lower animals and plants. In these there is found a fact which is technically known as the alternation of generations. The best popular description of it that I am acquainted with is to be found in the fifteenth chapter of Profs. Geddes and Thomson's "Evolution of Sex" (Revised Edition). It is often found that the immediate descendant of a pair of organisms, male and female, is not a creature like one of themselves, but is a sexless being whose progeny, in their turn, reproduce the sexual state of their grandparents. Space is not here available for the discussion of the various forms of this phenomenon. Many years ago, however, Dr. Beard declared, that, even in the higher animals which we call vertebrates, there is a disguised alternation of generations, just as there is in flowering plants. I have before me, as I write, twenty-three papers of various lengths which have been published by Dr. Beard during the last seventeen years, the first being communicated by Prof. Huxley to the Royal Society and received April 20, 1889. In that paper Dr. Beard first described the presence within the Bill-fish, Lepidosteus osseus and other fishes, of certain curious cells, which seemed to play a temporary part in development and then totally disappeared. Three years later he published at Jena a paper on "A Supposed Law of Metazoan Development," which contains the first enunciation of his theory that even in the Metazoa of higher animals the process of alternation of generations occurs. I may quote a few words from that remarkable paper. After describing the presence of the larval or a sexual form in many of the lower Metazoa, and pointing out "the analogy which would obtain between the suggested mode of Metazoan development and the accepted fact of an alternation of generations in the life histories of all plants above the lowest Thallophytes," Dr. Beard says:

Facts Upon Which Theory is Based

"I venture to attach most weight to the application of the principle to the vertebrata * * * It is undoubtedly the obstacles offered by the phenomena of vertebrate development which have hitherto prevented the enunciation of the law of development as an alternation of generations. Larvae are so commonly encountered among the invertebrata that the wonder is that no one has inquired why they are so rare in any guise in the vertebrata." Dr. Beard goes on to assert that larval structures can be found in several Amphibia and fishes, and that these degenerate. Speaking of one such structure, he says: "It is gradually broken down by some ferment action." Dr. Beard's conclusion is that "Metazoan development appears to be by means of an alternation of generations in that, from the fertilized organism arises the larva, upon which, in one way or another, according to the circumstances of each case, a new form, the adult or image, takes its origin." Fourteen years have elapsed. It has been found that, just as in various of the vertebrates, the egg gives rise to a larva which does not directly develop into the new organism, but "serves as the foundation on which the development recommences, as it were de novo;" so, according to Dr. Beard, in such vertebrates as the skate and chick, there is found to be an asexual larval stage, upon which the embryo proper develops. Such are the embryological beginnings which have in all probability led, as we shall see, to the conquest of cancer.

It is Dr. Beard's belief that the alternation of generations is common to all vertebrates including man. What then becomes of the asexual stage or generation, since there is no sign of it in the adult individual? In the case of the skate and the chick, Dr. Beard has discovered what he calls a "critical period," which marks the beginning of the disappearance of the transitory larval generation that has hitherto been growing. We may call the characteristic tissue of which this structure is composed by the convenient name of trophoblast. Dr. Beard appears to have shown that up to the critical period in the case, for instance, of the fish, all the digestive processes have depended upon an acid, intracellular digestion, very similar to that which occurs in the stomach of the adult. The critical period is determined by the development in the embryo of a new organ called the pancreas (or sweetbread). In each of us this is the most important organ of digestion. It produces various ferments, the most important of which is known as trypsin. This substance acts only in an alkaline medium, being thus contrasted with pepsin. Writing in the Lancet rather more than a year ago, Dr. Beard said:

"At this epoch, the critical period, the fish commences to feed itself on yolk, not by an (intracellular) acid, peptic digestion, but by an alkaline, pancreatic one. The commencing activities of the pancreas during foetal life initiate an alkaline digestion by the means of the most powerful and important of all the digestive juices, the pancreatic * * * If the secretion be absent, neither the asexual structures of a fish development nor the cells of chorio-epithelioma (a tumor) do or can degenerate. The solution of the problem of the functional relation of embryo and trophoblast—how the latter nourishes itself by an (intracellular) acid digestion and degenerates slowly by a pancreatic digestion—becomes at the same time the embryological, if not the medical resolution of the problems of malignant neoplasms * * *"

