he lost weight, felt much improved and performed part of his regular work; his blood pressure fell to normal levels. Troublesome pruritus was controlled with an antihistaminic. Seven weeks after the operation his condition deteriorated, as evident from increasing involuntary muscular twitching and beginning mental confusion. The downhill course was temporarily reversed by repeated peritoneal dialyses: each procedure afforded relief for about 2 days. The patient became despondent; dialyses were not repeated and he died.

Comment. The initial clinical improvement of this terminally ill patient (weight of both kidneys at autopsy: 50 g) was evident from the absence of dyspnea and chest pain and gradual disappearance of nausea and vomiting. Clinical deterioration was evident from malfunction of the central nervous system. Clinical improvement or deterioration were not related to changes of weight (*i.e.* edema), blood pressure, hematocrit, or abnormal serum cation patterns. The severity of uremic symptoms paralleled the magnitude of the unknown serum anion moiety.

Discussion. Mechanisms that bring about the typical clinical signs and symptoms of severe uremia will be understood only when the toxic molecules have been identified. It is shown here that true clinical uremia (as distinct from the chemical entity azotemia and from pseudouremic syndromes) was associated with the rise of an unknown fraction of serum anions above a concentration of 25 me/1. The patients described here had nearly normal serum cation patterns; serum phosphate and sulfate were measured and accounted for only a small fraction of the unknown anionic radicals; serum urea varied independently; serum creatinine and uric acid remained highly abnormal but relatively stable. Serum amino acid levels are not known to increase in uremia above 1-2 me/1 (4). The data support the concept that central nervous manifestations of true uremia are caused by unknown anions of low molecular weight.

Summary. In 2 patients the central nervous signs and symptoms of uremia were associated with rising serum levels of unidentified anions, but not with parallel changes of other chemical or physiologic parameters.

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Brain Hormone Activity in *Bombyx mori* of Sterols and Physiologically Vital Active Substances. (28662)

MASATOSHI KOBAYASHI, MIEKO SAITO, YUKIO ISHITOYA AND NOBUO IKEKAWA
(Introduced by W. J. Burdette)
Sericultural Experiment Station, Suginami-ku, Tokyo and Institute of the Physical and Chemical Research, Bunkyo-ku, Tokyo

In the silkworm, *Bombyx mori,* imaginal differentiation is brought about by 2 hormones, one secreted from neurosecretory cells in the brain and the other from glandular cells in the prothoracic gland(1-2) as in other insects(3). Extraction of the hormone from insect brains was first reported by Kobayashi and Kirimura(4). Recently, it was determined that one of the active principles of the brain hormone was cholesterol(5-7). Therefore, considering the importance of sterols as insect hormone, we have investigated the brain hormone activity of compounds known as the steroid hormones in mammalian organisms, of sterols related to cholesterol and of other sterols. Furthermore, the brain hormone activity of some compounds known as physiologically vital active principles

without inclusion of sterols has been studied by the *Bombyx*-test(5-6).

Material and method. 1. The *Bombyx*-pupae of *F.* hybrid between 2 races, *J.* 122 and *C.* 115 were used as material immediately after pupation at 25°C. After maintenance at 2.5°C for several hours to retard circulation of the blood(8), the brain was extirpated from each pupa and the wounded portion was sealed with melted paraffin. The resulting, artificially-diapausing, brainless pupa ('Dauer-pupa') which showed no sign of imaginal differentiation for about 6 weeks was used as test-object of brain hormone activity at 25°C.

2. Assay of mammalian steroid hormone, sterols and other physiologically vital active substances. Each compound shown in Tables I and II was dissolved in 0.002-0.005 ml of ether or methanol and injected into the first abdominal segment of the 'Dauer-pupae' using the dilution method in ranges of 0.02 to 50 μg in the case of C_{27}-, C_{28}-, and C_{29}-sterols. The test-object injected was observed for 30 days at 25°C following injection. Although not indicated in Tables I and II, control studies were carried out simultaneously with the bioassays.

Results and discussion. 1. Brain hormone activity of steroid compounds. The results obtained are presented in Table I. According to Kobayashi and Burdette(9), crude but active extract of the brain hormone has two actions. The first is its tropic action on the prothoracic gland and the second is its direct, synergistic action with ecdysone. The action of cholesterol as one of the active principles of the brain hormone, however, is known only as prothoracotropic hormone upon the *Bombyx*-test of the brain hormone (5-7). Both ovarian hormones, hexestrol and diethylstilbestrol, having either strong estrogenic activity or no sterol ring yielded positive bioassays, even though it is unknown whether the effect of the ovarian hormones derived from strong estrogenic activity (Table I). The corpus luteum hormone, a steroid compound, also has brain hormone activity. However, the threshold amount of the above 3 compounds for induction of imaginal differentiation is not known.

