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THE SIGNIFICANCE OF DEVELOPMENTAL ANOMALIES OF OVA IN THE AETIOLOGY OF ABORTIONS

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Considerable is the number of cases in wich the pathogenic cause of spontaneous abortion remains unexplained. Those inherent in the mother and in the ovum seem to play the predominant role. With spontaneous abortions due to an ovulogenic cause, signs of developmental disturbances of the ovum as a whole or of some part or parts of it are very frequently noticeable. Such pathologic ova are easily recognizable by close scrutiny even with the naked eye. A number of them has been gathered and studied by us for the purpose of

(i) accumulating data for a new, as yet undeveloped branch of science, intrauterine pathology (pathological embryology), considering that investigations into pathogenic life processes contribute as a rule to the better understanding of physiological processes ;

(ii) accumulating data concerning the early dying off and the pathogenesis of affected ova so very different in their form and outer appearance ;

(iii) elaborating the problem of heredity, a question far more important than that of the numerical frequency of spontaneous abortion of pathogenic ova.

Very often the causative factor of abortion remains inscrutable. To aggravate the situation, criminal interventions bringing about abortion are usually disguised or denied. In addition, even such causes remain frequently undetected for which nobody can be held responsible, as for instance infectious disease, previous inflammation of the genital organs, etc.

The frequency of recorded abortions greatly differs in the various parts of the country, in the capital, in the larger industrial centres, etc. In the period between 1946 and 1949, their average over the whole country was 13,96 per cent of all births and took place mostly in hospitals and infirmaries. (It should be noted, however, that the majority of these health institutions did not record as abortions cases where endometritis post abortum was diagnosed following the histological examination.) Thus, the factual number even of legitimate abortions cannot be assessed, one can but fall back upon estimates, and the same refers of course to criminal abortions. On the other hand, it is possible to determine with tolerable accuracy the number of those cases where the ovum

is expelled with an intact chorion and the maldevelopment of the embryonic membranes is fairly well recognizable.

Pathologically developed aborted ova have been known for a long time. *His* described them in detail without trying to establish interconnection between them and the aetiology of abortion. *Mall* (1910), and *Mall* and *Meyer* (1920) subjected them to exhaustive studies, and *Mall* realized that some of the abortive ova contain no embryo. They determined their characteristics

Fig. 1. Ovum expelled together with decidua. No embryo only a shapeless clot of the size of a millet seed in the amniotic sac surrounded by uninjured membranes. The chorion stains perfectly well. Under the microscope, very scanty capillary network in the villi, in many places capillary buds containing nucleated red blood cells. Cystic ovum.

and the proportions of size between the embryo and this membranes. (According to *Mall*, *Meyer*, *Evans* these are, 1 : 10 in the third, 1 : 6 in the fourth, 1 : 4 in the seventh and 1 : 1,2 in the eighth week of development, when the embryo almost completely fills the amionic cavity.) Lately, several authors (*K. W. Schultze*, *Bayer*, *Besold*, *Dolff*, *Hertig*, *Streeter*, *Paine*, *Kaeser* and others) have dealt with the pathology of aborted ova. It was *Bayer* who advanced the idea, which to day is almost generally accepted, that all maldeveloped ova of early pregnancy should comprehensively be termed moles. There are *cystic moles* in wich no embryo is recognizable ; *embryomoles* with a small, undeveloped,

shrivelled embryo ; *blood* or *carneous moles* with an amnionic cavity compressed by a severely haemorrhaged chorion ; *Breus haematomoles* with a small, distorted embryo, a usually short and thickset umbilical cord, or rather stalk, and with the subchorial, tuberous haematoma, from which the inner surface of the embryonic plate receives its characteristically clotty and knotty appearance. Originally, the designation »mole« was put forward by way of analogy on the

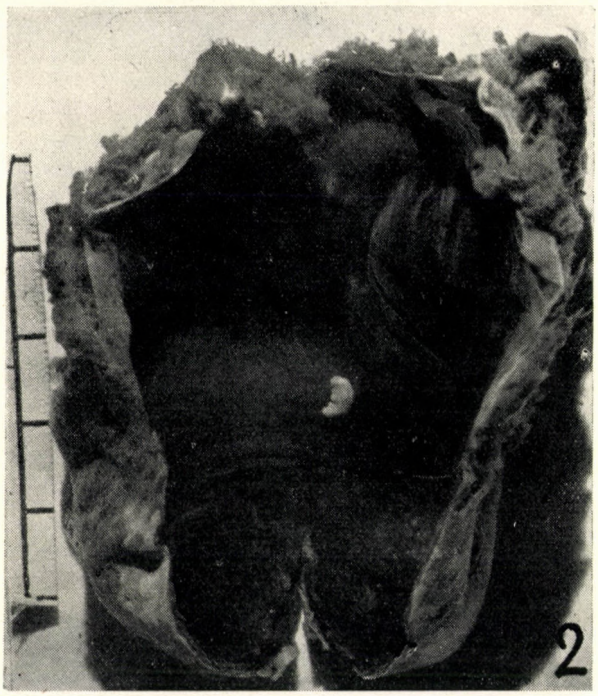

Fig. 2. Expelled cystic ovum in opened state. Maldeveloped embryo shrivelled to the size of a grain of rice. No chorionic vascularization, the oedematous chorionic villi stain well.

basis of a likeness to hydatiform mole. Really, in the course of our investigations we, too, have found that vesicular mole structurally and genetically does show similarity in many respects to the aforementioned mole-ova and that there exist intergrades. On these grounds the common denomination seems to be quite justified.

Our investigations are based on cases of abortion observed during a period of 15 years (1933—1949), in the Gynaecological Department of the University in Debrecen. Ova expelled in the course of impending or unavoidable abortions spontaneously as whole ova and with perceptibly undamaged chorions, have been studied. (Two of them were noticed while amputating myomatous, considerably distorted uteri, and one in an uterus extirpated because of cancer of the uterine cervix.) The pathologic (abortive) ova found in 5685 cases of threatening and inevitable abortions during the 15 years can be divided in the following groups.

