evidence suggests, however, that Neandertal was replaced by modern man at the peak of the cold phase. Furthermore, we know that modern forms survived through succeeding cold stadia without regaining "Neandertal" morphology, in areas where the exploitation of fish as a food source was unlikely to be a significant source of vitamin D.

Ivanhoe states that "Virchow's original hypothesis can be tested empirically". We claim that it cannot, by the method proposed by Ivanhoe. All the suggested tests can do is to determine the presence or absence of, as well as the severity of damage due to, vitamin D deficiency. This in no way proves that the taxonomic characters of Neandertal man are due to such deficiency. For example, Ivanhoe states that one of the diagnostic characters of rickets in children is "a high bulbous forehead (olympian front)" while the most characteristic feature of Neandertal man is precisely the opposite : a fleeting forehead with the total absence of a bulbous frontal. In so far as the Neandertal child has a more bulbous frontal than the adult, this can be satisfactorily explained from our knowledge of skull ontogeny in man and other higher primates.

Neither does the parallelism between the appearance of Neandertal characters and the Arctic climate prove that the characters are caused by vitamin D deficiency. If the characters of Neandertal man are of adaptive significance, and with Clark Howell[4] we agree that this is so, at least in part, then we can expect them to be correlated with climate and geography, and to become more pronounced as the climate deteriorated. A certain parallelism between the true Neandertal characters and the signs of rickets, thus, is not unexpected.

In spite of rickets and arthritis, the morphology of Neandertal man can be clearly recognized and interpreted as a harmonious functional adaptation to the environment in which he lived.

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Received November 5, 1970.

[1] Ivanhoe, F., *Nature*, **227**, 577 (1970).
[2] Virchow, R., *Z. Ethnol.*, **4**, 157 (1872).
[3] Straus, W. L., and Cave, A. J. E., *Quart. Rev. Biol.*, **32**, 348 (1957).
[4] Clark Howell, F., *Quart. Rev. Biol.*, **32**, 330 (1957).

Effect of Ethoxyquin on the Longevity of C3H Mice

SEVERAL workers have found that mice fed diets containing large amounts of added antioxidant live longer than those fed standard laboratory diets. The size of the effect varies with the substance added, but it has been obtained with a wide variety of agents, including α-tocopherol, 2-mercaptoethylamine, ethoxyquin, *tert*-butyl hydroxytoluene (BHT), dithiocarbamates[1,2] and (in rats) nor-dihydroguaiaretic acid[3]. These studies were prompted by the suggestion of Harman[4] and of other workers[5,6] that both natural and radiation-induced ageing may involve oxidative free radical attack on long term molecules or on lipids[6], including those of mitochondria[7,8].

In the course of antioxidant screening studies we have observed a lifespan effect in C3H mice of both sexes receiving ethoxyquin in a standard pellet diet. Forty male and forty female 3 month old C3H mice, bred at the National Institute of Medical Research, were assigned randomly in equal numbers to control and antioxidant-supplemented groups, caged by tens with sexes separated, and kept in life table conditions, that is weighed monthly but subjected to no other manipulations.

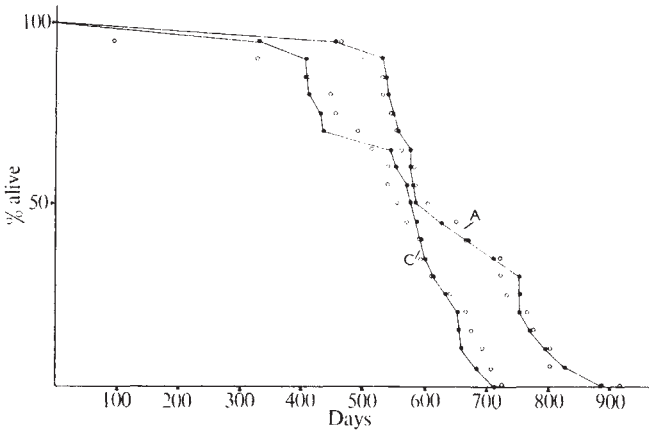

Fig. 1 Survival curves for mice on diet containing antioxidant (A) and on control diet (C). ●, Males; ○, females.

Control mice received a standard pellet diet ('Oxoid 41 B'), and treated mice received a diet of identical pellets moistened and reconstituted with 0.5% w/w ethoxyquin oil ('Santoquin', Monsanto), both given freely.

There was no sex difference in survival in either group, but survival curves for both sexes differed significantly in favour of the treated groups ($P < 0.005$, on a ranking test computed by Mr Peter Fayers, of the MRC Statistical Unit) with a curve displacement of about 100 days (Fig. 1). Tumour incidence in both treated and untreated groups seemed to be low for the strain. Mean expectations of life with standard errors and limit are given in Table 1.

