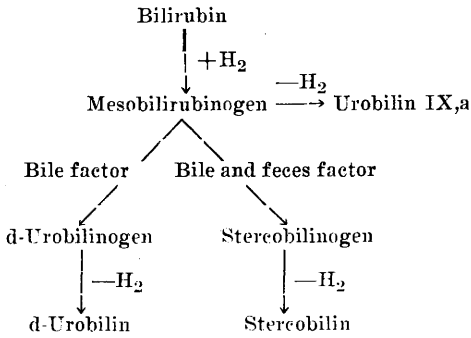

The primary reduction to mesobilirubinogen is probably effected by a number of bacterial reducing systems, while the secondary transitions to d-urobilinogen and stercobilinogen evidently depend on more complex factors, as indicated. The possibility cannot be excluded that bilirubin may be reduced directly to d-urobilinogen or stercobilinogen without mesobilirubinogen as an intermediate stage, also, that given the proper conditions, d-urobilinogen may be converted to stercobilinogen. Still another possibility is that stercobilin or d-urobilin may be formed directly from mesobilirubinogen without intermediary differing chromogens.

Summary and Conclusions. 1. The oral or intraduodenal administration of mesobilirubinogen resulted in an increased excretion of stercobilin in the feces. 2. The incubation of mesobilirubinogen with normal feces, or with acholic feces plus bile resulted in formation of stercobilin. Incubation with acholic feces alone resulted in no change; urobilin IX,a was subsequently isolated. 3. Mesobilirubinogen was not converted to stercobilin in the 3 urine samples studied. It is believed that mesobilirubinogen is the primary chromogen or urobilinogen formed by bacterial reduction of bilirubin. The further elaboration of d-urobilin requires bile, while that of stercobilin requires bile and feces.

13658

Experimental Studies in Metaplastic Ossification.

SHELDON A. JACOBSON. (Introduced by Valy Menkin.)

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Huggins[1-4] has discovered that transplanted epithelium of bladder, ureter, or kidney pelvis induces ossification of the connective tissue

of muscle or muscle sheath in the dog. He further found that this epithelium possesses the same potency in *fascia lata,* subcutaneous tissue or synovial membrane, but not in kidney, liver or spleen. These experiments, successful in the dog, failed (except for one case) in the rabbit, despite the administration of viosterol and parathormone. Dragstedt and Kearns[5] and the author were able to reproduce his results. The former succeeded also in demonstrating ossification about a bit of fascia used to close a surgically produced defect in the bladder walls of dogs.

Sacerdotti and Frattin[6] found that if the vessels of one kidney of a cat, or one renal vein of a rabbit, were tied off, bone would be produced in the organ. It has been shown by Jaffe[7] and others that elementary phosphorus is a stimulus to osteosclerosis. Barth[8] reported ossification in the cat's omentum in response to the implantation of burned bone.

To study the mechanism involved more easily and on a larger scale, albino rats of both sexes and from 105 to 385 g in weight were selected. Under amytal anesthesia pieces measuring several mm in diameter were excised from the bladder and implanted into one or more pockets in the rectus muscle or elsewhere as mentioned. Variations of this and other procedures were employed as indicated in Table I. After a period of time varying from 3½ to 7 weeks, the animals were sacrificed, unless found dead. The experimental areas, when identifiable, were removed for microscopic section. Cysts resulted from the transplantations. They were lined by epithelium of the lower urinary type, varying markedly in thickness, and had many branching pockets. Besides the cysts, solid or almost solid clusters of epithelial cells often appeared. Granulation tissue surrounded the transplants, with lymphocytes and histiocytes in varying numbers. The occasional abscesses are not included in this report.

Three of the animals were found to be pregnant at autopsy. (None of these was among the 5 cases with positive results.)

The results are summarized in Table I. (The excess of number

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[1] Huggins, C. B., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 349.

[2] Huggins, C. B., and Compere, E. L., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 753.

[3] Huggins, C. B., PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 125.

[4] Huggins, C. B., *Arch. Surg.*, 1931, **22**.

[5] Dragstedt, C. A., and Kearns, J. E., Jr., *Am. J. Physiol.*, 1932, **100**, 262.

[6] Sacerdotti, C., and Frattin, G., *Gior. d. r. Accad. di Med. di Torino*, 1901, **7**, 825; *Arch. Path. Anat.*, 1902, **168**, 431.

[7] Jaffe, H. L., *Arch. Path.*, 1933, **16**, 63, 236.