89 cystic, cavernous ova without embryos (Fig. 1—2) ;

92 ova with small, disproportionate embryos showing different stages of developmental malformation (Fig. 3—4) ;

23 embryomoles ; ova with small, undeveloped, shrivelled, often almost irrecognizable embryos (Fig. 5—6) ;

31 blood moles with macerated embryos, of a soft consistency, 5 Breus haematomola tuberosa (Fig. 7) ;

Fig. 3. Cystic ovum expelled in toto. Thinned and considerably flattened chorion. A very deformed embryo, the size of a grain of wheat, attached on an exceedingly short umbilical stalk to the inner surface of the chorio-amniotic cavity representing the cavity of the ovum. The remnants of the amnion are strained onto the embryo showing traces of the limb buds.

53 missed abortions with the ova dying off, yet fairly well recognizable, shrivelled embryos in them ;

3 ova containing embryos developed without the amnion ;

19 case of coiling of the umbilical cord, and ova snared by Simonart's threads with distorted embryos (in the first 3—4 months) ;

34 mola hydatidosa.

Thus, in altogether 349 cases did it prove successful to establish an ovulogenic cause of abortion, i. e. one that is most probably inherent in the maldevelopment of the ovum. This

however does not mean that it is easy to determine any true proportion of the pathogenic ova. So, for instance, all the ova which had suffered injuries, became lacerated or fell asunder in the course of abortion, have had to be excluded from the present study irrespective of the fact that in several cases there was room for suspicion of pathologic maldevelopment. In other words, only definitely undamaged specimens were considered.

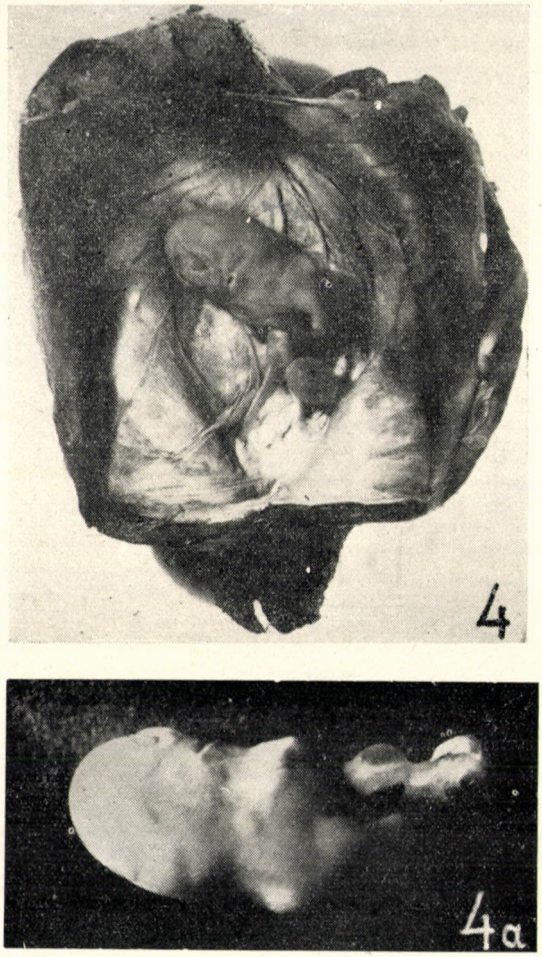

Fig. 4. Ovum expelled in toto. Embryo exceedingly deformed. Spina bifida, shortness of umbilical cord, hydropic swelling easily discernible on picture magnified 2x. Disproportionally expanded cavity. Chorionic vascularization faintly discernible. Empty capillaries in many of the villi.

The proportion of 6,1 per cent (that of 349 ovulogenic causes to 5685 abortions) does not approximate the true position at all. It needs correction, which in the present case is based on the facts a) that of the 5685 abortions 1467, or 25,8 per cent, progressed spontaneously, and b) that practically all the 349 abortive ova studied derived from spontaneous abortions. On this basis, the frequency of pathologically developed ova is 23 per cent of all spontaneous abortions. It is remarkable that according to observations, amassed quantities of abortive ova occurred in those cases where abortions resulted in spite of the patients' prolonged lying and of all medicinal and hormonal treatments applied.

In literature, the views on the frequency of abortions of pathologic ova in proportion to all abortions differ greatly. *Grosser* puts it at 30 per cent, *K. W*

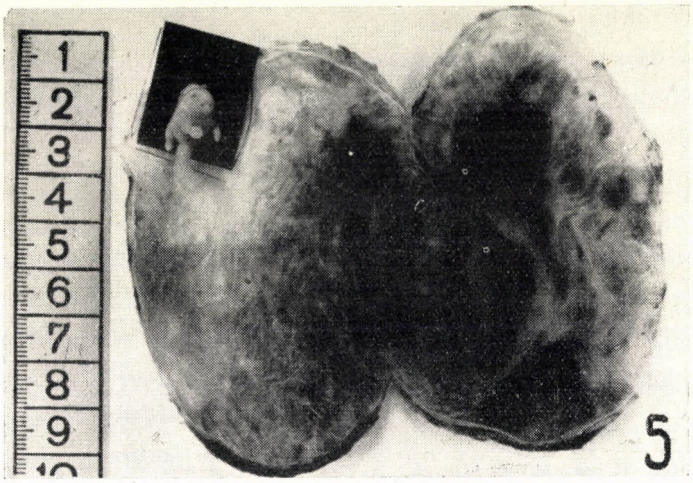

Fig. 5. Deformed, shrivelled, dead embryo within the disproportionally enlargened cavity. No vascularization discernible on inner surface of ovum. Microscopically well staining chorion. Capillary buds and many stromatic wandering cells with frothy plasm in the stroma of the villi. Embryomole.

