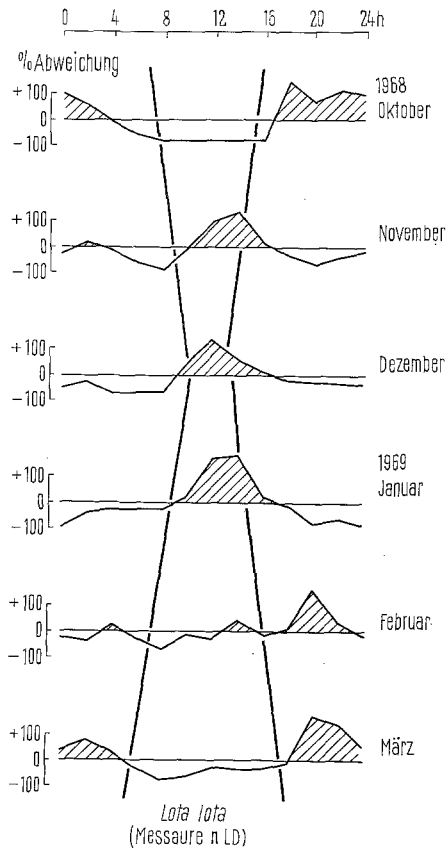


Fig. 1. Die Aktivitätsperiodik der Quappe (*Lota lota* L.) bei natürlichem Licht-Dunkelwechsel (nLD) in Messaure (Schwedisch-Lappland). Darstellung der Monatsmittel vom 1.10.1968–31.3.1969. Abzisse: Tageszeit in Stunden. Ordinate: Prozentuale Abweichung der 2 h-Werte des Monatsmittels vom 24 h-Mittel des Monats.

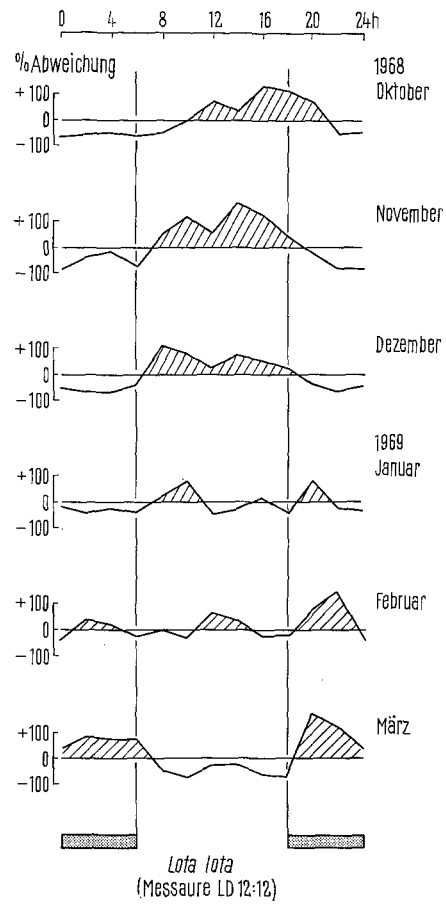


Fig. 2. Die Aktivitätsperiodik der Quappe (*Lota lota* L.) in künstlichem Licht-Dunkelwechsel (LD 12:12) vom 1.10.1968–31.3.1969. Abzisse und Ordinate wie in Figur 1.

	1968						1969		
Monat	Juli	Aug.	Sept.	Okt.	Nov.	Dez.	Jan.	Febr.	März
°C	12,6	11,7	8,1	3,6	2,7	2,0	2,0	1,5	1,5

Dass wir den Phasenwechsel von *Lota lota* im Jahresablauf auch bei künstlichem LD (12:12) nahezu zeitgleich mit dem natürlichen Wechsel der Phasenlage beobachten konnten, spricht für eine endogene, circanuale[8] Jahresperiodik dieser Fischart, d.h. dass die Quappe über eine innere zeitliche Orientierung im Jahreslauf verfügt, wie es an Zugvögeln nachgewiessen werden konnte[9]. Eine zusammenfassende Darstellung der Untersuchungen und Beobachtungen an *Lota lota* ist bei Müller[10] gegeben.

Summary. Investigations on daily rhythm in the burbot (*Lota lota* L.) in the Arctic Circle showed that a phase-shift in the locomotor activity occurred under nLD; the fish, which is night-active in the summer, phase-shifted 180 degrees in relation to the phase-timing factor. This phase-shift was also found in a fish kept in artificial light (LD 12:12) which occurred at almost the same time of year. Accordingly an endogenous circa-annual rhythm is suggested.

K. Müller[11]

Ökologische Station Messaure, S-960 36 Messaure (Schweden), 25. Februar 1969.

[8] K. Immelmann, Studium gen. *20*, 15 (1967).
[9] E. Gwinner, J. Orn., Lpz. *109*, 70 (1968).
[10] K. Müller, Oikos, im Druck (1969).
[11] Die Untersuchungen erfolgten mit Unterstützung der Max-Planck-Gesellschaft zur Förderung der Wissenschaften und des Staatlichen Schwedischen Naturwissenschaftlichen Forschungsrates.

Induced Myotonia in Fast and Slow Muscles of the Rat

In a recent paper[1] we reported that induced myotonia in rats affects the fast-twitch muscles much more than the slow-twitch muscles. This finding is similar to the observation that slow skeletal muscles of the mouse, in contrast to the fast muscles, are relatively resistant to muscular dystrophy[2]. Further studies in our laboratory, however, revealed that after prolonged treatment the slow-twitch muscles can develop a high-degree of myotonia, and that obvious clinical symptoms of myotonia become grossly manifest.

