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## PASTEUR

#### AS THE

## FOUNDER OF STEREO-CHEMISTRY

BY

#### Alex. CRUM BROWN, M. D., F. R. S.

PROFESSOR OF CHEMISTRY IN THE UNIVERSITY OF EDINBURGH

FROM THE REVUE FRANÇAISE D'ÉDIMBOURG

Adresser toutes communications concernant la Rédaction à M. Charles SAROLEA, Université, Édimbourg.

#### EDINBURGH

WILLIAMS & NORGATE, Publishers SOUTH FREDERICK STREET, 20

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### PASTEUR AS THE FOUNDER OF STEREO-CHEMISTRY (\*)

The name of Pasteur is known wherever anything is known of modern progress, and even those who do not take - do not even pretend to take - an interest in science know something of Pasteur and of his work. But it is only his later work in which everybody takes an interest; his earlier investigations are known only to those who make a special study of the branches of science to which these investigations belong. And this is unavoidably so. The great majority of men, of educated men, are perfectly indifferent to the question of the symmetry or asymmetry of the ultimate molecules, of which scientific men tell them matter is made up, but they can take an intelligent interest in the work of a man of science, if they see that it has something to do with the well-being or the safety of the human race. And thus it is that, as being of more general human interest, Pasteur's later work is infinitely better known to the public than his earlier; that, while he is known to everybody as the discoverer of a method for the treatment of hydrophobia and the introducer of new principles of preventive medicine, only the few who know what stereochemistry is, reverence him as its founder.

Each of Pasteur's admirers can only bring his own special tribute.

Here in Edinburgh, a splendid gift has been presented to the University in memory of Pasteur. The late Mr. A. L. Bruce bequeathed a large sum towards the foundation

<sup>(&</sup>lt;sup>1</sup>) An address delivered at the Edinburgh Meeting of the Franco-Scottish Society. 14<sup>th</sup> July, 1897.

of a chair of Public Health in token of his sense of the great work done by Pasteur. Mr. Bruce's family has supplemented his bequest and Mr. John Usher has most munificently completed the sum necessary for the foundation of the chair, from which, no doubt next year, the discoveries of Pasteur will be proclaimed.

Many of us recollect Pasteur's visit to Edinburgh thirteen years ago, when he was one of the five delegates who represented the Institute of France at the celebration of the Tercentenary of the University of Edinburgh, and can recall his enthusiastic reception by the students and the words of kindly wisdom he addressed to them.

I feel very highly honoured by having been asked by the organisers of this meeting to address you. It is not an easy thing to do. I have to speak to representatives of the highest culture of France and to fellow citizens active and able in the prosecution of all branches of learning. A teacher must carefully consider what he says to his pupils; a scientific worker does not, without a good deal of thought, lay his views before his colleagues, but habit enables us to do these things without much embarrassment. It is more difficult to address such an audience as this on a very special scientific subject. I can only hope that those of you who are acquainted with stereochemistry may not think that I treat Pasteur's great work in too slight a way, and that I may not be intolerably tedious to those of you whose studies have not led them in that direction.

Perhaps I should apologise to our French visitors for addressing them in English, but I do indeed believe that mutual intelligibility will be better attained if I use the language with which I am most familiar.

Pasteur began his independent scientific work, as he tells us in the memorable Lectures delivered in 1860 before the Chemical Society of Paris, with the subject of crystallography, because he felt sure that this would be of great use to him in his study of chemistry. By a

happy chance, or perhaps by a more conscious premonition, he selected La Prevostaye's work on the crystalline forms of tartaric acid, paratartaric acid (racemic acid) and their salts, for careful review. He was able to confirm La Prevostaye's observations, but found a most important point which that acute and accurate observer had left unnoticed, namely that the tartrates are all hemihedral. Not that faces of hemihedral forms always occur on crystals of tartrates, but that some crystals of every tartrate show such faces. The hemihedry which Pasteur discovered in the tartrates is of the sort which is called nonsuperposible, it may be illustrated by means of the models which I show you. These two models resemble each other in every point but one : the one will not fit into a mould made from the other, the one is exactly like the mirror image of the other. We are quite familiar with that sort of difference. Our right hand will not fit into a mould made from our left hand. Our right hand is exactly like the mirror image of a left hand. If we stand before a mirror and hold up our right hand, the man in the mirror - exactly like us - holds up his left hand. We call a form symmetrical if it is identical with its mirror image. If it is not, we call the two forms, the thing itself and its mirror image enantiomorph. Pasteur gives us one example of a symmetrical thing, the human body. But an actual, real human body is not strictly symmetrical even as regards its outside. Leaving out of consideration what we may call accidental deviations from symmetry, such as the marks we carry with us of encounters we may have had with external forces, scars of battle, for instance, there is none of us whose right hand is exactly the mirror image of his left hand; in most of us the nose is slightly inclined to one side, it is unusual to find the two eyes quite the same in optical properties; in fact, if we examine our own body with care, we are sure to find many points in which there is manifest want of symmetry. And if we look within, the most