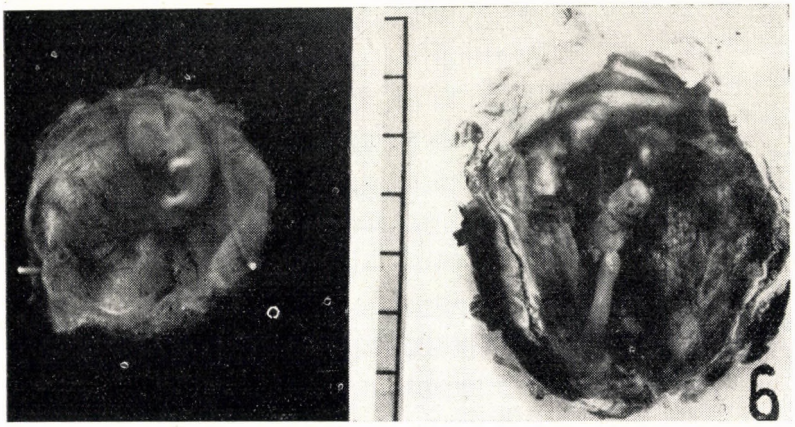

Fig. 6. Left, normal ovum, perfectly developed embryo, clearly visible chorionic vascularization. Right, pathologic ova, shrivelled embryo, hydropically swollen umbilical cord, microscopically missing chorial vascularization, surviving villi of chorion stain well. Embryomole.

Schultze at 41 per cent. (within the first 3 months at 75 per cent), *Bayer* at 45 per cent, *Hertig* at 70 per cent, *Livingstone* at 49 and *Kaeser* at 34,1 per cent. Apart from the differences in percentage, these authors obviously all agree that faulty distorted forms indicative of impeded development play a very significant

role in the aetiology of spontaneous abortion. Relying on our studies, we may draw the same conclusion.

Human embryology as a whole is a fairly well worked out branch of knowledge, but the morphogenesis and histogenesis of the chorionic villi still offer problems unsolved in their details. There is a definite interconnection between the primary adhesive villi forming on the surface of the ovum that

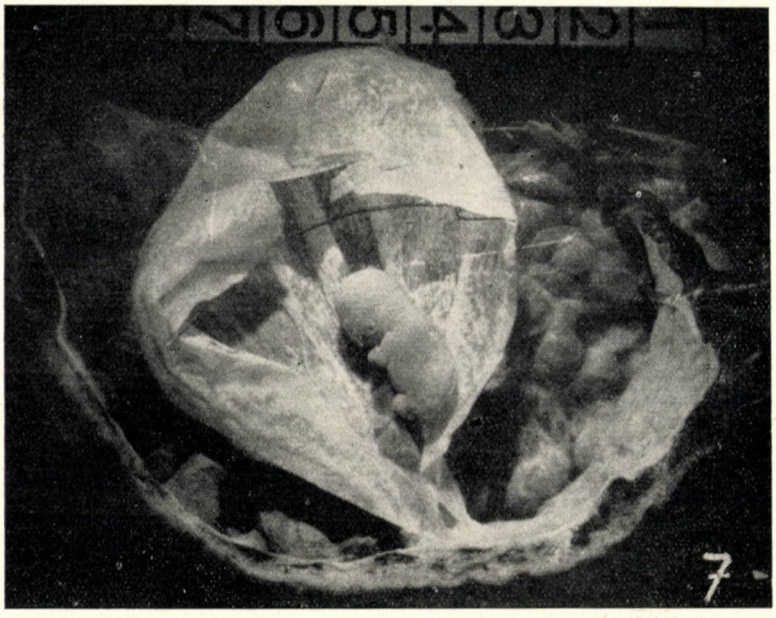

Fig. 7. Breus mole expelled in toto. On the embryonic surface ot the chorion inwardly bulging, knotty, subchorial haemorrhages. Very expanded chorio-amniotic cavity. Within the opened amniotic vesicle disproportionally small, shrivelled, dead embryo. In some places traces of imperfect vascularization in the chorion still staining faintly.

sits in the trophoblast nest, the appearance of the resorptive villi and their proliferation, on the one hand, and the grade of that trophoblastic activity, on the other hand, which is really a struggle going on between the maternal tissues and the ovum seeking to attach to and embed itself in them. Chorion-gonadotrophin secretion also is the greatest during the period of trophoblastic activity. As long as the trophoblast is extensive there is an increased inclination to abort *(Grosser)*, and the ovum cannot be considered to be safely anchored until the fibrinoid degeneration of the trophoblastic mass has begun in the direction of the maternal areas or, more exactly, until a state of equilibrium has taken the place of the struggle proceeding in the borderland. The fibrinoid settles in several layers *(Nitabuch, Langhans, Rohr)*, particularly in the border-belt which is the arena of the fight between the ovum and the maternal

tissues. These fibrin layers differ from each other in many respects and under pathologic conditions they may precipitate in very large masses. If they do so, they envelop the villi and by constricting and obstructing the intervillous spaces impede their activity or even completely paralyze the nutrition of the ovum. This tissue process is closely connected with the allergic processes of the struggle between mother and ovum, and on the basis of our histological examinations of pathologic ova we feel convinced that it plays a very significant role amongst the factors causing spontaneous dying off of ova.

The ova studied by us had some characteristic features in common. The embryo was either missing (the amnionic cavity was empty), or it was rudimentary, a hardly recognizable clot, or it was very small compared to the embryonic membranes and, as a rule, perceptibly deformed. The question arises whether it is the embryo as the organizational guiding factor which in case of early developmental impediments or early dying off secondarily gives rise to a maldevelopment of the chorionic plate, or whether this maldevelopment, together with the disturbances in vascularization of the chorionic plate and the villi is the primary factor, the one which deprives the embryo of its ideal conditions of life. In connection with the ova studied we have established that where the embryo is missing (or where there are only remnants of a shrivelled, died off embryo very small in comparison to the size of the ovum) there the chorionic plate and the villi show considerable independence and, frequently, the tissues stain fairly well. In spite of the dying off of the embryo, which in a great many cases happened at a rather early stage, in the stroma of the villi an organizational process could be noticed accompanied by extensive tissue differentiation and by the formation of blood and blood vessels.

