increased synthesis of para-aminobenzoic acid.[10] That the same mechanism is not involved in the development of penicillin-fastness is evidenced by susceptibility of sulfonamide-fast strains of staphylococci and pneumococci[5,11] to penicillin. Furthermore, it is evident that penicillinase does not hold analogous relationship to penicillin-fast staphylococci as para-aminobenzoic acid does to sulfonamide-fast staphylococci. Other factors as yet unknown must be concerned in the development of resistance by bacteria to penicillin.

That development of resistance to penicillin is not dependent on penicillinase is not surprising inasmuch as inability to produce penicillinase does not appear to be the determining factor in the sensitivity of an organism to penicillin. The factors concerned in the development of resistance to penicillin by bacteria no doubt are related to the factors which determine their susceptibility to penicillin.

It is to be expected that organisms producing penicillinase would not be highly susceptible to penicillin. The susceptibility of the two penicillinase-positive organisms to higher concentrations of this antibiotic may be attributed to production of penicillinase in smaller amounts. Furthermore, 24-hour cultures were used in the susceptibility tests whereas cultures 4 days or older contain much greater amounts of penicillinase.

Conclusions. Inability to produce penicillinase is not a determining factor in the sensitivity of an organism to penicillin. However, penicillinase-producing bacteria are not likely to be highly susceptible to penicillin. Development of resistance to penicillin by a bacterium is not associated with acquisition by the bacterium of the ability to produce penicillinase.

10 Landy, M., Larkum, N. W., Oswald, E., and Streightoff, F., *Science*, 1943, **97**, 265.

11 Powell, H. M., and Jamieson, W. A., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 387.

14623

Production of Labyrinthine Paralysis by Application of Local Anesthetics to External and Middle Ear.*

E. A. SPIEGEL.

From the Department of Experimental Neurology, Temple University School of Medicine, Philadelphia, Pa.

In the course of experiments dealing with other problems of abnormal labyrinthine excitability, methods of eliminating the impulses from the labyrinth were developed that may be able to make more radical measures (Dandy,[1] Putnam,[2] Mollison[3]), at least in some instances of Ménière syndrome, unnecessary. While Brown-Séquard's[4] procedure of producing symptoms of labyrinthine paralysis by instillation of chloroform into the external auditory canal in guinea pigs is not applicable to cats or dogs, paralysis of the labyrinth was obtained, in cats, by electrosmosis of solutions of local anesthetics introduced into the external auditory meatus. Two per cent solutions of cocain, pontocain, or metycain in 80% alcohol were instilled into the external meatus, and the meatus was plugged by an electrode that was wrapped by cotton soaked with the

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Temple University.

1 Dandy, W. E., *Acta Otolaryngol.*, 1934, **20**, 1.

2 Putnam, T. J., *Arch. Otolaryngol.*, 1938, **27**, 161.

3 Mollison, W. W., *J. Laryng. and Otol.*, 1936, **51**, 38.

4 Brown-Séquard, C. E., *C. R. Soc. de biol.*, Ser. 7, 1880, **2**, 383.

same solution. The ear electrode was connected to the anode, an indifferent electrode fastened to the abdomen was connected to the cathode of a constant current. When 5 milliamperes were applied for 5-10 minutes, typical symptoms of labyrinthine paralysis appeared such as nystagmus to the opposite side, rotation of the head (see Fig. 1), pleurostonus, circus movements, falling to the same side. These symptoms persisted for from 3-4 hours. When the cocain was bilaterally introduced into the labyrinths by this method, a transient definite reduction of the labyrinthine excitability to rotatory stimuli could be obtained (*e.g.*, duration of the postrotatory nystagmus in cat 39, 13-17 sec. before, 6-9 sec. 20 min. after bilateral cocain electrosmosis; in cat 40, 12-15 sec. before, 3-6 sec. 10 min. after this procedure; next day normal values). In dogs and in man, it was not possible to obtain symptoms of labyrinth paralysis by electrosmosis of cocain solutions.

FIG. 1.
Cocaine-electro-endosmosis of right ear 3:33-3:43. Photographed at 4:36. Note, besides abnormal position of head, rightsided Horner (paralysis of sympathetic fibers to eyeball on their way over promontory).

† R. Magnus and A. de Kleyn (Bethe's Handb. d. Physiol., 1926, **11**, 875) erroneously quote C. J. König (Contribution a l'étude expérimentale des canaux semicirculaires. Thèse de Paris, 1897) and J. Breuer (Sitzungsber. d. Akad. d. Wissensch. Wien, Mathem. naturw. Kl. III, 1905, **112**, 315) as observing labyrinthine paralysis following injection of cocain into the middle ear in guinea pigs. These two authors applied cocain to the semicircular canals directly, in pigeons. For "cats, etc." Magnus and de Kleyn recommended only injection of cocain into the labyrinth.