[8] von Korff, K., *Birch. Arch.*, 1940, **276**, 111.

TABLE I.
Metaplastic Ossification Experiments on Rats.

Transplants (autoplastic unless otherwise stated)	Area of implantation	Supplementary treatment	No. animals	No. Exp.	Animals with cysts	No. instances of ossification
Bladder, segment	Rectus muscle		14	28	9	0
" dome	" "		4	4	3	1
" minced	" "		4	4	2	0
" segment	Peritoneum		2	3	0	0
" "	Spleen		2	2	0	0
" "	Liver		1	1	0	0
" "	Kidney		1	1	0	0
" "	Rectus muscle	1 cc $CaCl_2$ 1½% sub-cu. daily in graft area	8	16	0	1
" "	" "	Ca lactate ½% as drinking water	2	4	1	0
" "	" "	Viosterol 50 × normal conc. daily *per os* 0.1 cc	9	18	7	1
" "	" "	Viosterol 500 × normal conc. daily *per os* 0.1 cc	2	4	0	0
" "	" "	Elementary phosphorus 0.025 mg daily *per os*	2	2	3	1
" "	" "	Elementary phosphorus 0.05 mg daily *per os*	1	2	0	0
" "	" "	Radium emanation seed implanted in one kidney with variable degrees of destruction, elementary phosphorus 0.05 mg daily *per os*; kidney and transplant sites examined	3	6	2	0
Bladder and boiled rat bone	" "		2	4	1	0
Bladder and boiled rat bone	" "	Viosterol 50 × normal conc. daily *per os* 0.1 cc	2	4	1	0
Bladder and boiled beef bone	" "		3	6	3	0
Bladder and $AgNO_3$ crystal	" "		3	5	0	0
Kidney segment	" "		1	1	0	0
" cortex	" "		3	3	0	0
" medulla	" "		3	3	1	0
" pelvis	" "		7	13	3	0
Ureter	" "		5	9	2	0
Boiled rat femur	" "		2	4	0	0
" beef bone	" "		3	6	1	0
$AgNO_3$ crystal	" "		2	4	0	0
Vessels of one kidney ligated			4			1
Dome of bladder removed and replaced by fascia			5			0
Dome of bladder removed, everted and replaced inside out			1			0
Dome of bladder removed, everted and replaced inside out		Elementary phosphorus 0.025 mg daily *per os*	1			0
Totals			102			5

of experiments over number of animals refers to multiple transplants.) Five experiments out of a total of 170 yielded evidence of metaplastic ossification. In each of these the bone was represented by a minute islet only.

Nine guinea pigs of both sexes and from 200 to 350 g in weight were next used for bladder transplants into the rectus muscle. At the end of a month, the animals were sacrificed. In other cases animals were initially sacrificed and their bladders cut up for homoplastic transplantation into 17 others. Takes were comparable in the two groups. Eighteen of the 26 cases manifested ossification at the transplant sites. Five were completely negative. In all 5, epithelium was absent. (It is, therefore, possible that the grafts did not take. This cannot be inferred, however, because bone was sometimes found when epithelium had disappeared.) The 3 remaining presented considerable areas of non-calcified ground substance.

13659

Action of Curare on the Brain of the Frog.

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It is generally accepted that curare action is peripheral. An effect of curare on the brain has been occasionally assumed (Koelliker,[1] Steiner,[2] Meyer[3]), but never demonstrated conclusively.

We have attempted to present a definite proof of a central action of curare by the investigation of electroencephalograms on frogs.

Procedure. Frogs *(Rana esculenta)* were divided into 2 groups. One group was poisoned by curare (injection in the ventral lymph sac). Following this the electrical activity of the brain was investigated. The frogs of the second group were first pithed. After the electrical activity of the intact brain was determined, these frogs were poisoned by curare, and a second determination of the cerebral electrical activity was made. In a separate series of control experiments (12 frogs) it was ascertained that the electroencephalographic

* Aided by a grant from the Dazian Foundation for Medical Research.

† Aided by a grant for apparatus by the Ella Sachs Plotz Foundation.

1 Koelliker, A., *Virchow's Arch.*, 1856, **10**, 58.

2 Steiner, J., *Das Amerikanische Pfeilgift Curare*, Leipzig, 1877, p. 36 f.

3 Meyer, H. H., Gottlieb, R., and Pick, E. P., *Experimentelle Pharmakologie*, Vienna-Berlin, 1936, p. 36.