Under the microscope, in case of spontaneously expelled ova the structure of the chorion may show very different pictures according to how long the ova were retained. Notwithstanding the absence or dying off of the ovum, the chorion appears strikingly viable and in the sections it could be established that its stroma and epithelium may even stain normally. In some other cases where the embryo presumably died off at an early developmental stage the blood-vessels of the villi were found to be missing or very sparsely developed. Later, when the ovum is lastingly retained, the initially hydropically transformed stroma becomes fibrous, more compact, and only the epithelia of the villi show any activity (Figs. 8 and 9). On this basis, it is possible to recognize with great probability the abortive ova even if they be injured to an extent where only their chorion can be examined. The study of the abortive ova from this particular point of view can also be of importance to forensic medicine. Especially in connection with young and quite young ova *Grosser* speaks of such as have a scanty trophoblast and are lacking in villi, and reports to have frequently found among them pathologic embryos or embryos in the state of being absorbed. *Hinselmann* emphasizes the decisive importance of the complete lack of veins

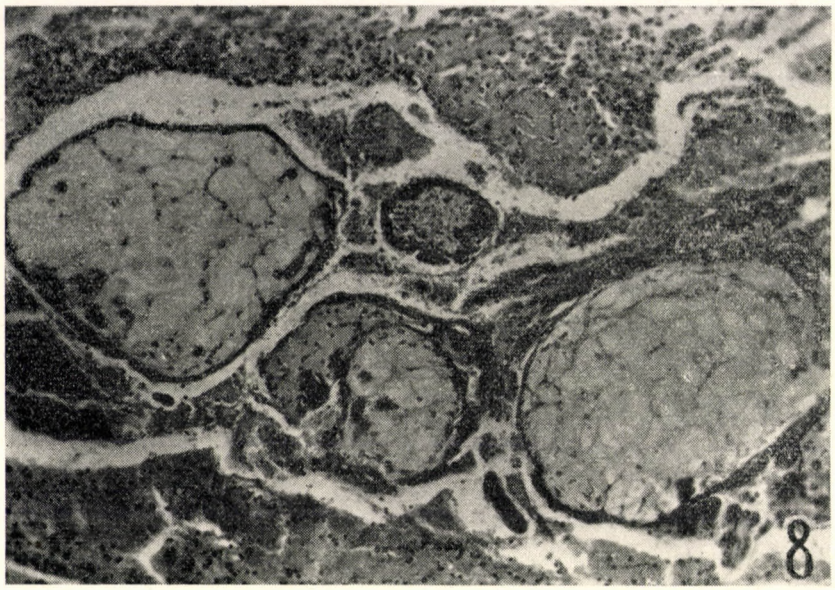

Fig. 8. Cystic ovum, chorion (considerably magnified microphotograph). Well staining chorionic epithelium showing great activity. Stroma of villi dense and of fibrous character. No capillaries to be found.

Fig. 9. Cystic ovum, chorion (considerably magnified microphotograph). Chorionic plate without vascularization. Epithelium of villi still staining well, their stroma fibrous, rich in cells, dense without capillaries.

in vesicular moles and points out, as a causative factor of them, the developmental inhibition of the venous system of the villi. *K. W. Schultze* found 43 abortive ova in 100 consecutive abortions and in his diagnoses layed stress on the oedema in the villous stroma and on the fact that regular vascularization was missing. In his opinion, however, neither the behaviour of the epithelium of the villi, nor the Chaletzky-type cells are in any connection with the abortive ova.

Odor and *Székely* (1949) described an embryoless ovum found while extirpating a myomatous uterus. Its chorionic villi contained no blood-vessels whereas within the area of the chorial elements (epithelium and stroma) cell division and proliferation was noticable. After the embryo had died off and been absorbed the embryonic membranes continued to live independently. It is known of chorionic vascularization that the first blood-vessels arise autochthonously at a very early stage in the chorionic plate and the villi, and that later the vascular primordia thus produced establish contact between each other. Further vascularization of both the older and newer villi starts from these primary processes. In other words, vascularization does not take place only by ingrowing vessels from the direction of the embryo. Yet in other words, it occurs simultaneously from the direction of the embryo, and locally, in the chorionic mesoblast. However, if the organizing and directing power inherent in the ingrowing embryonic vessels along the allantois ceases to have effect then, in our opinion, chorionic vascularization can evolve but very rudimentarily. According to *Hertig*, the vascular buds arise in the villi prior to the vascularization of the mesoderm of the yolk sac and the embryonic primordium. Haematopoiesis also takes place in the villi during the first two months of pregnancy ; a fact generally agreed upon on the ground of the investigational results of *Jaegerross*. Following the conclusion of the embryotrophic phase (about 38 days after the last menstruation) megaloblasts are usually to be found in the vessel of the villi, which later, after the 11th week, gradually cede their place to erythrocytes.

In the cystic, embryoless ova studied it was often possible to demonstrate primordiate vessels in the usually oedematous stroma of the villi (Fig. 10). These capillary buds are filled with erythroblasts which, however, did not yet enter the circulation. — The processes are crammed with erythroblasts connected with the vein walls. Yet, compared with the chorionic villi in normal early pregnancy the stroma is exceedingly poor in vessels. In its loose, intercellular network a considerable number of cells with a frothy, vacuolated cytoplasm is demonstrable *(Chaletzky, Neumann, Hofbauer, Stieve)*. The great number of frothy cells seems to be characteristic of mole-ova and their presence certainly facilitates the recognition of such ova in the sections (Fig. 11). According to *Stieve*, the frothy cells almost completely disappear in the second developmental phase of the young villi (after the fourth month) when the latter have become rich in blood-vessels that, too, had completed their evolutionary course. Also

Grosser has observed in the stroma of young ova great, protoplasma-rich, granulated, sometimes vacuolar cells, without, however, realizing their significance. *R. Meyer* considers them to be a degenerative product of the mesoderm cells. *Numers* (1949) has recently studied the structure of Chaletzky's cells in cases of normal pregnancy interrupted in the 2nd and 3rd months, and found them to be peresent in great numbers in the stroma of the villi. In view of the fact