Theory of Misplaced Germ Cells

And now let us return to cancer. What are we to regard as the nature of a cancer, in the light of our discovery of trophoblast? The answer which Dr. Beard returns is that cancerous tissue is none other than "irresponsible trophoblast." In order that the justification for this dictum may be advanced, we must consider our modern knowledge of germ cells. That this term corresponds to a reality, Weismann and Beard have definitely taught us. Every individual, produced as the higher animals are produced, is derived from a united pair of germ cells. The old view was, that these are derived from the individual who bears them; but Weismann taught us that this is not so. He has familiarized us with what he calls the "continuity of the germ-plasm." From the point of view of the race, the individual is merely the ephemeral bearer of the immortal germ-plasm, which is as old as the race and is subject to no law of death. Weismann employs the phrase germ-plasm since he is unable to demonstrate the actual continuity of germ cells in every case. Dr. Beard, however, believes that he has demonstrated the actual continuity of germ cells as cells from generation to generation. If we take a special instance, such as the smooth skate (Raja batis) which Dr. Beard began to study nearly twenty years ago, we find, according to him, that an actual continuity of germ cells is demonstrable. When he studies the very young skate—and the same is true of many other fishes and of the chick—he finds that the germ cells are by no means confined to their proper and characteristic site in the body. He has found them in the head, the skin, the gill region, the liver, the blood, "in fine, there is hardly a place in the whole trunk or head in which such aberrant germ cells have not been observed." He has figured them again and again. There is no possibility of mistaking their identity under the microscope. Where have these aberrant germ cells come from these cells, the malign possibilities of which are soon to be indicated? The common view would be that they had wandered from the part of the body of the embryo which gives rise to the germ cells. But to Dr. Beard such an assertion is nonsensical; the germ cells are older than the embryo. They are not products of any part of the body of the individual; they have arisen outside the embryo and have migrated into it. Dr. Beard has proved that this is so. In the smallest embryos of the skate no germ cells are visible. Later on, germ cells appear, but only a very few of them are found in their characteristic site in the body. For instance, in embryos twenty millimeters long 50 per cent of the germ cells are misplaced, whilst in embryos half as long again only about 30 per cent are misplaced. In the very youngest embryos, containing no germ cells, hosts of germ cells are to be found lying in the tissue immediately outside the embryo and preparing to enter it. In a word, the germ cells precede the embryo and gradually wander into it as it develops. Many of the germ cells never reach the proper position. They wander along what is called the germinal path, but may find themselves misplaced in all parts of the body. Commonly their fate is to degenerate, but apparently they do not always do so.

It follows that the germ cells, not being developed from the embryo, are direct products of the original cell (of bisexual origin) which gives rise, on the one hand, to them, and on the other hand to the embryo itself. Thus the germ cells within the embryo are its own immature "twin" brothers and sisters. In other words, the embryo is the product of one of the primary germ cells, whilst the remainder come to be regarded, quite erroneously, as its own sexual products.

According to Dr. Beard, all malignant tumors are products of aberrant germ cells, so that a death from cancer is, so to speak, a case of fratricide, since the individual and the tumor which kills him are both derived alike from one parent cell. There are a host of instances in the lower animals, if not also in man, of the development of these aberrant germ cells into tumors which show distinct signs of the attempt to produce a second individual.

Of these extraordinary cases Dr. Beard seems to have provided an explanation. But far more commonly such an aberrant germ cell does not give rise to any such tumor, but passes on to the asexual stage or generation, producing the trophoblastic tissue of which we have already heard. In a word, a cancer results from the attempt of an aberrant germ cell to continue its life cycle, the attempt having ended merely in the indefinite production of larval, asexual or trophoblastic tissue.

If this theory be correct, the conditions which lead to the destruction, digestion and complete absorption of the normal trophoblastic tissue that begins to vanish at the "critical period," should have similar effects upon "irresponsible trophoblast." In a word, trypsin should cure cancer by digesting its cells. The rest of the pancreatic secretion should destroy and dispose of the products of this digestion.