rudimentary knowledge of anatomy discloses an essential asymmetry. Pasteur was of course quite aware of all this, and his use of the human body as an illustration of a symmetrical form is to be taken only in a rough and general way; we shall see that it is a point of his argument that living things are asymmetric. To return however to the tartrates, Pasteur observed that of the three axes to which their crystalline form may be referred, two have in all tartrates nearly the same ratio, while it is the variation of the third axis which gives the variety of form to the different tartrates. Orienting the crystals by these corresponding axes, he saw that the hemihedry of all the tartrates is in the same sense; we may call it right or left, the name is a matter of convention, but they are either all right or all left. Thirty five years before Pasteur's work on the tartrates and racemates, Biot had discovered that certain substances in the liquid state such as oil of turpentine, in a vitreous non-crystalline form such as barley-sugar, or in solution, have the property of rotating the plane of polarisation of a ray of polarised light. Tartaric acid is one of these substances. The coincidence of this sort of optical activity and non-superposible hemihedry has a certain analogy with the case of quartz. In that substance also we find these two characters conjoined. But it is only in the crystalline form that quartz affects the position of the plans of polarisation, while it is in an uncrystallised form or in solution that tartaric acid does so. In quartz the molecules are symmetric, but are arranged in an asymmetric order in the crystal; in tartaric acid the molecules themselves are asymmetric.

A communication sent by Mitscherlich to Biot and, by him laid before the Academy of Sciences had puzzled Pasteur from his student days.

It was to the effect that not only in chemical composition, but to the minutest detail in crystalline form and all physical properties but one, the double soda and ammonia

salts of (a) paratartaric (racemic) acid and (b) tartaric acid were identical. The one point of difference was that the solution of the first did not and the solution of the second did affect the position of the plane of polarisation. Pasteur supposed that Mitscherlich must have overlooked another point of difference, namely the absence of hemihedry in the one case and its presence in the other, and having prepared the two salts, he carefully examined the crystals. As he expected he found those from the tartrate solution hemihedral, but to his great surprise found that those from the racemate solution were so also. He saw however that some of the crystals from the racemate exactly resembled those of the tartrate while some of them had the enantiomorph form. He laboriously picked out and separated from one another the two sorts of crystals and he now had in his hand what no one had previously seen, except in a looking-glass, a specimen of an antitartrate. It was easy now to prepare the anti-tartaric acid, to show that in every respect it is the mirror-image of tartaric acid, and to reproduce racemic acid by mixing equal quantities of the two enantiomorph acids.

It is well for us to try to realize the feelings of a discoverer of a really fundamental truth of nature, and Pasteur has in a singularly modest way enabled us to do so. He says little of what he himself felt, but he tells us what Biot, then an old man, did and said. I quote from Pasteur's lecture : « L'annonce des faits qui précèdent me « mit naturellement en rapport avec M. Biot, qui n'était « pas sans concevoir des doutes au sujet de leur exacti-« tude. Chargé d'en rendre compte à l'Académie, il me fit « venir chez lui pour répéter sous ses yeux l'expérience « décisive. Il me remit de l'acide paratartrique qu'il avait « étudié lui-même préalablement avec des soins particu-« liers, et qu'il avait trouvé parfaitement neutre vis-à-vis « de la lumière polarisée. Je préparai en sa présence le sel « double avec de la soude et de l'ammoniaque qu'il avait « également désiré me procurer lui-même. La liqueur