TABLE I. Brain Hormone Activity of Steroids.

Tested compounds		Dose (μg)	Activity
Corpus luteum hormone	Progesterone	.2	+‡
Ovarian hormone (estrogens)	Estradiol	40	—
	Hexestrol	5	+
	Diethylstilbestrol	5	+
Male hormone (androgens)	Testosterone	40	—
Corticosteroids	Cortisone	.2	—
	Corticosterone	40	—
Pregnenolone		.2	—
C_{27}-sterols	Cholestanol	2	+‡
	Cholesterol	.02	+
	Cholesterol acetate	30	—
	7-dehydrocholesterol	10	+‡
C_{28}-sterols	Campesterol	.2	+‡
	Ergosterol	50	—
C_{29}-sterols	Purified β-sitosterol*	20	—
	Commercial β-sitosterol†	2	+
	Stigmasterol	50	—
Bile acids	Cholic acid	.2	—

+, positive; —, negative.

* β-sitosterol contained about 1% of campesterol.

† β-sitosterol contained about 20% of campesterol.

‡ It was confirmed by means of gas chromatogram(10) that the chemical does not contain cholesterol.

C_{27}-sterols related to cholesterol, such as cholestanol and 7-dehydrocholesterol, had brain hormone activity like cholesterol, confirming previous results(5.) Of C_{28}-sterols only campesterol which has one double bond in the sterol ring yielded positive results. C_{29}-sterols without commercial β-sitosterol had no activity, even though commercial β-sitosterol (NBC) showed positive hormonal activity in the previous(5) and present work. The gas chromatogram(10) of commercial β-sitosterol was shown to be associated with campesterol as an impurity (Table I). This was also confirmed by Thompson *et al*(11).

2. Brain hormone activity of physiologically vital active substances. According to our previous report(7), the chemical property of the active fraction other than cholesterol, obtained by means of the counter-current distribution method, was similar to that of other workers' extract(12). We are now studying the separation and purification of the active principle and searching for active

TABLE II. Brain Hormone Activity of Physiologically Vital Active Substances.

Tested compounds	Dose (μg)	Activity
Farnesol	40	—
Squalene	40	—
Ascorbic acid	40	—
Gibberellin	40	—
Thyroxin	5	±
Adrenaline	50	—
Noradrenaline	.5	+
Parotin	60	—

+, positive; —, negative.

substances as a brain hormone without sterols from compounds known as vital active substances.

Noradrenalin yielded a positive bioassay but other substances a negative bioassay, though the result was inconclusive in the case of thyroxine (Table II).

Summary. The brain hormone activity of compounds known as biologically vital active substances in mammalian organisms or in insects was studied by the *Bombyx*-test. Several compounds, such as progesterone, hexestrol, diethylstilbestrol, cholestanol, cholesterol, 7-dehydrocholesterol, campesterol, and noradrenalin yielded positive bioassays.

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Ciliated Epithelial Cells in Normal Murine Intrahepatic Bile Ducts. (28663)

J. W. GRISHAM*† (Introduced by E. L. Alpen)
U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.

Prior to use of the electron microscope, ciliated cells in bile ducts of mammals had not been described(1). In recent studies using this instrument cilia have been noted on epithelial cells of proliferated intrahepatic bile ducts in rats with various experimental alterations(2,3,4) and in human beings with extrahepatic biliary obstruction(3). In these studies ciliated cells were not noted in normal intrahepatic bile ducts although the possibility of their existence was pointed out (3). This report describes the rare occurrences of ciliated cells in small interlobular and intralobular bile ducts of normal adult rats and discusses their possible significance.

Materials and methods. Livers from many untreated normal rats, both male and female, of the Wistar albino strain were examined as controls during many investigations of experimental alterations of hepatic ultrastructure. Small blocks of tissue were fixed in 1% osmium tetroxide in veronal buffer or in Dalton's chromate buffer at pH 7.6. Fixation was carried out at 5°C for 1 hour. Dehydration was accomplished by passage through

* The opinions or assertions contained herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Dept. or the naval service at large.

† Present address: Department of Pathology, Washington University School of Medicine, St. Louis, Mo.