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.

O. V. BATSON

UNIVERSITY OF CINCINNATI

[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).

McClosky, of the U. S. Hygienic Laboratory, and these workers have applied both the pressor and oxytocic assay methods. They found that the two types of activity show identical diffusion rates, thus suggesting the presence of a single hormone.

Smith and McClosky have so adequately described the technique of preparing and using collodion membranes for this dialysis work that further experimental details are unnecessary. The only variation in the present work consisted in the use of a volume of solvent outside of the membrane exactly equal to that contained inside and provision for uniform stirring. The collodion membrane, cast in the form of a large-size test-tube, was suspended in a glass cylinder of such diameter that the liquid level inside was exactly equal to that outside.

In the following experiments the active material was dissolved in one fourth per cent. aqueous acetic acid and dialyzed against acetic acid of the same strength. At the beginning of the experiment the outside concentration was, of course, 0 per cent. The maximum per cent. attainable in the outside chamber (50 per cent.), obviously was not attained since the experiment was not run to final equilibrium. Samples were withdrawn for assay usually at 15, 30, 60 and 120 minute intervals and subjected to assay. The experiments were conducted at a temperature of 25° C.

EXPERIMENT I

Dialysis of Pituitrin

Assay by Pressor Method

Time	Concentration Inside	Concentration Outside
0 min.	100 per cent.	0 per cent.
30 "	.....	12 per cent.
60 "	.....	20 per cent.
180 "	50–60 per cent.	40 per cent.

In all cases the potency of the pituitary solutions is expressed in terms of the U. S. P. standard. The potency of adrenalin is expressed in terms of 1:1000 adrenalin solution.

In order to rule out the error due to variations in permeability of the collodion membranes, the adrenalin was dialyzed through the same membrane used in the first experiment and with the following results:

EXPERIMENT II

Adrenalin Dialysis

Time	Concentration Inside	Concentration Outside
0 min.	100 per cent.	0 per cent.
15 "	.....	13 per cent.
30 "	.....	22 per cent.
60 "	60 per cent.	35 per cent.

From the above figures it is apparent that adrenalin dialyzes twice as rapidly as does the pressor principle of pituitary extracts and if the laws of diffusion of gases are applicable to the dialysis of these complex substances through collodion membranes one might conclude provisionally that the pituitary principle is approximately four times as complex, from the standpoint of molecular magnitude, as is adrenalin.

In the following two experiments a different membrane was used and also a more concentrated pituitary solution. The samples were assayed by both the pressor and oxytocic methods.

EXPERIMENT III

Dialysis of the Pressor Activity

Time	Concentration Inside	Concentration Outside
0 min.	400 per cent.	0 per cent.
15 "	.....	40 per cent.
30 "	.....	80 per cent.
60 "	.....	100 per cent.
120 "	250 per cent.	160 per cent.

EXPERIMENT IV

Dialysis of the Oxytocic Activity

Time	Concentration Inside	Concentration Outside
0 min.	480 per cent.	0 per cent.
15 "	.....	70 per cent.
30 "	.....	100 per cent.
60 "	.....	120 per cent.
120 "	325 per cent.	175 per cent.

Although the above results are not as uniform as the physical chemist might expect in a quantitative experiment, it must be remembered that the results are all based upon physiological assays on animals and are actually within the accuracy of the experimental methods. For this physiological work I am greatly indebted to Messrs. L. W. Rowe and E. P. Bugbee.

The results of experiments III and IV verify the claim that the pressor and oxytocic activities dialyze at practically uniform rates and agree with the assumption that a single active principle is responsible for both types of physiological activity. Indirect evidence of this kind, however, is not final and we must still consider the possibility of two active principles that are similar not merely in chemical constitution but also in molecular magnitude.

The molecular weight of the active principle (or principles) may be considered as approximately 600 until direct measurements are available.

OLIVER KAMM

CHEMICAL RESEARCH DEPARTMENT,
PARKE, DAVIS AND CO.,
DETROIT, MICHIGAN