

PATHOLOGY OF THE TROPHOBLAST

Presented by
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<http://www.navi.net/~rsc>
Journal of the American Medical Association, 1946
VOLUME 131 NUMBER 18 Page 1527
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To the Editor: During the past four years my associates and I have been conducting an intensive study of the biologic and morphologic properties of the mammalian trophoblast. And although we have attempted to classify and systematize from the available literature the consensus on the subject, we realize that there must be a considerable body of unpublished data on this greatly neglected component of the mammalian life cycle. We should therefore be grateful for any such data that the readers of THE JOURNAL are able to supply on the human trophoblast.

The following list, I believe, represents the consensus on the mammalian trophoblast. I should welcome any questions or criticisms of, or additions to, these data :

1. The trophoblast is segregated from the "embryo-forming cells" during the early cleavage stages of the conceptus and does not form the definitive embryonic cells nor can such cells ever form trophoblast. The trophoblast cell is thus the most primitive cell in the ontogeny of the animal.
2. The trophoblast cell (cytotrophoblast or Langhans cell) of normal pregnancy is cytologically and otherwise indistinguishable from the cytotrophoblast of primary uterine chorionepithelioma.
3. The definitive trophoblast cell of primary uterine chorionepithelioma is likewise indistinguishable from such cells in genital and primary extragenital chorionepitheliomas in the male.
4. The presence of cytotrophoblast in all such situations yields a qualitatively identical gonadotropic substance, the quantity of which varies directly with the number of Langhans cells present.
5. The trophoblast cell is the only cell of the animal's life cycle that has never been found in the male except as cancer, nor so in the female outside the canalization of normal pregnancy.
6. In the course of normal gestation the human trophoblast erodes, infiltrates and phagocytizes the maternal decidua; and metastases are normally discharged into the circulation, where they lodge in the lungs, brain and other structures and are then normally destroyed.
7. The trophoblast is the only normal tissue that regularly metastasizes.
8. When the cellular trophoblast is directly exposed to the blood it undergoes a syncytial adaptation.
9. In growing human trophoblast in tissue culture it is found that the cellular element predominates and that this element produces gonadotropin, whereas the syncytium produces estrone-like and progesterone-like steroids.
10. In culturing the trophoblast and its definitive embryo in vitro the trophoblast may, through erosion, infiltration and phagocytosis, completely devour the nontrophoblast elements (definitive embryo).
11. Although the trophoblast cell or the syncytium has never been found in the male-- except as cancer, when these elements are found in the male they comprise the most malignant of tumors-the chorion- epitheliomas.

12. Microscopic examination of various exhibitions of cancer in the male have in some cases disclosed genital as well as primary extragenital chorionepitheliomas which have graded by imperceptible degrees into adenocarcinoma or sarcoma ; and primary adenocarcinoma of the testis has been reported as

exhibiting overt chorionepithelioma in pulmonary metastases. It is also reported that chorionepithelioma, adenocarcinoma and hypernephroma are indistinguishable in their metastases to the liver.

13. Extragenital chorionepitheliomas in both sexes produce identical gonadotropic substance duplicated only by the gonadotropic substance of the normal pregnancy trophoblast. In testicular tumors, in which the trophoblast cells are not morphologically overt, so-called chorionic gonadotropin is produced. It is also produced in detectable quantities in some extragenital nonchorionepitheliomatous exhibitions of cancer. And the more closely a cancer comes to exhibiting overt Langhans cells, the higher its gonadotropic titer and, generally, its degree of malignancy.

14. Ectopic trophoblast cells are susceptible of being "masked" morphologically.

15. The trophoblast arises from the activation (by fertilization or parthenogenetically) of a gametogenous cell produced, through meiosis, from a diploid totipotent cell.

16. Diploid totipotent cells are ubiquitous within the soma and not restricted solely to the gonads.

17. Cells which are alike (e. g. trophoblast cells) arise from preexisting cells that are alike.

18. The normal pregnancy trophoblast cell duplicates all the properties of the cancer cell, but these inherently malignant properties are prevented, under normal conditions of gestation, from being exhibited at the pathologic level because of the resistance of the maternal host.

19. The cytotrophoblast of chorionepithelioma is the same as the cytotrophoblast of normal pregnancy, except that the growth of the latter is restricted by the host.

20. A trophoblast cell has never been observed ectopically-- masked or overt, alone or in conjunction with a teratoma-- except as one of the malignant exhibitions of cancer; and the trophoblast cell and syncytium are the only normal elements in the life cycle that are indistinguishable from cancer. And in tissue culture the degree of malignancy of normal pregnancy trophoblast toward nontrophoblast is not surpassed by any known exhibition of cancer (9).

These data suggest that the trophoblast cell per se is malignant in ectopia. They further suggest that the trophoblast cell is not always exhibited as chorionepithelioma but may be so masked as to be exhibited, in some cases, as carcinoma or sarcoma. Thus these malignant exhibitions seem all to stem from a common cell type : the progenitor of trophoblast or the gametogenous cell.

Experimental data suggesting the trophoblastic nature of cancer are to be published elsewhere. At present a common basis of agreement is sought in this communication for the foregoing theses.

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(J.A.M.A., 1946, 131(18):1527)

Current page location: <http://www.navi.net/~rsc/cancer/krebs46a.txt>

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