ADAMI (Principles of Pathology) defines a teratoma or dermoid as "an autonomous growth, the product of the continued development within one individual of another individual of the same species." By this definition the normal foetus is excluded, as its development is only of a temporary nature. All gradations can be traced from ordinary twins through attached twins, in which one individual is weaker, and so atrophies, to the inclusion of a twin inside the stronger individual, the last being a teratoma or dermoid. Quite clearly it must be from some totipotent cell that the dermoid takes origin, because the latter contains all types of tissue found in the fully-developed foetus—is in fact an attempt at a new individual. In a majority of cases it is in all probability from the germinal blastomeres or mother cells of the ova and spermatozoa that the teratomata arise. These germinal blastomeres are the direct descendents of the sexual cells of the previous generation. They are set apart at the very earliest period of segmentation of the fertilised ovum. They eventually become lodged in the generative glands and give origin to ova or spermatozoa of the new individual. They may, however, become misplaced and lodge in some unusual part of the body, hence, although dermoids are much more common in the neighbourhood of the sexual glands, they also occur in the neck and other parts.

It is now some considerable time since experiments were first carried out by inoculating animals with embryos in an attempt to produce tumours. Numbers of workers have taken part in this investigation, but the name most usually associated with the more modern work is Askanazy of Geneva, and it is his work which is now under review. A paper of his published in 1909 (Wien. med. Woch., pp. 2518 and 2578) gives a good résumé of the work up to that date. After trying a number of animals the author found the white rat to give the best and most uniform results. One might be inclined to imagine that the younger the embryo the more likely would it be to develop a tumour. That, however, is not the case. Embryos measuring $\frac{1}{2}$ to $\frac{3}{4}$ cm. often give negative results, while older ones of 1 to 4 cm. give almost constantly positive results. The embryo may be that of the animal injected or it may be from another white rat. The male is susceptible to inoculation as well as the female, but the female exhibits a greater predisposition. The embryo is pounded up into a sort of mash, although results are also obtained by implanting the whole embryo. The mash may be injected into the subcutaneous
tissue, peritoneal cavity, or, indeed, into any part of the body. The best positions are undoubtedly the subcutaneous tissue and the peritoneal cavity, with a preference for the latter. Injection into the brain and the parenchymatous organs gives almost uniformly negative results. In many cases the material is simply absorbed; in other cases development occurs for a time and then stops; in others, again, retrograde changes take place after a tumour has developed. In a considerable percentage, however, the resulting tumour continues to grow, in some cases for as long as two years or even more. Borst (Atti del 1° Con-

gresso Internazionale dei Patologi, Torino, 1911, p. 24) has obtained 74 per cent. of positive results by intra-peritoneal injection. This author notes a number of further interesting facts, such as that animals in which subcutaneous injection was a failure were not protected from subsequent intra-peritoneal injection.

As regards the appearance of these tumours, the size varies very much. Occasionally one would develop measuring $5 \times 5 \times 3$ cm., but most were somewhat smaller. The tumours are rounded, obviously consisting of a series of cysts in most cases where the injection has been made into the peritoneal cavity. Sometimes these are aggregated together, at other times they are separate. They are yellow or grey in appearance according to the nature of the contents, which may be epithelial debris or mucinous material. In short, the appearance at once suggests that of the ovarian dermoid.

Microscopically all types of tissue are found, the most common being cartilage, bone, skin, teeth, non-striped muscle, but liver, lung, brain, and other organs were occasionally present. An interesting point is that these tissues need not necessarily be already pre-formed in the embryo injected in order to appear in the resulting teratoid. The cysts are lined sometimes with ciliated, sometimes with stratified squamous epithelium, and sometimes with chalice cells. The contents, as already mentioned, may be epithelial debris or mucinous material. From the point of view of microscopic appearances, therefore, these tumours resemble the ordinary ovarian dermoid very closely.

With regard to further variations in conditions which modify the growth, the age of the animal used for experiment was found to be a matter of indifference. Both Askanazy and Borst noted that the gravid state increased the tendency to the tumour formation in an animal. Cooling the embryo mash seemed to increase the rapidity of the growth of the tumour which developed after its injection. Injury to the growth after it had started seemed to increase the rapidity of growth subsequently.

An attempt was made to see if it were possible to enhance the virulence of a tumour by sub-inoculation from animal to animal, as was done by Ehrlich in the case of certain malignant mouse tumours. This was, however, found not to be the case. Sub-inoculation of
already growing teratoids occasionally succeeded, but the resulting tumours were small.

As previously stated, cooling the embryo mash did not kill it. After preservation on ice for 16 and even for 25 days the mash still retained its capacity to produce tumours.

A number of interesting results were obtained by treating the embryo mash with various chemical agents previous to inoculation. A 4 to 5 per cent. ether water was prepared and the mash mixed with this. The mixture was immediately implanted and a very marked increase in the rate of growth of the subsequent tumours was noticed. This was not merely due to increase in the size of the component cysts, but to more rapid proliferation in the embryonic cells composing the various tissues. The same effect is not produced if ether be injected into the tumour after it has commenced to grow.

Röntgen rays were found, as might have been anticipated, to exercise a restraining influence upon the growth of the tumours. Even 30 seconds' exposure was sufficient to produce a perceptible amount of diminution in the rate and amount of growth.

