *de novo*, when we wish to use it. We find here the same difficulty which presented itself to Jenner. After he had demonstrated that inoculated cow-pox is a preservative against variola, he thought that it was necessary to start from the cow-pox of a cow. Jenner soon discovered, however, that he could get along without cows, and make vaccine pass from one arm to another. We may try to do the same by causing our germ to pass from one cultivation to another. Under these circumstances, will the germ become actively virulent or will it remain moderately so? Although this may appear very astonishing, I can say that the last supposition is the correct one. The virulence of the germ, in the small number of cultivations which I have attempted, has not increased, and everything seems to point to the existence of a true vaccine. I may even add that one or two trials favor the idea that the attenuated virus keeps its character of mildness after passing through the bodies of Guinea pigs. Will the same thing happen after repeated cultivations and repeated inoculations? Only by experiments can such a question be answered.

At any rate, we now know of a disease caused by a microscopic parasite, which may be obtained in such a condition, that it does not recidivate, as other diseases caused by similar parasites. Moreover, we have a variety of its virus, which behaves towards it as vaccine towards variola.

The Academy may allow me a digression worthy of attention. From what has been said, we can easily obtain chickens affected with the disease called *chicken cholera*, in which death is not a necessary consequence of the disease. We may then witness as many cases of cure as we may wish. Now, I do not believe that experimental surgery has ever met with more curious phenomena than those which are present when the animal returns to health, after inoculations have been made in the large pectoral muscles. The germ of the disease multiplies in the substance of the muscle as it would in a vessel. At the same time, the muscle swells, hardens, and becomes bleached at the surface and below the surface. It becomes filled with globules of pus, but does not suppurate. Its histological elements are easily torn, because the parasitical germ is scattered through them in numerous pockets, and it feeds on a portion of their substance. I will, later on, exhibit colored figures, showing the disorders caused by the parasitical germ in case of cure. The parasite is gradually arrested in its development and disappears, while at the same time the portion of muscle which has been attacked, unites, hardens and lodges itself in a cavity whose surface resembles that of a healthy granulating wound. The portion which has suffered from the disease finally forms a sequestrum, and is so well isolated in the cavity that holds it, that it may be felt by the finger under the skin, and, by the least incision, it may be seized with forceps and extracted. The small wound left in the skin heals immediately, and the cavity is gradually filled by the renewed elements of the muscle. I will now place some of these demonstrations before the Academy.

I have now to close by an explanation relating to the non-recidivation of the disease which occupies our attention. Let us take a chicken thoroughly vaccinated by one or more previous inoculations of the enfeebled virus. What will happen if we inoculate the same chicken again? The local lesion will be insignificant, while the first inoculations, and in particular, the very first, had been the cause of such marked change in the muscle, that a large sequestrum can be easily felt by the touch. The cause of the difference in the effects of these inoculations, is to be found entirely in a greater relative facility of the development of the germ of the disease at the first inoculations, and, in the last inoculation, in the development being either entirely wanting or very feeble and promptly stopped. The consequence of this seems evident, and it is that the muscle, which has been seriously diseased, has become, even after it has been cured, unfit for the cultivation of the germ of the disease, as if this germ, by a preceding cultivation, had suppressed some principle which life does not bring back, and whose absence prevents the development of the microscopic organism. I have no doubt that this explanation, to which we are led by palpable facts in this case, will be found to be generally applicable to all virulent diseases.

It must appear superfluous to point out the principal consequences of the facts which I have had the honor to present before this Academy. There are, however, two of these which may be mentioned. One is, that we may hope to obtain artificial cultivations of every virus, and the other is, the idea of obtaining vaccines of the virulent diseases which afflict humanity, and which are the greatest plague of agriculture, in the breeding of domestic animals.

It is a duty and a pleasure for me to add, that in these delicate and lengthened researches, I have been assisted with great zeal and intelligence by Messrs. Chamberland and Roux.

Abstracts from American and Foreign Journals.

Bulletin de la Societe Chimique de Paris.

Abstractor, E. H. S. BAILEY, PH.B.

Various Thermochemical Data, BERTHELOT (**32**, 385).—From his recently published work, the author gives various data, the result of careful experiments, in regard to the heat of formation of cyanogen, of diamylene in the gaseous state, and the heat of fusion of glycerine, and its specific heat.

On the Elimination of Bromine from Bromocitraconic Acid, and on a New Organic Acid, E. BOURGOIN (**32**, 388).—By partially saturating a solution of bromocitraconic acid with caustic potash, and slowly evaporating the solution, crystals of bromide of potassium separate out, and the mother liquor consists of a new acid corresponding to the formula $C_{10}H_4O_8$. It appears to be related to pyrotartaric acid ($C_{10}H_8O_8$), and also to citraconic acid ($C_{10}H_6O_8$).

Note upon the Solubility of Benzoic and Salicylic Acids, E. BOURGOIN (**32**, 390).—A re-assertion of facts previously stated, and a description of the methods used (see Bull. Soc. Chim., **31**, 53, and this JOURNAL, **1**, 272)

On the Chlorhydrate of Phosphoretted Hydrogen, J. OGIER (**32**, 483).—In the apparatus devised by M. Cailletet, at a temperature of 14°, hydrochloric acid combines with phosphoretted hydrogen, producing hydrochlorate of phosphoretted hydrogen. It appears in the shape of small, snowy flakes. At a little higher temperature it is a liquid.