« fut abandonnée dans l'un de ses cabinets à une évapo-« ration lente, et lorsqu'elle eut fourni environ 30 à « 40 grammes de cristaux, il me pria de passer au Collège « de France, afin de les recueillir et d'isoler sous ses yeux « par la reconnaissance du caractère cristallographique, « les cristaux droits et les cristaux gauches, me priant de « déclarer de nouveau si j'affirmais bien que les cristaux « que je placerais à sa droite dévieraient à droite et les « autres à gauche. Cela fait, il me dit qu'il se chargeait « du reste. Il prépara les solutions en proportions bien « dosées et, au moment de les observer dans l'appareil « de polarisation, il m'invita de nouveau à me rendre « dans son cabinet. Il plaça d'abord dans l'appareil la « solution la plus intéressante, celle qui devait dévier à « gauche. Sans même prendre de mesure, par l'aspect « seul des teintes des deux images ordinaire et extraor-« dinaire de l'analyseur, il vit qu'il y avait une forte « déviation à gauche. Alors, très visiblement ému, « l'illustre vieillard me prit le bras et me dit : « Mon cher « enfant, j'ai tant aimé les sciences dans ma vie que cela « me fait battre le cœur. »

Pasteur goes on to say : « Vous excuserez, messieurs, « ces souvenirs personnels qui ne se sont jamais effacés de « mon esprit. De nos jours, avec nos habitudes, on y répu-« gnerait dans le cours d'un mémoire scientifique, mais ils « m'ont paru de mise dans une exposition orale; et peut-« être que l'intérêt biographique de semblables souvenirs « constituera l'un des avantages du genre d'enseignement « que la Société chimique inaugure au ourd'hui.

« Du reste, il y a plus que des souvenirs personnels.
« A l'émotion du savant se mêlait chez M. Biot le plaisir
« intime de voir ses prévisions réalisées. Depuis plus de
« trente années, M. Biot s'était efforcé vainement de faire
« partager aux chimistes sa conviction que l'étude de la
« polarisation rotatoire offrait l'un des plus sûrs moyens
« de pénétrer dans la connaissance de la constitution
« moléculaire des corps. »

Besides the method just described of separating the two enantiomorph constituents of racemic acid, Pasteur discovered two other and quite distinct ways of effecting this separation, or at all events of obtaining one or other of the asymmetric forms. He says in introducing the first of these methods. « A right-handed and a left-handed screw will with equal readiness pierce through a block of wood, if the fibres of the wood are straight and parallel. But if the fibres of the wood have themselves a right or left handed twist the two screws will not equally well penetrate the block, and so if we form the salts of right and left tartaric acid with asymmetric base such as cinchonicine, which deviates the plane of polarisation to the right, as ordinary tartaric acid does, we should not expect these two salts to have the same physical properties. » He accordingly neutralised cinchonicine with racemic acid, and evaporated the solution. At first there crystallised out in a perfectly pure condition the cinchonicine salt of left-handed tartaric acid, the salt of the right-handed acid, being much more soluble, remained in solution. On further evaporation this salt crystallised in a form quite different from that of the salt of the right handed acid. Great use is now made of this method for separating the constituents of what we now call « racemoid » mixtures of compounds, that is substances resembling racemic acid as being mixtures or compounds of substance composed of enantiomorph molecules, for we now know a large number of such substances, and many of them have been thus split up. The third of Pasteur's methods is of very special interest on account of its bearing on his later work.

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It had long been known that tartrates mixed with water containing nitrogenous organic matter were liable to undergo fermentation especially in warm weather. Pasteur studied the conditions of the fermentation of ammonium tartrate, button examining the fermenting liquid by means of the polariscope it was seen that the originally and then subjected ammonium racemate to exactly the same treatment, using the same ferment, Fermentation took place as in the case of the tertrate;- inactive solution was gradually acquiring left-handed optical activity, that when this ceased to increase, the fermentation came to an end. The solution now contained none of the right-handed salt, and pure left-handed tartrate of ammonia could be obtained from it. He thus proved the surprising fact that the ferment, a minute fungus, is physiologically asymmetric, and causes the decomposition of the one enantiomorph, while leaving the other unchanged. Later investigations have shown that this asymmetric character of organised ferments is general, some micro-organisms causing the destruction of the one, some, of the other constituent.

Pasteur saw in this a confirmation of a view which he had adopted from a consideration of the fact that the known substances having molecular asymmetry are produced in living things, plants or animals.

Pasteur drew from these facts the conclusion that a great, perhaps, the only distinction between the chemistry of living matter and that of dead matter is that the former can and the latter cannot produce substances having molecular asymmetry.