In view of the above-mentioned results with ether, Askanazy (Atti del 1° Congresso Internazionale dei Patologi, Torino, 1911, p. 27) has investigated the effect of allied chemical substances. In a series of four experiments ethyl alcohol in 8 per cent. solution, when mixed with the embryo mash, caused in two cases tumours of an unusually large size. Other experiments with xylol, benzol, and acetone were entirely negative. In one experiment with lipase (steapsin) a very large subcutaneous teratoid was obtained. Chloroform gave negative results, but with chloral hydrate in one case out of four an exceptionally large tumour was produced. In another a teratoid tumour developed, in connection with which, after an interval of 1½ years, a malignant (squamous epithelioma) tumour arose, which caused the death of the animal.

All these later experiments were suggested by the work of Meyer, which goes to show that lipoid dissolving substances act more energetically upon cells than those not capable of dissolving lipoids. Wacker and Schmincke (Münch. med. Woch., 1911, Nos. 30 and 31) have investigated this question more fully with a view to finding some tumour-producing chemical. These observers injected a series of chemical substances into the ears of rabbits and noted the amount of subsequent epithelial proliferation. They found that indol dissolved in rabbit fat produced marked epithelial proliferation, and similarly acetone. On the other hand neither ether nor chloroform produced proliferation. As a result of their investigations they conclude that only those substances which are lipolytic are capable of producing proliferation of epithelium, although not all lipolytic bodies have this effect.
It should be stated that Borst (*loc. cit.*) also carried out some experiments by treating embryo mash with chemicals such as ether and indol, but failed to note any increased energy in the growths which resulted from the injection of the material.

These various results as to the influence of chemicals upon cell proliferation are obviously conflicting. At the same time positive results, such as those of Askanazy, must be susceptible of some explanation.

A point upon which Askanazy lays some stress is that in three instances malignant tumours have arisen in connection with experimental dermoids. This is all the more noteworthy as in the many generations of white rats observed by him no instance of a spontaneous malignant growth was found. One of these tumours was a carcinoma, one a sarcoma, and the other a myxosarcoma. In two of these instances the embryo mash had been previously treated with lipolytic chemical substances. In both cases the fœtuses inoculated were relatively young, and in both a period of a year elapsed between the inoculation of the embryo mash and the development of the malignant growth. Askanazy considers that there are two possible explanations of this occurrence—either the more advanced age of the rats made them more liable to malignant disease, or some change took place in the teratoid cells whereby certain of them assumed malignant characters. Askanazy himself inclines to the latter explanation, and regards the previous treatment with lipolytic substances as having something to do with this change.

A further observation made by Askanazy is that excision of the sexual organs in animals has no effect upon the subsequent development of teratoids. On the other hand, unilateral excision of the kidney in a series of animals led to a uniformly rapid development of tumours. Extirpation of the spleen had an exactly opposite effect. Out of 9 animals injected after extirpation 6 showed no growth at all, and in the other three slight growth only was observed.

As already mentioned, experiments were tried with whole embryos. These were implanted in the peritoneal cavity, and after the lapse of months the animals were examined. No tumour formation had occurred, but the embryo, still preserving its outward form, was found to contain a series of cysts lined by epithelium of various kinds.

To sum up, tumours macroscopically and microscopically resembling dermoids or teratomata can be produced by inoculating white rats with a mash of white rat embryo. Admittedly these tumours are not true dermoids. They arise from tissues already partly differentiated, and not, as is generally believed of the dermoid, from a single ovum or germinal blastomere. They may be regarded, as Askanazy puts it, as a sort of adopted daughter instead of a sister product. A number of interesting observations have already been made as to the con-
ditions under which these teratoids grow and as to factors which hinder or stimulate growth. It may be that further observation will throw light upon certain factors in connection with tumour growth in general.

NEW BOOKS.

Acronegaly—A Personal Experience. By Leonard Portal Mark, M.D. London: Baillière, Tindall & Cox. 1912. Price 7s. 6d.

This remarkable work must be of the deepest interest to everyone conversant with recent observations upon the ductless glands. Consisting as it does in a detailed account of the personal experiences of a trained observer suffering from acromegaly, it is undoubtedly unique.

The most valuable part of the work will probably be found by most readers to lie in the careful analysis and description of the symptoms as observed by the author himself. At the age of 24 he began to suffer from very varied symptoms connected with the head, such as tinnitus, photophobia, and drowsiness; but it was not until the age of 50 that the knowledge of his affection suddenly dawned upon him. He appears rather inclined to the belief that his condition may have been caused by early adventures after the fashion of the antenatal misfortunes of Tristram Shandy. It is certainly true that many a cerebral tumour may be dated back to some accident to the head, yet it does not follow that acromegaly and gigantism are results of cranial compression.

The author dates the commencement of his symptoms from the age of 24, and it is really very remarkable how many of those who suffer from acromegaly have begun about that time of life to show objective appearances of the disease. In his youth he was evidently above the average in physical strength and hardiness. He mentions, for example, that without any training, at the age of 19, he ran one day a distance of two miles and 236 yards in fourteen minutes. Here, again, we have a circumstance which has been mentioned in connection with a large number of previous cases. In acromegaly it is very common to find great strength at, and soon after, adolescence, followed by rapid diminution of energy, so that by middle life the victim is reduced to a very weakly condition.

About the age of 30 Dr. Mark became subject to great suffering, on account of his inability to resist cold, and during the four succeeding years he constantly suffered from catarrh of the nares and fauces. When 35 years old he recognised the fact that there was a gradual advancement of the lower jaw, preventing the bite of the teeth, and at the same time he felt a quite extraordinary sense of fatigue, with an increase of the discomfort in the head. At the age of