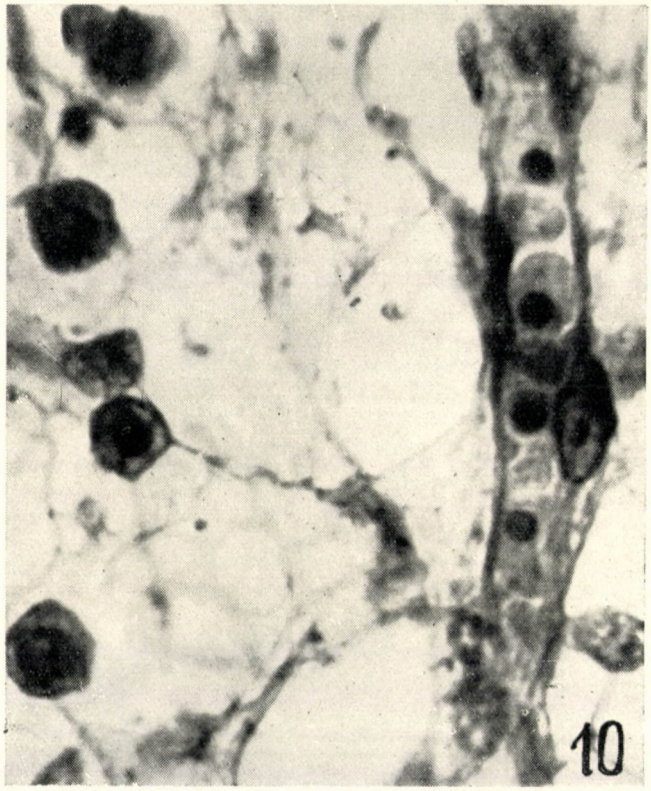

Fig. 10. Cystic ovum. Portion of stroma of chorionic villi. (Oil immersion.) Imperfect capillary formation. Nucleated red blood cells in the lumen. Around the vein and pressing to its wall large masses of wandering cells, their plasma staining characteristic of haemoglobin.

that the plasm of the Chaletzky-type cells connected with the stroma reticulum, stained positively with secretion dyes he refutes the view that these cells be merely degenerated stroma cells without any function of their own.

Our studies seem to confirm interconnection between the functioning of the Chaletzky-type cells of the stroma and the formation of haematopoietic centres in the primary villi. By means of staining with May-Grünwald-Giemsa we have been successful in obtaining in the plasm of the frothy cells secretion staining corresponding to haemoglobin (Fig. 12.). By way of histochemical

tests according to *Lepehne's* method (benzidin-peroxidase) it has also been possible for us to elucidate the prohaemoglobin character of the secretion in the vacuoles. It appears that the Chaletzky-type cells abound in great numbers near the capillary processes and play either a direct role in the formation of blood cells within the capillaries, or an indirect one by surrendering their haemoglobin

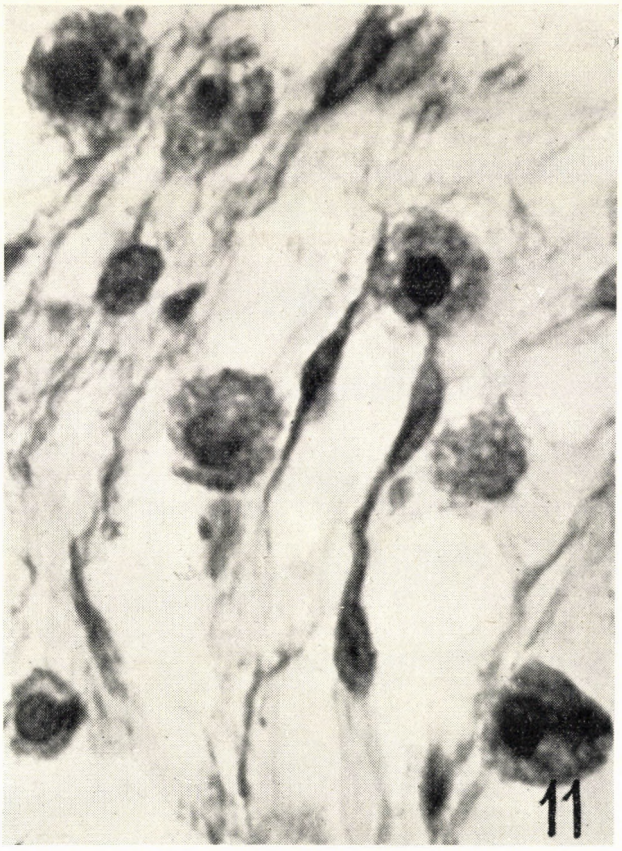

Fig. 11. Cystic ovum. Portion of stroma of chorionic villi. (Oil immersion.) The long, spindle-shaped, mesenchymal cells of the stroma are wandering cells. No vascularization demonstrable.

contents. Surrendering takes place either by haemoglobin transport or through cell division (Fig. 13). In the stroma of the villi of ova with pathologically developed veins extravasal erythropoiesis has been observed by us. Erythroblasts could be seen scattered single or in groups, and it was plainly noticeable that these newly arisen erythrocytes are in direct contact with the wandering cells of the villi, which fact seems to justify the presumption that in the loose stroma of the villf and at this earliest stage of chorionic blood formation, erythropoiesis must somehow be connected with these cells. The azur-eosinophil granules of

the Chaletzky-type cells stain similarly to the plasm of the young nucleated red blood corpuscles ; with the benzidine peroxidase method both take a brownish stain, though the erythrocytes take one a shade darker. From this it follows that in the histochemical sense a genetical correlation exists between the Chaletzky-type wandering cells and the blood cells formed the villi, and

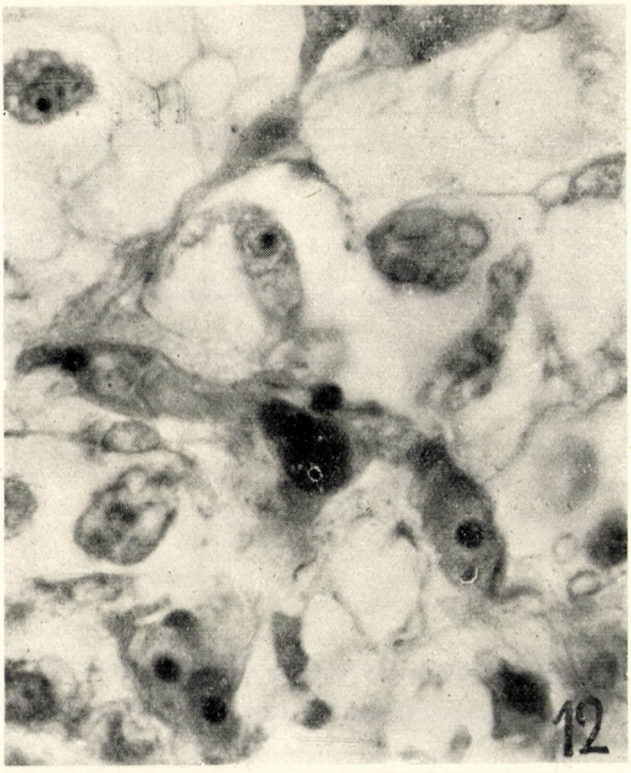

Fig. 12. Cystic ovum. Portion of stroma of chorionic villi. (Oil immersion.) Secretion-filled Chaletzky-type cells in direct contact with extravasal nucleated red blood cells. May—Grünwald—Giemsa staining ; the plasm of erythroblasts stains a vivid red, in the stroma of the wandering cells many lighter red granulations.