To understand this, me wust look at another most important discovery made by Pasteur. He found that when the tartrates of certain organic bases are raised to a pretty high temperature they undergo a molecular change, such that when the acid is extracted from the mass it is no longer optically active : it is now a mixture of racchic acid and a new acid having the same composition. This new acid is, like racemic acid, quite without action on the position of the plane of polarisation, but it cannot be separated into two enantiomorph constituents. It was called by Pasteur Inactive tartaric acid, or tartaric acid inactive by compensation. It is now often called « Meso-tartaric acid », the name given to it by Dessaignes. There are thus four forms of tartaric acid, (1) the righthanded, (2) the left-handed, (3) racemic acid, the compound in equal proportions of (I) and (2) and therefore

inactive by compensation, and (4) inactive, or mesotartaric acid. Now it was almost unavoidable that Pasteur should suppose (as we now know erroneously) that in a similar way every substance capable of asymmetry at all should have four forms corresponding to those wich he had shown to exist in the case of tartaric acid. Of these four forms the fourth is the only one which Pasteur, at the date of his Lectures, 1860, admitted might be made without the aid of living things. That this was indeed his opinion at that time appears from his remark in speaking of the inactive form of malic acid, which he had obtained from Dessaignes's aspartic acid had been prepa- This red from fumaric or from malic acid, and therefore from ex symmetric substances without the aid of living things. Pasteur says : « On pourrait se demander si le nouvel acide malique n'est pas le paratartrique de la série, c'està-dire la combinaison de l'acide malique droit et de l'acide malique gauche. Cela est bien peu probable, car alors non seulement avec un corps inactif on aurait fait un corps actif, on en aurait fait deux, un droit et un gauche. »

It is obvious that at this time Pasteur's opinion was that life was necessary for the production of racemoid (paratartriques) as well as of separated, single substances with molecular asymmetry from symmetrical, inactive substances. But it was impossible for him to retain this view long unmodified. Soon after the delivery of the Lectures, Perkins and Duppa obtained a form of tartaric acid from dibromosuccinic acid, which Pasteur, after a complete examination, recognised as racemic acid. In his note to the « Annales de Chimie et de Physique », in which he records the result of his examination of the acid of Perkin and Duppa, he says : « Je m'empresse de mentionner ici un scrupule que j'ai toujours eu en ce qui concerne l'acide malique que j'ai appelé inactif. Est-ce bien l'acide malique inactif par nature? Ne serait-ce pas l'acide malique inactif par compensation, le racemique malique, si

je puis ainsi parler? On le saura dès que les quatre acides maliques auront été obtenus. »

It is plain that already, in 1861, he had revised his opinion as to the distinction between the Chemistry of living and that of dead matter in consequence of the discovery that racemic acid could be produced in the laboratory from succinic acid. His only doubt was that perhaps succinic acid itself might be racemoid. This doubt, he says, would be removed if racemic acid could be prepared from Maxwell Simpson's synthetic succinic acid which could not be suspected of any kind of asymmetry. This was accomplished by Jungfleisch, so that all doubt was set at rest.

Pasteur's time and attention were now taken up with the question of fermentation and of the origin of ferments, and it is not until 1874 that we have one, and again in 1875 another reference to the question of the origin of molecular asymmetry. These are, however, particularly interesting as showing his mature opinion on the matter, an opinion which we have no reason to think he ever changed. In 1874 he writes : « Tous les produits miné-« raux, toutes les substances organiques qu'on obtient « artificiellement en si grand nombre dans les laboratoires « sont privés de la dissymétrie moléculaire et de l'action « corrélative sur la lumière polarisée, propriétés qui sont « au contraire, l'une et l'autre, inhérentes à un grand « nombre de substances organiques naturelles et des plus « considérables sous le rapport physiologique, telles que « la cellulose, les sucres, l'albumine, la fibrine, la caséine, « certains acides végétaux, etc.

