When the embryos have been thoroughly dehydrated they are cleared in oil of cedar or origanum. They should remain in the clearer for one hour after sinking to the bottom of the container to insure thorough clearing. The embryos are then removed and washed in xylol for ten minutes to prepare them for subsequent treatment by removing the oil which adheres. Next, the embryos are placed in a solution of paraffin-xylol. The most satisfactory solution is prepared by dissolving at ordinary room temperature 24 grams of paraffin in 100 cc of xylol. It is well to have this solution prepared a few days in advance to prevent delay. The amount of solution used should be three or four times the bulk of the embryos. The embryos are left in this solution from two to six days depending on their size. (See Schema at end.) After removing the embryos dip them once or twice in xylol, then place them in melted paraffin and put in oven. The melting-point of the paraffin should not exceed 52 degrees Centigrade nor should the temperature of the oven. At the end of fifteen minutes the paraffin is poured off and fresh-melted paraffin put on. This procedure should be repeated at least three times. At the end of forty-five minutes it is wise to smell of the embryos to make certain that all the xylol has been removed. If the slightest trace of xylol is detected change the paraffin a fourth time. All the xylol must be removed, otherwise the imbedding paraffin will crystallize and great difficulty will be experienced in sectioning.

It is a well-known fact that heat is detrimental to all tissue, even adult tissue, not to mention its effect upon embryonic. In infiltrating tissue it is most essential to submit it to heat for the shortest time possible. Heat shrinks, hardens and distorts tissue, thereby rendering it worthless. We have found pig embryos to shrink from 1/16 to 1/4 their natural size when submitted to heat for as short a period as two hours at 52 degrees Centigrade. The tissue shrinks and hardens so rapidly that it is impossible for the paraffin to penetrate and as a consequence imperfect infiltration results, particularly in those parts of the embryo where shrinkage is the greatest. In sectioning, the parts not infiltrated crumble and fall out. This is invariably the case with the liver of the embryo. The liver is very compact, the interstices minute and the shrinkage great. By using a paraffin-xylol solution a sufficient amount of paraffin penetrates the tissues so that when the embryo is placed in the melted paraffin and put in the oven, the paraffin, which has already penetrated the embryo from the paraffin-xylol solution, melts and by capillary action rapidly draws in the fresh paraffin and forces the xylol out in less than one hour. The maximum shrinkage in pig embryos takes place after the first ninety minutes in the oven.

An objection which might be raised against the use of paraffin-xylol is that tissue left in xylol for many hours becomes brittle and brittleness is as ruinous to tissue as heat. This objection is true when xylol is used as the clearer—but when cedar oil or oil of origanum is used as the clearer the embryos may remain in paraffin-xylol for a week without becoming brittle.

Below is a Schema which shows the relative amount of time necessary for embryos of various sizes to remain in the paraffin-xylol solution in order that they may be thoroughly infiltrated after being in the oven from 45 to not more than 60 minutes.

SCHEMA

Size of Embryo	Length of Time Embryo is in Solution of Paraffin-Xylol
7 mm. to 10 mm.	48 hours
11 mm. to 15 mm.	54 hours
16 mm. to 20 mm.	65 hours
21 mm. to 24 mm.	77 hours
25 mm. to 29 mm.	88 hours
30 mm. to 34 mm.	95 hours
35 mm. to 39 mm.	104 hours
40 mm. to 45 mm.	110 hours
46 mm. to 50 mm.	119 hours

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SPECIAL ARTICLES

THE ANATOMY OF THE CORIUM

IT was pointed out by Dupuytren[1] in 1836 that a round, pointed awl thrust into the human skin produced not round openings but linear slits. This property of the corium was very fully studied by K. Langer in 1861.[2] From the work of Langer it is evident that in the human there are very definite directions in which these cleavages take place and that these directions are constant for an anatomical part. Nussbaum[3] and Burkard[4] have studied these cleavage lines in the human foetus and have shown the changes that take place during development.

[1] Quoted by K. Langer.

[2] Langer, K. "Über die Spaltbarkeit der Cutis." *Sitz. berichte d. K. akad. d. Wissenschaften S.* 19 Bd. 44, 1862.

[3] Nussbaum, Ilse. "Über die Spaltungsrichtung Menschlicher Embryonen." Inaug-Diss. Berlin, 1923.

[4] Burkard, Otto. "Über die Hautspaltbarkeit Menschlicher Embryonen." *Arch. f. Anat. u. Physiol. Anat. Abt.* S. 13, 1903.