our presumption is that the former surrenders its haemoglobin content to the latter by direct division. Very probably, this is the phenomenon of cell-birth proceeding as interpreted by *Törő*. Even in the earliest phase of chorionic vessel and blood formation this process only takes place in the capillary buds, where the new cell, the nucleated red blood cell appearing in the plasm of the planocyte develops — »is born« — into the vascular lumen of the thickness of just one cell, whereas the mother cell helps building up the vascular wall.

Our observation that many wandering cells accumulate around the capillary buds (which are already full of erythrocytes but have not yet canaliculized)

seems to indicate that it is these cells that are passing on the material required for haemoglobin formation. The Chaletzky-type cells do function in this manner under normal conditions, too, but there the importance of this function to blood formation prevails only in the very early embryonic phase and persist for an exceedingly short period, whereas in the chorion of the pathogenically developed ovum (out living the perished embryo, and prior to the commencement of the degeneration of the stroma of the villi) it itself appears to be the extravasal

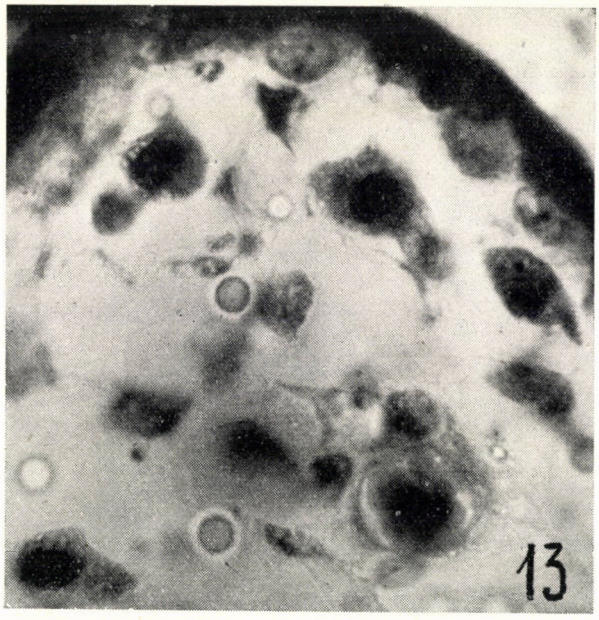

Fig. 13. Cystic ovum. Portion of chorionic villi. (Oil immersion.) Under the epithelium of the villi, stromatic cells full of secretion. Incomplete capillary formations with nucleated red blood cells in their centre.

blood cell formation. Many Chaletzky-type wandering cells can also be found in the reticular magma of embryoless ova.

As is commonly known, vessel and red blood corpuscle formation in the villi occurs equally in normal and pathologic ova. It is this phenomenon which in connection with the embryonic vessel formations invading through the allantois renders possible the rapid inversion of the histiotrophic into the haemochorial nutrition of the ovum. In human this sudden great change in the metabolism of the ovum is compensated by the insertion, for a short time, of nutrition through the yolk sac. Undoubtedly, the nidation of the ovum and the formation of the trophoblast (which mean the combined struggle between the maternal and embryonic tissues) are among the greatest shocks in the life of the ovum. In our opinion, the so-called mole-ova or abortive ova are the consequences

of disturbed vasoformation. However, the primary cause of abnormalities in vascularization is not always the same. In the course of our studies we found far-reaching similarities between the mole-ova, especially the cystic ova, and the real vesicular moles, both in respect of vasoformative irregularities and the great number of wandering cells in the stroma. Nor is the degree of proliferation and increased activity of the chorionic epithelium (the syncytium and Langhans' cells) the same even with the genuine moles, there being many transitions observable in the direction of the abortive ova. This fact explains why in the latter chorion-gonadotrophin secretion remains positive for a long time.

Endogenous and exogenous causes are supposed to underlie the development of pathologic ova, and they deserve to be also studied from a general biological point of view. Formerly, embryonic malformations were ascribed chiefly to endogenous factors, such as defects in, or injuries suffered by, chromosomes, or to changes in the cytoplasm gametes or zygotes. By now, these views have come to be ruled out in various respects. When studying embryonic maldevelopment in Greater Berlin in the years following the second world war *Eichmann* and *Gesenius* came to the interesting conclusion that following the war the number of neuroectodermal maldevelopments (anencephalus, spina bifida, hydrocephalus, meningocele) had considerably increased in comparison to that of hereditary maldevelopments. They now conceive the germinative ovarian insufficiency — this harmful effect on the germ plasm — to be disturbances consequent upon environmental or nutritional changes or other adversities due to the war. And, indeed, they all perceptibly affect the development of the embryonic central nervous system. No doubt, this is further valuable proof of the fact that environmental influences exert a significant effect on the germ cells. In the aetiology of spontaneous abortions, a sharp distinction between maternal and ovulogenic causes can only be approximated; their definite separation is exceedingly difficult. The development of the ovum embedding itself is not a simple evolution, but one a passing, at the nodal points, from continuous quantitative processes of growth into decisive qualitative changes. The efforts of the ovum to achieve transition from histiotrophic to haemochorial nutrition, on the one hand, and the mother's elaboration of enzymes, cells and tissues to ward off ingrowing embryonic cells and foreign proteins and hormones, on the other hand, constitute a fierce allergic struggle, the decisive stages of which are the embedding of the ovum, the coming into existence of the chorionic circulation and, finally, the formation of the placenta.