Dr. Beard's First Experiments with Animals

Plainly this was a matter that must be put to the test, and Dr. Beard forthwith proceeded to do so, availing himself of the work of Prof. Jensen, and with the assistance of Dr. H. Wade. Several mice were inoculated with tissue from the mouse-tumor to which we have already referred. After about five weeks, when a number of them had well-marked tumors, two were selected for treatment, their history being carefully compared with that of the untreated mice whose tumors were of the same age. A solution of trypsin was employed for injection into the two mice in question. Says Dr. Beard: "After ten days, when four injections in all had been made into each mouse, one of them was found dead by the laboratory servant. The post-mortem examination made by Dr. Wade revealed no cause of death. But for the presence of a tumor mass the mouse appeared to be quite healthy. The laboratory attendant thought that it had got caught between the cage and food vessel and so (when intoxicated?) had caused its own death. The microscopical examination demonstrated that every single cell of the tumor was in degeneration, fully half of them being represented by shapeless masses of particles, probably remains of nuclei, and all the rest were mere skeletons of cells. Even these seemed in very many cases to be crumbling and falling rapidly away, as though in a hurry to quit the scene. The somatic tissues of this mouse, as represented by the leucocytes and connective-tissue stroma cells, were quite normal, and in the following instance also. The treatment of the second mouse lasted for twenty-two days, when it was killed, since on that day one of the untreated mice died of its tumor. In the case of that mouse the tumor was as large as the last segment of a man's thumb, whilst in the treated mouse it was only as big as a lentil. Microscopically this latter apology for a tumor was in advanced degeneration, shrinking away to nothingness and quite harmless. * * * Even without further treatment the tumor would have in all probability been absorbed shortly or its remains cast out."

The conclusion from these experiments, which are now, of course, being repeated, was that "the action of trypsin upon the cancer cell is to pull down the cancer albumin—a living substance—and the cancer ferment—malignin—produced by this. * * * In addition to their confirmation of the conclusion that trypsin is the substance which will destroy the cancer cell with ease, and without danger to the individual (Beard and Shaw Mackenzie), these experiments go far to prove that in its nature cancer is neither germinal nor somatic, for trypsin, the architect of the soma (the body), does not in life destroy the soma or sexual individual or its sexual products, whilst its action is direct and utterly ruinous upon trophoblast or asexual generation." (British Medical Journal, January 20, 1906.)

What Trypsin Has Done for Man

Can trypsin do for man what it did for these two mice? In the above quotation there is the assertion that it can. Dr. Shaw Mackenzie, to whom the reference is made, has obtained apparently satisfactory results from the administration of trypsin in man, in order to prevent the recurrence of cancers after operation. Evidently, however, this is not a conclusive or satisfactory means of demonstrating the value of trypsin in man, if it has any. Its value must be tested in cases of present cancer, the diagnosis and the active growth of which at the time of treatment are beyond dispute. For preference we must choose cases in which the growth is visible and the results therefore more certain. On the other hand, it is necessary also to choose cases in which the growth is inaccessible, so that we may test the value of the treatment where the local application of trypsin is impracticable. Trial is now being made in many parts of the world, and the present writer's personal knowledge of the results warrants him, he considers, in giving publicity to the whole matter. Warrants, indeed, is too weak a word. The giving of the widest and most immediate publicity to these facts seems to be a proceeding from which it would be cruel and cowardly to refrain, even though one may be accused of rushing in where wiser people fear to tread. If the cases I have seen be not miraculous in the common sense of the term—that is to say, due to Divine interference with natural law—one has no choice but to speak.