Therefore, it was determined whether substances injected through the drum into the cavum tympani are able to permeate into and to influence the activity of the labyrinth.† The experiments were performed on dogs and cats, and the following substances were tested: alcohol 95% 1-2 cc, alcohol-glycerin āa 0.5-1 cc, alcohol-physiologic NaCl āa 0.5, alcohol 0.5 cc plus vasoconstrictors (0.5 cc ¼% neosynephrin, 1% propadrine HCl, or 1% paredrine HBr), 0.5 cc 2% cocain solution in 80% alcohol with equal amounts of the above-mentioned vasoconstrictors. All these substances were able to produce symptoms of labyrinth paralysis, except injections of the vasoconstrictors alone (diluted by equal amounts of saline).

The paralytic effect as indicated by nystagmus to the normal side appeared within 10-45 minutes; its duration varied. It was shortest (about 1 hour) after injection of 95% alcohol diluted with equal parts of physiologic NaCl solution, longest after injection of alcohol plus the vasoconstrictors or 2% alcoholic cocain solution plus equal amounts of vasoconstrictors (above 5 hours). All these effects were transient, the animals showing no manifest symptoms of labyrinth paralysis on the day following the injection. Repeated intratympanic injections, *e.g.*, of alcohol on 5 successive days, produced each time a transient nystagmus of several hours' duration.‡ However, even after a single intratympanic injection of alcohol or of an alcoholic cocain solution the tonic impulses from the affected labyrinth seem to be somewhat diminished for a week. This is indicated by the fact that an injection of the same solution into the opposite ear after an interval of several days produces a nystagmus of shorter duration and lower frequency than the first injection (*e.g.*, after injection of 2% cocain in 80% alcohol, 1% propadrine HCl āa 0.5 into the left ear: nystagmus to right, duration 5

‡ Occasionally the injections failed to produce the labyrinth paralysis or repeated injections were necessary, probably because the fluid escaped through the Eustachian tube. This factor may also interfere in man and may necessitate plugging of the pharyngeal ostium of the tube. These problems of clinical application are now being studied with Dr. M. Ersner.

hours, frequency 140 decreasing to 108; after injection into right ear several days later: nystagmus to left 3½ hours' duration, frequency 102 decreasing to 76).

Summary. In cats, paralysis of the labyrinth can be obtained by electrophoresis of cocain solutions from the external auditory meatus. In cats and dogs, such an effect can be produced by injection of local anesthetics into the tympanic cavity. The effect can be prolonged by combination of the local anesthetic with vasoconstrictors. The use of such intratympanic injections for the treatment of abnormal states of labyrinthine irritation is proposed.

14624 P

Insensible Perspiration and Keratinization Process.

STEPHEN ROTHMAN AND ZACHARY FELSHER. (Introduced by G. F. Dick.)

From the Section of Dermatology, Department of Medicine, University of Chicago.

The keratinization of the epidermis is associated with considerable dehydration since the Malpighian layer contains 70% to 80% water, whereas the water content of the horny layer does not exceed 30%.[1] If the liberated water is lost with the insensible perspiration, conditions in which keratinization is accelerated must show increased insensible perspiration values. Earlier observations seemed to be in accord with this supposition.[2,3] Lately, Pinsen[4] found 2- to 3-fold values of insensible perspiration in dry, scaling skin. Further experiments on this subject are reported in the present study.

Method. The insensible perspiration was measured by absorbing water vapor from the skin in linen bags filled with anhydrous calcium chloride. These bags were weighed, suspended under glass bells which were firmly taped to the skin, and weighed again after 60 minutes.*

Results. Parallel values obtained in simul-

TABLE I.
Insensible Perspiration in Psoriasis.
Measurement on Adjacent Areas of Normal Skin and Psoriasis Patches.
Diameter of glass bells 4.71 cm.

Date	Name	Sex	Age	Region	Room temp., F°	I.P. in mg: Normal skin	I.P. in mg: Psoriasis skin	Increase of I.P. in psoriasis
11-27-43	H.H.	M	42	Back	—	9.4	73.4	8x
12-28	L.	M	43	Abdomen	75	23.8	109.1	4x
2- 7-44	C.E.	M	77	Chest	77	—	92.3	—
2- 8	E.M.	M	56	"	76	13.1	88.9	6x
2-12	E.M.	M	56	Abdomen	74	—	58.4	—
2-19	D.S.	M	66	Sacrum	76	25.5	98.6	4x
2-22	—	M	—	Back	—	18.6	55.5	3x
3-11	A.K.*	M	33	Abdomen	77	—	97.4	—
3-11	A.K.*	M	33	"	77	—	90.8	—
4-17	M.R.†	F	40	Thighs	77	14.7	56.3	4x

* Two adjacent areas measured in generalized psoriasis.
† Symmetrical areas measured.

[1] Rothman, S., and Schaaf, F., Chemie der Haut, *Jadassohn's Hand. d. Haut- u. Geschlechtskr.*, 1929, **1**, 161, J. Springer, Berlin.

[2] Rothman, S., *Strahlentherapie*, 1930, **35**, 381.

[3] Rothman, S., *Zentralbl. f. Haut- u. Geschlechtskr.*, 1931, **37**, 30.

[4] Pinsen, E. A., *Am. J. Physiol.*, 1942, **137**, 492.

* A detailed description of the method is given in Felsher, Z., Hereditary Ectodermal Dysplasia, *Arch. of Derm. and Syphil.*, in press.