« J'ai reconnu, il est vrai, que l'acide succinique ordi« naire, corps inactif, avait fourni, entre les mains de
« MM. Perking et Duppa, de l'acide paratartrique réso« luble en acide tartrique droit et en acide tartrique
« gauche, et postérieurement, M. Jungfleisch, dans une
« série de travaux accomplis avec une rare habileté, est
« arrivé au même résultat, en partant de l'acide succi-

nique de synthèse, que M. Maxwell Simpson avait
réussi à préparer au moyen des éléments carbone et
hydrogène. Ces derniers faits n'entachent pourtant en
quoi que ce soit la vérité de cette proposition, que,
jusqu'à présent, on n'a jamais formé un corps actif
simple à l'aide de corps inactifs. Je suis même très
porté à croire que le nombre des *paratartriques et des paratartriques résolubles* est considérable. Les *para tartriques* sont une des formes des corps qui ont un plan
de symétrie, et ils prennent naissance sous l'influence
d'actions qui n'ont rien de dissymétrique. »

In 1857 he writes : « Il n'existe pas dans la science « un seul exemple d'un corps inactif qui peut être, jus-« qu'à présent, transformé en un corps actif par les « réactions de nos laboratoires.

« Transformer un corps inactif en un autre corps inactif, « qui a la faculté de se résoudre simultanément en un « corps droit et en son symétrique, n'est en rien compa-« rable à la possibilité de transformation d'un corps « inactif en un corps actif simple. C'est là ce qu'on n'a « jamais fait; c'est là, au contraire, ce que la nature « vivante fait sans cesse sous nos yeux, et telle est la « proposition formulée dans les citations précédentes. Ce « que je ne crois pas possible, par le jeu des forces non « dissymétriques auxquelles sont soumises nos réactions « artificielles, c'est la transformation d'un corps ou d'élé-« ments non dissymétriques en des corps dissymétriques. « Toutefois, c'est une distinction de fait et non de prin-« cipe absolu que j'ai établie en 1860, ainsi que le lecteur « peut s'en convaincre par la note que j'ai insérée dans « les comptes rendus, séance du 1er juin 1874. Non seule-« ment je ne crois pas que cette barrière entre les deux « règnes minéraux et organiques soit infranchissable, « mais j'ai assigné, le premier, des conditions expé-« rimentales qui seraient propres, selon moi, à la faire « disparaître. Tant que ces conditions n'auront pas « été réalisées avec succès, il est sage de croire à la

« distinction dont il s'agit et de la prendre pour guide. »

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I have quoted thus at length partly on account of the interest of the subject, partly because it appears to me that Pasteur has not been fully understood, and has been unfairly accused of a sort of unreasoning and perverse obstinacy, in adhering to an opinion which he himself had helped to disprove. The opinion which he helped to disprove was that racemoids as well as single, separate asymmetric substances require the presence of living things for their formation from symmetrical substances, and to this opinion he did not continue to adhere. What he continued to hold was the fact, discovered by him, that there is a most striking, we might almost say a mysterious difference between the way in which we can form asymmetric substances and the way in which they are formed in animated nature. I think that now, in 1897, we can put the question more distinctly than it could be put in 1860. I shall try to do so.

When by methods not involving asymmetric substances or agencies we prepare a substance containing in its molecule an asymmetric carbon atom, our product is always optically inactive. Leaving out of account the meso-compounds, which occur only in special cases, and cannot be regarded as sub-species, in the same sense as the enantiomorphs, our product is a « racemoid ». From this racemoid we can often by one or other of Pasteur's methods, obtain the two enantiomorph forms, or one of them. In Pasteur's second method a simple asymmetric substance (cinchonicine, or something analogous to it) is used, and we must go back to see whence this substance was obtained. In his third method a living thing (Penicillium glaucum or something analogous to it) is used, so that, if we are to keep clear of asymmetric substances and living organisms, we have only his first method, that of separation of the enantiomorphs by crystallisation. The question has often occurred to me. Do we here get rid of the action of a living organism? Is not the observation and deliberate choice by which a human being picks out the two kinds of crystals and places each in a vessel by itself the specific act of a living organism of a kind not altogether dissimilar to the selection made by Penicillium glaucum? But I do not insist on this, although I think it is not unworthy of consideration; what I do insist upon is that this method gives us the two enantiomorphs in equal proportion and without any kind of preference for the one or for the other. But in organic nature we find a very marked preference. We find in living things no anti-glucose, no anti-sucrose, no anti-cellulose, no anti-form of any of the optically active alkaloids. Very few racemoids have been observed among the products of vital action, there may of course be many others yet undiscovered. I shall here only refer to the two cases that occur to my memory. The lactic acid of fermentation is the product of the action of a living ferment on the asymmetric substance glucose, and yet it is racemoid\_/Piutti has found that the ordinary asparagine, the left form, is accompanied in plants by a small quantity (about one half per cent), of the enantiomorph right Asparagine. I may in passing point out that Piutti's observations prove the asymmetric character of our sense of taste, for while left asparagine is tasteless, right asparagine, its perfect enantiomorph is intensely sweet. Such exceptional cases of racemoids in organic nature may be of great use in the search for the explanation of the mystery, the existence of which was so strongly insisted upon by Pasteur. In looking for such an explanation he was inclined to turn to cosmic influence, and to see in the asymmetry of organic nature a reflection of the asymmetry of the Universe. I think the immediate explanation is to be found in Pasteur's own observations. He has shown us that living things are asymmetric, and we may therefore expect to find asymmetry in their products. There are two ways in which such asymmetry may be produced. I shall take an example of each of these ways from the