By the courtesy of the physician in charge, to whose notice I first brought the trypsin treatment, and solely for my own pleasure and instruction, I have personally watched, from the first, the treatment of a case of cancer in an outlying district of London. The diagnosis was beyond dispute and had been independently confirmed at two hospitals—one of them world-famous. The growth was visible and evidently full of vitality. The surgeons had pronounced the case inoperable and the patient was evidently sinking. Writing two days less than four weeks after the tentative and partial commencement of treatment by trypsin, I am able to report that, so far as all the indications go (and they are abundant), the tumor has already been killed outright. The patient is now apparently on the high road to recovery, though some difficulty has yet to be apprehended by reason of the poisonous action of the disintegration products of the growth. So far as my small experience goes, this is certainly the most amazing thing I have ever seen. Several practicing physicians —not mere on-lookers like myself—have already made similar reports to Dr. Beard. Erroneous diagnosis, coincidence, miracle, spontaneous death of the tumors—none of these explanations is adequate in these cases, any more than in the two mice of happy memory.

I might quote another case of the same kind which I have myself seen, but I prefer merely to mention another which, at the time of writing, has been under treatment for six weeks, three successive operations having been performed by a distinguished surgeon who declined to undertake a fourth. In this case it is possible to say, even at this stage, not only that the growth of the tumor has been arrested, but that it is now dead. The patient is apparently making a rapid recovery and it is expected that in a few weeks more no signs of the tumor will be discoverable.

In the present tentative and merely experimental stage of the treatment the plain duty of any one who tries it is to adopt all the possible means of bringing the action of the potent ferment to bear upon the cancerous cells. Those practicing pioneers who have already ventured to act upon the Augustinian advice to prove all things, are therefore administering trypsin or pancreatic extract by the mouth, under the skin, and, where possible, by local application. My interest here is merely, having seen what I can scarcely believe myself to have seen, to avail myself of my peculiar opportunity to perform what I believe to be a public service. It is not for me to state doses and methods. Dr. Beard has formed provisional opinions upon these, but his practical experience and authority are superior to mine by only the measure of two mice. His advice, however, is at the service of all properly qualified physicians in any land who care to avail themselves of it. The treatment has to be seriously undertaken. In all probability Dr. Beard is correct when he asserts that trypsin exerts no action whatever upon the cells of the sexual generation of vertebrates, such as we represent. This must indeed be so, since trypsin in considerable strength passes from the pancreas of each of us, yet causes no injury. On the other hand, if there be a cancer or "irresponsible trophoblast," nourishing itself upon the tissues of the body, and if this be destroyed by trypsin, the products of its digestion must be absorbed and must give rise to disturbance. Hence very marked symptoms of poisoning or auto-intoxication are witnessed at first in human patients. Similar symptoms were observed in Dr. Beard's mice, being due, he believes, to poisoning by some product, possibly an alcohol of the tryptic digestion of the tumor. A healthy mouse, similarly treated with trypsin, never displayed any symptoms. Hence, at present, important difficulties are to be expected in the application of the treatment, though the case I have myself watched shows that they are surmountable. This is another reason for haste, if my beliefs are correct. If the treatment does all that we hope it will shortly be applied, in early stages, when the tumor mass is of inconsiderable size and the products of its digestion negligible.*

Dr. Beard is naturally far too busy with his work for him to assume the labor of publishing his results broadcast. It is by his wish that I am undertaking this task, from which practicing members of my profession are excluded by that extremely necessary and admirable professional etiquette, which is so constantly misunderstood and maligned by the public, in whose interests it exists and whom it most effectually serves. If Dr. Beard is right he could well afford to wait for his inevitable reward of glory. If he be wrong, such an article as this can only injure him. But he prefers to take his chance, since, whilst he can afford to wait, the victim of cancer cannot; and, besides, what we call a chance is for Dr. Beard a certainty. The event will prove. I will refrain from laudation or words of triumph and even from what would be peculiarly attractive to me—a discussion of the manner in which a worker in pure science has been enabled, after nearly twenty years, to contribute to a practical subject of which he had no thought in starting, and the connection of which with his own work it has remained for that work itself to elucidate. If, as I believe, there is a moral here, it must be pointed out in due course. Meanwhile, I submit to the civilized world generally, the proposition that the "trypsin" or pancreatic treatment of cancer is worthy of immediate trial in the behalf of the many persons to whom it alone offers a possible chance of escape from an otherwise inexorable fate. C. W. SALEEBY, M. D., F. R. S. (Edin.)—McClure's Magazine.

* It is now found that if all pancreatic ferments be employed the symptoms of poisoning are averted.