The correlation between these cleavage lines in the human and the direction of the supporting fibers in the tela subcutanea was reported by me before the American Association of Anatomists in Nashville in 1927.[5] On the basis of earlier experimental work (Batson and Zinninger[6]) which shows that tension physiologically applied produces connective tissue fibers in the direction of the pull, it was postulated that the manner of distribution of the retinacula cutis and the anatomy of the more extensive deposits of fibrous tissue, now going under the name of various fascias, together with the connective tissue fibers of the corium responsible for the cleavages (earlier studied by von Langer) were the result of the tension placed upon these structures by their own weight, and by the weight of associated structures (*i.e.*, capital hair, mammae and genitalia). Naturally both the circumferential and linear growth of the parts covered by the skin must not be overlooked as a source of tension. This growth factor is significant in studying the direction of fibers and cleavages in the developing organism. Skin muscles likewise play their part.

It has been found that the "splitability" of the corium may be studied after it has been detached from the underlying structures, and this has made possible the gathering of much additional information on the human and opened up the possibility of the study of the detached animal skin. These split-like cleavages have been produced in the corium of the following: the dog-fish, the frog, the dog, the pig and the chimpanzee. It would appear that if the arrangement of the corium fibers were due to functional factors, that the direction of these cleavages should have a direct relationship to the posture of the animal. Further with the knowledge of the habits of any form it should be possible to foretell the directions of the principal cleavages in that comparative form. Parenthetically it might be added that these cleavages in addition to being present in the skin and mucous membranes may be demonstrated in the serous membranes of the body, vessels, periosteum, dura mater, cartilages and in the capsules of parenchymatous organs as well. The specific study of these ramifications of the problem are now in progress in this laboratory. The lines of cleavage in the corium of the dog which have been more specifically studied do not resemble the human but correspond to what would be supposed, considering the postural habit of the animal. This correlation strengthens the previously proposed idea that the anatomy of the corium was developed through function. The wide variety of animals showing cleavage lines in the corium can leave no doubt that this property of the corium is common to all animals.

Leather, that is tanned corium, shows this same property. The cleavages may be at any angle to the furrows of the animal's skin or to the "grain" of the leather. Laboratory tests show that leather is stronger in the direction parallel to the direction of the cleavage. This idea negates a common one that an area of leather has its strength uniform in all directions. This finding applied to the manufacture of leather articles should secure the maximum of strength and a greater uniformity of product.

Studies of the microscopic anatomy of the corium responsible for these splits occurring in a longitudinal direction are now under way. Three possibilities suggest themselves as explanations; 1. More connective tissue fibers in the direction of tension. 2. Greater length of connective tissue fibers in the direction of tension and 3. Difference in character of the fibers running in the direction of tension. The first notion, *i.e.*, that the cleavages are due to a greater number of connective tissue fibers lying in that direction seems the most probable.

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[5] Batson, O. V. "The Anatomy of the Tela subcutanea." *Anatomical Record*, p. 4, Vol. 35. 1927.

[6] Batson, O. V., and Zinninger, M. M. "The Experimental Production of Annular Ligaments, as an Example of the Influence of Function upon the Differentiation of Connective Tissue." *Bull. Johns Hopkins Hospital*, p. 124, Vol. XXXVIII, 1926.

THE DIALYSIS OF PITUITARY EXTRACTS

THE physiologically active material contained in extracts of the posterior lobe of the pituitary gland diffuses readily through the ordinary dialyzing membranes.[1] The rate of dialysis suggests that the active principle (or principles) is considerably more complex than adrenalin, but somewhat simpler than insulin or the parathyroid hormone.

In a preliminary report[2] I compared the relative rate of dialysis of pituitrin with that of a compound of known molecular weight (adrenalin) and suggested 600 as the approximate molecular magnitude of the pituitary principle. This early work appeared deficient because it relied only upon the pressor assay method but the actual laboratory results have now been verified and are presented below.

In the meantime an excellent report[3] on the dialysis of pituitary extracts has been published by Smith and

[1] *J. Physiol. 25,* 87 (1899); *Am. J. Pharm. 86,* 291 (1914); *Biochem. J. 9,* 307 (1915); *Brit. Med. J.* I, 502 (1900); *Proc. Roy. Soc.* (London), B. *77,* 571 (1906); *J. Pharmacol. 15,* 81 (1920).

[2] Washington Meeting, Amer. Chem. Soc., April, 1924.

[3] *J. Pharmacol. 24,* 391 (1924).