Soviet biological science has realized and acknowledged the decisive importance of the unity of the organism and its environment. To the ovum settled in the uterine cavity, the latter together with all the conditions prevailing in it represent the external environment; the direct nursing and training factor is the decidua, the indirect one is the mother's entire organism, and they produce an effect upon the formation of the developing organism. *Lyssenko*

has expressed this by stating that »the living organism and its indispensable conditions of life form a unity«.

Western authors display a certain predilection for explaining abortive ova by damages to the germ plasm or the genes, which through the so-called »lethal factor« should manifest themselves as inheritable injuries. However, this »lethal factor« of a mystical character is recessively transmitted, and could thus be found in the homozygous state, at the utmost, in 25% of all fertilized ova. Were the decisive role really rested in the inheritable factors, repeated abortion of pathogenic ova by the same mother would have to be a frequent phenomenon. On the other hand, if the anomaly is caused by external effects only, in the developmental phase of the ovum when it most sensitively reacts with qualitative changes to any influence, it is not to be expected that maldevelopment reveals itself in any subsequent pregnancy.

The results of many observations are at our disposal to-day proving that injurious effects befalling the pregnant organism cannot cause such lasting developmental impediments in the ovum as, in their turn, are liable to call forth permanent disturbances in it, unless they occur in a quite early period of pregnancy. To exogenous effects the ovum reacts most sensitively in its very initial phase of development. In the evolution of every important organ-system there is a phase when it is particularly sensitive to influences reaching it from its environment. The chorion, which is one of them, also has its developmental period in which it is very open to exogenous effects (toxic, or viral) or to the over-active maternal defence against a potentially weak trophoblast or to other harmful influences which, then, affect the entire developing organism or such organ-systems of it as just happen to be in the course of development or formation. Quite a number of external factors are already known which undoubtedly play a role in the pathogenesis of maldeveloped ova. Among them, stress must be laid upon acute virus disases and, first of all, upon German measles, for its virus penetrates the ovum and in the first weeks definitely attacks the embryo's central nervous system, the evolution of the brain and the formation of the primitive structures connected with sight (microphtalmia). It is probable, that as a rare exception injuries to the zygote might be caused by other acute infectious diseases, such as variola, toxoplasmosis and even malaria. Also, interconnection has been registered between vaccination during pregnancy and inborn deformity. Mention should still be made of the various hypovitaminoses, nutritional deficiencies, hormonal disordens, chemical and mechanical influences, radiating energies, injuries resulting from the action of X-rays, and — what is most important from the point of view of our study — nutritional injuries owing to the ovum having embedded itself unfavourably. In our opinion, peristatic effects exert the greatest influence in the period of nidation upon the rise of abortive ova. This view is evidenced by data in the literature *(Aschoff)* according to which in the greatest part of ova embedded

outside the uterus such structural changes of the chorion can be demonstrated already at an early stage which are completely missing in the normal chorion. In our own material, we could often observe in ova from extrauterine gravidity partial or complete absence of the vascular system of the villi, oedematous imbibition of the stroma and a very lively activity on the part of the trophoblast. This is a good example of the exceedingly important role of the maternal organism, representing the external environment of the ova if the ovum is embedded ectopically.

Many of the women under our observation, who had expelled abortive ova, later gave birth to healthy infants. Nor has any repetition of pathologic ova been noticed at later abortions, except in one case of mola hydatidosa pregnancy. On the basis of our case records, it had been established on a vast material that 20,4 admitted abortions could be apportioned to each 100 births. This proportion was somewhat higher for women who had ejected abortive ova ; it was 24,7 per cent. However, this slight increase cannot be taken for conclusive evidence in favour of inheritable injuries to the germ plasm. On the contrary, we believe that on the strength of our investigations we are justified to state, similarly to *Kaeser*, that the capacity to conceive is not less and the chances to have later normal pregnancies are not worse in the case of women who suffered mole-abortions than in the case of those who had abortions owing to some other causes. True, *Schultze* established reduced fertility subsequent to mole-abortions, but there was nothing in our material to verify this statement.

For practical purposes, our investigations are meant to draw attention to the significance of certain dangers to health in the initial stage of pregnancy, to the necessity of increased protection during that period, and to the fact that a certain percentage — and a large one too — of impending abortions are caused by pathologically developing ova. Early recognition of maldeveloping and gradually dying ova would save much nursing and expensive treatment during the period of impending abortion usually protracted for weeks. Thus, *Árvay* emphasizes the importance of elaborating diagnostical procedures which would allow earlier and more reliable indications made for the evacuation of the uterine cavity to take the place of costly and drug-wasting therapeutic attempts. Obviously, from a practical point of view this question is of considerable significance. The evaluation of our investigational results concerning hormones indicating ovum-activity is in progress. However, recognition of pathologic ova by biological tests is still hampered by the fact that the tissues and hormones of the chorion of cystic ova and embryomoles remain very active even after the death of the embryo that organizes and directs the development of the ovum.

Yet, in many cases of impending abortion with protracted bleeding in spite of long hospital treatment, and in cases of incomplete abortion where the uterus definitely discontinued growing or even showed retrogression, we have succeeded in proving the considerable decrease or complete stopping of the

chorionic activity by quantitative estimation of chorionic gonadotrophin by titration on the frog. Realizing this in practice, we abandoned waiting and evacuated the uterus.

Summary

All ova spontaneously expelled as whole ova in the course of 5685 cases of impending and inevitable abortions in our Department in Debrecen have been examined. Among them 349 pathologic ova have been found, their maldevelopment explaining the cause of the abortions. Cystic ova, containing no embryo, and ova with disproportionally small, shrivelled or dead embryos showing malformations have received special attention. The proportion of ovulogenic causes to all abortive cases was found to be 6, 1, and that of pathologically developed ova to all spontaneous abortions 23 per cent. It has been established that those of the threatening abortions which proved to be unavoidable were mostly due to disorders in the ova.

According to our investigational results, evacuated ova and pathologically developed ova show common features, genetically, in the formation of chorionic vascularization and its developmental derangements, respectively.

