Aurothioglucose Sensitivity of *CBA* Mice injected at Two Different Times of Day

Some years ago Brecher and Waxler[1] described for the first time obesity in mice resulting from aurothioglucose (ATG) injection. Since then it has been found that ATG can cause lesions in different areas of the brain[2–4]. Among these, the lesions in the ventromedian hypothalamic nuclei are held responsible for the observed obesity. However, it was also found that the most effective ATG doses caused a high mortality[5].

As the susceptibility of animals to certain drugs, toxic substances, etc., is well known to be strongly dependent on their diurnal rhythm[6], we have carried out experiments to see to what extent this is true for ATG. *CBA* mice (males and females) were kept under a day–night rhythm of 12 h light (0700–1900 h) and 12 h darkness (1900–0700 h). The ages of these animals varied from 4 to 6 months, that is, they were all full-grown. Two different ATG doses were used (0·4 mg/g and 0·5 mg/g bodyweight) of a 10 per cent ATG suspension in oil ('Solganal *B* Oleosum', Schering). The mice were divided into two equal groups of comparable composition with respect to age and sex. One group was injected during their inactive phase (1200 h), the other group during their active phase (2000 h). All the animals were deprived of food for 3 h immediately before injection. The animals were weighed daily at 0830 h.

The results are summarized in Table 1.

Table 1

Group	I		II	
Time of injection:	Day	Night	Day	Night
ATG dose	0·4 mg		0·5 mg	
No. of animals	19	19	31	31
Weight *a**	21·9	22·2	27·3	25·1
Weight *b*†	32·7	31·6	36·2	33·9
Died	1	0	22	5

* Mean body-weight (g) before injection.
† Mean body-weight (g) 1 month after injection.

These data show that the ATG injection strongly promotes weight increase, considering the fact that the weight of normal mice of the same age increases by only 1–3 g per month. There is also a striking difference in mortality between the 'day' and 'night' animals of group II. Apparently the animals are much more sensitive to the toxic qualities of ATG at 1200 h than at 2000 h. To a much lesser degree this can be found in group I. One of the 'day' animals died, some were sick for some days after the injection, whereas of the 'night' animals in this group none showed any sign of illness. I never observed illness or mortality in animals injected with a dose of 0·3 mg/g mouse (23 animals). In this latter case weight increase is only slightly greater than normal.

From these data it can be concluded that the susceptibility of mice to the toxic effect of ATG clearly depends on their metabolic state. It may be that this decreased susceptibility is comparable with that described after food deprivation[7]. There are no indications that there is a difference in the resulting obesity of the comparable day and night groups.

It is noteworthy that twelve of the twenty-seven animals that died in group II went through a phase (starting about 24 h after the injection and lasting for some hours) of frantic biting. During these hours the tongue is seriously injured and becomes a swollen bloody mass protruding from the month. These animals then stop eating and drinking and die after some days. Whether this frantic biting is an aggressive or an exaggerated feeding activity cannot yet be decided.

What the precise cause of death of all these animals may be is unknown to me, but I now know that ATG mortality can be decreased considerably by injecting the animals at the beginning of their active phase.

Because ATG plays a part in the treatment of, for example, rheumatism and asthma, the findings reported here may also have a medical significance. It would seem important to examine more systematically the effect of drugs, medicines, radiation treatment, etc., in relation to the natural day–night rhythm of the organism treated.

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Haplospora globosa Kjellm. and *Scaphospora speciosa* Kjellm. in Culture

The reproduction and life-cycle of the order Tilopteridales have attracted the interest of phycologists for a long time. Reinke[1] was the first to investigate these problems and, although he was unable to provide any definite evidence, he concluded that the algae in question represent alternating generations of one species, a sporophyte producing non-motile quadrinucleate monospores and an oogamous gametophyte. Reinke's view was adopted by such authorities as Kylin[2,3], Oltmanns[4] and Smith[5], but rejected by Sauvageau[6] and Christensen[7].

Reinke[1], Nienburg[8] and Dammann[9] tried to culture *Haplospora globosa* Kjellm. and *Tilopteris mertensii* (Turn. in Sm.) Kütz. but without great success. In the former species, only germlings from monospores were obtained.

Haplospora globosa is widely distributed on North Atlantic coasts. In the Oslofjord, the *Haplospora* stage as well as the *Scaphospora* stage, originally described as *Scaphospora speciosa* Kjellm., are rather common in spring (Sundene[10]). Specimens of the *Haplospora* stage were collected in May 1964 near the Biological station, Dröbak, in the middle of the fjord, and cultures were established in Erdschreiber at 5° C with daylight. The specimens were fertile, with stalked monosporangia. Monospores were released and some were isolated before settling, while most of the cultures were started from sporelings attached to the bottom of the mother-dishes. The majority of these sub-cultures were contaminated by diatoms, but some

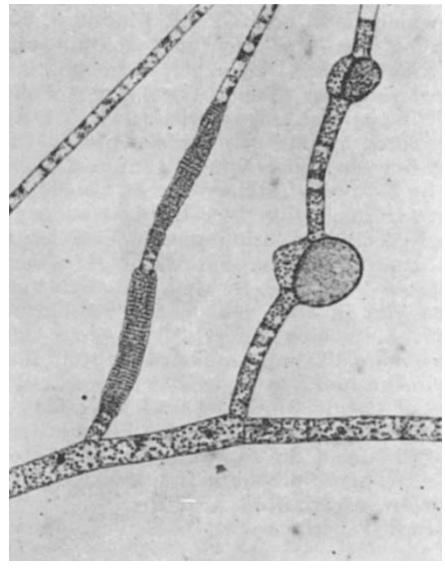

Fig. 1. Branch of the *Scaphospora* stage of *Haplospora globosa* with two antheridia and two oogonia. (× 95)