right Borneol and left Borneol occur together

products of the living organisms which we know best, human beings.

If you go into an ironmonger's shop and ask for a dozen screw nails, you will certainly get right-handed screw nails; if you wished to have left-handed screw nails, I think you would have to get them specially made for you. This preferential manufacture of one of the two enantiomorph forms of screw nails depends of course upon the fact that most men are right-handed. Similarly with scissors. I do not believe that a left-handed pair of scissors was ever made. These are cases in which the asymmetry of the organism determines the production of only one of the enantiomorph forms. But there is another way in which this presence of one enantiomorph may be produced. I had a friend who had the misfortune in early youth to lose his right arm. He thus became more pronouncedly asymmetric than most of us. Like many other men he wore gloves, or rather I should say a glove, for he could only use the left one. He had, however, always to buy a pair, and he wore the left one, putting the right one into a box in the hope that he might find a man with the same size of hand who had lost his left arm. He never succeeded in this research, and so had a large stock of right-hand gloves in his box. May it not be that one or other of these ways in which the asymmetry of living things produces asymmetry in their products may be the cause of the presence of only one of the two enantiomorphs in vegetables and animals? We should perhaps be inclined to favour the view that it is rather preferential consumption than preferential production that is the cause, if we look at the case of the lactic acid of fermentation.

It is difficult to imagine any sort of use which the quinine and cinchonine in the bark of the cinchona tree can be to the plant. But if we suppose that racemoid quinine and cinchonine are first formed, and that the plant prefers for its consumption the right-handed quinine

and the left-handed cinchonine, rejecting their enantiomorphs, we can understand how these should be found among the debris in the bark. But this explanation, if it can be called an explanation, leaves still the question, whence comes the asymmetry of the living cells? Now I am/inclined to put forward a theory on a question which belongs to a subject so far removed from the department of science with which my work has been specially connected, but every man is necessarily interested in such discussions, and I may perhaps be allowed to hazard some crude speculations. And first let me say that the asymmetry of which we are now speaking is not at all necessarily an anatomical or even in a strict sense a physiological asymmetry. It has more analogy to the asymmetry of habit, examples of which are familiar to us all. We cannot put on both of our boots at once, but must put on first the one and then the other and most men have I think, grown into a habit of always following the same order, some beginning always with the right, some always with the left. In this case, the asymmetric habit is acquired. But may there not be also what we should call innate habits, instincts, of a similar sort? And may not some of these innate habits or instincts, these asymmetric habits be common to all the individuals of a species as other instincts are? May such an instinct not sometimes be so inveterate that the organism can only do the thing in the one way? It would seem that we must go very much further down in the scale of animate existence than Buridan's ass, before we come to a being incapable of giving practical expression to a distinct preference for one of two objects differing only in being one to the right and the other to the left.

It is difficult to speak of a great discovery without thinking and speaking of what has grown from it. For the greatness of a discovery is not to be measured by its beauty or its novelty, but by the effect which it has on the development of human ideas. The tree is known by its

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fruit. We do not expect to see in the seed all that we see in the growing plant, it would be a very poor sort of seed of which that was true. This tree, Pasteur's seedling, produced good fruit when still under his care, and it has continued to produce much good characteristic fruit when tended by his successors. The results attained must have far exceeded his most sanguine expectations. As I said at the beginning of this discourse, these results do not as yet attract the public attention as do those of Pasteur's work on the effect of micro-organisms on chemical and vital phenomena, but we have not yet seen the end. There may be a more intimate relation than that of common authorship between these two different lines of research.

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