Under normal conditions, the blood processes arising independently in the chorionic plate and the villi unite at a later stage with the ingrowing embryonic veins. If the organizing and directing effect of the latter is discontinued, independent chorionic vascularization can give rise only to very rudimentary primordial vessels. Our investigations show that as long as the stroma of the villi of mole-ova stains well, the number of the Chaletzky-type cells increases whereby the recognition of the chorionic tissues of pathologically deficient vascularization is made easier. According to our observations there exists an interconnection between blood formation in the stroma of the villi and the Chaletzky-type cells.

We attribute the appearance of pathologic ova to occasional exogenous causes and not to inheritable injuries to the germ. We have not observed repeated abortions of such ova, but have established that the capacity to conceive is not less and the chances to have later normal pregnancies is not worse in the case of women who suffered mole-abortions than of those who had abortions owing to some other cause. Derangements turning the ova abortive befall them in the very early phase of gravidity, and chorionic developmental disturbance is caused primarily by disturbance of the nidation and external influences effective at that evolutionary stage.

REFERENCES

1. *Árvay, S.—Gavallér, I.—Nagy, T.:* (1952.) Therápiás eredményeink kiértékelése a vetélések korszerű kezelésében. O. H. 35. sz. (Hung.)

2. *Eichmann, E. u. Gesenius, H.:* (1952) Die Missgeburtenzunahme in Berlin und Umgebung in den Nachkriegsjahren. Archiv f. Gyn. Bd. 181. 168—184.

3. *Grosser, O.:* Über die Ursachen des Abortus. Archiv. f. Gyn. Bd. 176. H. 1. — (1927) Frühentwicklung, Eihautbildung und Placentation. Bergmann, München, V. Bd. Deutsche Frauenheilkunde. — Vergleichende und menschliche Placentationslehre. Halban-Seitz, Biologie u. Path. des Weibes. 1925. VI. Bd.

4. *Hertig, A. T. and Rock, J.:* Series of potentially abortive ova recovered from fertile women prior to first missed menstrual period. Am. J. Obst. and Gynec. 58, 968.

5. *Hinselmann, H.:* (1931) Erneuter Beitrag zur Theorie der Blasenmole. Zbl. f. Gyn. 55. Jahrg. 261. — Normales und pathologisches Verhalten der Placenta und des Fruchtwassers. Biologie und Path. des Weibes. Halban-Seitz VI. Bd. 1925.

6. *Kaeser, O.:* (1945.) Die Bedeutung der Molenschwangerschaften in der Abortaetiologie. Monatsschrift f. Geb. u. Gyn. Vol. 119. 159. — (1949.) Studien an menschlichen Aborteiern mit besonderer Berücksichtigung der frühen Fehlbildungen und ihrer Ursachen. Schweiz. med. Wschr. No. 23. 511.

7. *Lissenko:* (1948.) A biológiai tudomány állásáról. Szikra kiadás. (Hung.)

8. *Numers:* (1949.) Über die Struktur der Chaletzkyschen Zellen im Stromagewebe der Chorionzotten bei normaler Graviditaet. Acta obst. Scand. 23. Ref.: Zbl. Gyn. H. 8. 847.

9. *Nürnberger, L.:* Biologie und Path. des Weibes. 2. Aufl. VIII.: Fehlgeburt und Frühgeburt.

10. *Odor, B. u. Székely, K.:* (1949.) Ein Beitrag zur Frage der Abortiveier. Gynaecologie. Vol. 128. 130.

11. *Schultze, K. W.:* (1941.) Entwicklungsströrungen des Eies (Abortiveier), eine der wichtigsten Ursachen von Fehlgeburten. Zbl. f. Gyn. No. 4. 161. — (1944.) Zur Histologie der Abortiveier. Geburtshilfe u. Frauenheilk. H. 1—2. 50. — Über Missbildungen bei Aborten ihre Ursache u. ihre klinische Bedeutung. Ztschr. f. Geb. u. Gyn. 121. Bd. 242.

12. *Törő, I.:* (1953.) Über eine neue Form des Zellvermehrungmechanismus. Acta Morph. II. 363.

О ЗНАЧЕНИИ ПОРОКОВ РАЗВИТИЯ ЯЙЦА В ЭТИОЛОГИИ АБОРТА

Д. Рузичка

Р е з ю м е

Из материала дебреценской клиники, мы, среди 5.685 угрожающих и неотвратимых абортов, изучали те яйца, которые спонтанно целиком выкинулись. Среди последних мы нашли 349 абортивных яиц, порочное развитие которых объясняло причину аборта. Заслуживают внимание кистозные яйца, не содержащие зародыш и зародышные заносы, т. е. яйца, содержащие разные уродливые зародыши, слишком, или же мертвые, сморщенные. Абортивные яйца встречаются в 6,1% всех абортов и в 23% спонтанно окончившихся абортов.

Можно установлять, что среди угрожающих абортов, те у которых уже нельзя было предовратить аборт, были вызванны, заболеванием яйца.

Тщательное исследование выкинутых и порочно развитых яйц дает единое, стройное объяснение возникновения разных мол. Согласно результатам наших исследований, эти яйца генетически обнаруживают сходные черты, как в образовании васкуляризации хориона, так и в пороках развития его.

Зачатки сосудов, самостоятельно возникающие в листке хориона и в ворсинках при нормально-физиологических условиях, лишь более поздно вступают в соприкосновение с врастающими сосудами зародыша. Если организирующее и управляющее влияние последних отсутствует, васкуляризация хориона самостоятельно создает только весьма рудиментарные зачатки. По результатам наших исследований, в строме ворсинок заносных яиц, дающей еще удовлетворительное окрашивание, клетки Халецкого размножаются и своим большим числом облегчают гистологическое распознавание хориона с порочной, недостаточной васкуляризацией. По нашим данным имеется связь между образованием сосудов, происходящем в строме ворсинок с одной стороны, и ролью клеток Халецкого — с другой стороны.

Возникновение патологических яиц нами объясняется не наследственным повреждением зародыша, а влиянием случайных внешних причин. Повторение аборта таких яиц обычно не наблюдалось и как способность к зачатию женщин проходивших заносную беременность, так и перспективы доношения дальнейших беременностей, не хуже, чем у женщин, аборт которых вызвался другими причинами.

В случае абортивных яиц вредные влияния поражают яйцо в самом раннем периоде беременности и порок образования хориона вызывается прежде всего пороком иннидации или же внешними факторами, действующими в этой фазе развития.