Myotonia was induced in 20-day-old white, male and female Wistar rats with daily s.c. injections (0.2 mg/kg) of 25-azacholesterol. After 5 weeks of injections laboratory evidence of myotonia was clearly established in the anterior tibialis and gastrocnemius muscles of male rats. The soleus muscle of these animals remained completely normal. Electromyographic examination of the fast-twitch muscles showed persistent spontaneous activity and myotonic responses (trains of muscle action potentials oscillating in frequency and amplitude). At the end of this 5-week period clinical manifestations of the disease were not apparent in either the male or female rat.

Female rats treated equivalently showed either very little or no abnormal electrical activity in the fast-twitch muscles. Thus, after the 5-week period of administration of the cholesterol analog only the fast-twitch muscles of male rats develop electrical evidence of myotonia whereas female rats and the soleus in the male remain normal.

When daily injections were continued for an additional 2 weeks the effects were quite striking (see Figure). Clinical symptoms of myotonia became obvious. This was especially so in male rats, resembling those seen in humans. The animals were reluctant to move, ambulation became slow and awkward and limbs were spread far apart. The eyes were usually half closed. The fur, instead of being white, was yellow in color and very shaggy.

Coincident with these symptoms, 2 important factors were observed: (1) female rats which after 5 weeks of treatment showed no spontaneous activity, now were clearly myotonic; (2) the soleus muscles were consistently and strongly affected.

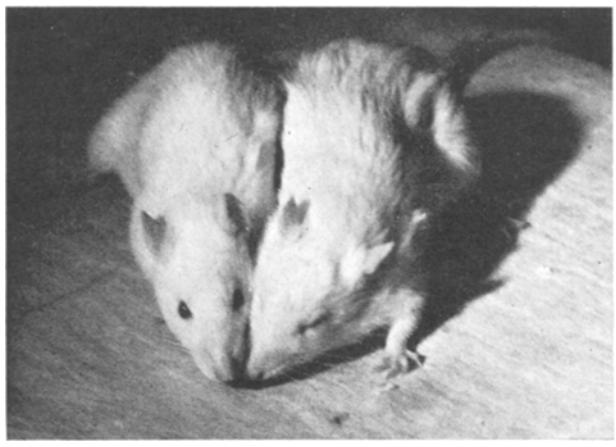
Myotonia was demonstrable electromyographically for about 10 weeks after cessation of drug administration. After 12 weeks the myotonia disappeared. This agrees with Burns et al.[3] who found that myotonia disappeared by the 81st day after termination of diazacholesterol administration in goats.

These results demonstrate conclusively (1) that the fast-twitch muscles develop myotonia earlier than the slow-twitch muscles, (2) that with prolonged drug administration the soleus muscles become as involved as the anterior tibialis, and (3) female rats follow the same delayed time course in developing myotonia as the soleus of male rats.

Although the mechanism by which 25-azacholesterol induces myotonia is not completely understood, an explanation for the difference in myotonic development between red and white muscles may be proposed. Since 25-azacholesterol is a steroid inhibitor of cholesterogenesis, it has been suggested by Winer et al.[4] that myotonia might result from 'the combined effect of desmosterol accumulation and agents with specific structural features, namely, a steroid nucleus with a side chain containing a nitrogen atom at or near a terminal dimethyl or diethyl group'. Winer et al.[4] reported a large accumulation of desmosterol and a reduction of cholesterol in the plasma in the myotonic rats.

A recent paper[5] has shown that rat red muscle contains about 50% more cholesterol and phospholipide than white muscle. Thus the delay in development of myotonia in the soleus may be due to the longer time necessary to change the cholesterol level and/or configuration in the muscle fibers. Similarly, the fact that female rats have higher plasma cholesterol than do male rats[6,7] may explain the longer period of drug administration necessary to induce myotonia[8].

Zusammenfassung. Nach chronischer Applikation von 25-Azacholesterol kann auch in den langsamen Muskelfasern Myotonie erzeugt werden.



Normal (left) and myotonic (right) rat of the same age.

A. Eberstein and J. Goodgold

New York University Medical Center, Institute of Rehabilitation Medicine, New York (N.Y. 10016, USA), 28 April 1969.

1 J. Goodgold and A. Eberstein, Expl. Neurol. *21*, 159 (1968).
2 M. Brust, Am. J. Physiol. *210*, 445 (1966).
3 T. W. Burns, H. E. Dale and P. L. Langley, Am. J. Physiol. *209*, 1227 (1965).
4 N. Winer, D. M. Klachko, R. D. Baer, R. L. Langley and T. W. Burns, Science *153*, 312 (1966).
5 S. D. Froberg, Biochem. biophys. Acta *144*, 83 (1967).
6 L. Aftergood and R. B. Alfin-Slater, Lipid Res. *8*, 126 (1967).
7 L. C. Fillios, Endocrinology *60*, 22 (1957).
8 This work was supported by Public Health Service Grant No. NB 07191-01 and Grant No. 8-0162-814 from the John A. Hartford Foundation. The authors would like to thank G. D. Searle and Co. for supplying the drug used in this study.

Mucosal Growth Effect of Vitamin D on the Duodenum[1]

The biochemical details of the mechanism of action of vitamin D on the small intestinal mucosa are being intensively investigated. A specific metabolite of vitamin D_3, 25-hydroxycholecalciferol has a direct stimulatory effect on small intestinal calcium transport[2]. Vitamin D_3 stimulates template activity of rat intestinal mucosa chromatin[3] as well as synthesis of RNA[4]. A chromosomal receptor for a vitamin D metabolite has been isolated from the chick small intestine[5]. The specific relationship of these findings to a calcium binding protein[6] localized to the luminal border of the intestinal mucosal cell[7] is as yet uncertain. Recently, vitamin D has also been shown