Table 1 Longevity of C3H Mice on Standard Diet and Diet plus 0.5% w/w Ethoxyquin

	Control			Ethoxyquin	
♂	551.6±24.7	(711)	♂	651.5±27.3	(887)
♀	541.4±33.3	(722)	♀	649.4±27.4	(907)

Values are mean, s.e. and limit (days). n=Twenty per group.

Mice of both sexes fed antioxidant grew into significantly lighter adults than did controls, and lost weight earlier (Table 2). Activity and condition were strikingly better retained with age in the treated series. Pathological studies on a parallel series will be reported later.

Increased longevity in mice fed antioxidant is compatible with, but does not demonstrate, the hypothesis of free radical ageing. In the converse experiment, Gerschman[9] found a decrease in mouse lifespan when oxygen tension was greater than 1 atmosphere, the effects being reversed by the administration of diethyl dithiocarbamate or Co^{2+} (ref. 10). In acute experiments, mice deficient in α-tocopherol increased in sensitivity to oxygen[11,12]. Sobel[13] failed to shorten life by intermittent exposure to 1.08 atmosphere of oxygen during youth and early adulthood.

In the antioxidant feeding experiments so far reported, alternative explanations are at least equally likely. None of the published survival curves, including our own, were obtained in a special purpose lifespan colony. The maximum lifespans obtained with antioxidants are within the recorded natural performance of the strains, and the increments are smaller than those regularly obtainable by calorie restriction.

Among alternative explanations, it could be suggested (1) that large amounts of chemicals hinder assimilation or spoil the appetite of mice, in the absence of strict pair-feeding measurements, and the effect may be due to covert calorie restriction; (2) that for mice, as for broiler fowls[14,15], excess antioxidant merely reduces the toxicity of a "normal" laboratory diet[2]; (3) that (according to unpublished studies by R. B. Cumming) many antioxidants, especially BHT, are powerful enzyme

Table 2 Weights of C3H Mice on Control (C) and Antioxidant-containing (A) Diets (Gm)

	97	125	197	248	310	409	533
♂ C	25.4±1.86 (22–30) n=20	27.7±2.62 (23–31) 20	31.9±2.84 (29–36) 20	32.6±2.64 (29–34) 20	30.5±1.73 (26–33) 20	30.5±2.12 (26–32) 19	29.2±3.04 (26–31) 13
A	26.0±1.79 (23–29) n=20	28.3±2.11 (25–34) 20	28.9±2.29 (25–36) 20	27.9±2.44 (24–34) 20	25.2±2.72 (22–29) 20	26.3±2.87 (22–30) 20	26.0±3.04 (22–36) 19
♀ C	20.2±1.30 (18–23) n=20	22.1±1.70 (20–25) 20	26.8±2.59 (22–31) 19	28.7±3.15 (24–33) 19	27.3±3.03 (23–33) 19	26.6±3.45 (21–31) 18	25.9±2.99 (25–32) 13
A	20.9±2.27 (16–28) n=20	22.3±1.78 (20–28) 20	24.4±2.37 (21–29) 20	24.1±2.05 (22–28) 20	20.6±2.04 (18–25) 20	21.0±2.51 (17–25) 20	20.3±1.78 (17–24) 18

Values are mean, s.d. and range.

inducers—ethoxyquin in these doses causing marked liver enlargement[16]: in Ross's experiments, hepatic enzyme concentrations were found to correlate strongly with further rat life expectancy on various diets[17]; (4) that with the doses used a hypothesis of straightforward "chemical stress", with or without suppression of a predominant tumour, is a feasible cause of longer gross survival. None of these possibilities has been excluded. Experiments with other potent enzyme inducers, such as DDT or barbiturates, seem to be necessary.

The form of the curves, and their response to a mortality incident affecting all groups after between 500 and 600 days, which was probably infective or environmental, would be consistent with a postponement of some predominant age-dependent process by about 15%, rather than with the suppression of one incidental cause of senile mortality. Non-actuarial indices of ageing (pigment deposition, tumour incidence) remain to be examined and will be reported later. We wish, however, to confirm the existence of the effect in a strain previously reported to be unaffected by antioxidants[18].

The Research Group was maintained by the Medical Research Council. We thank Monsanto Ltd for samples of 'Santoquin'.

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Received October 14, 1970.

1 Harman, D., *Gerontologist*, **8**, 13 (1968).
2 Harman, D., *J. Gerontol.*, **23**, 476 (1968).
3 Buu-Hoi, N. P., and Ratsimamanga, A. R., *CR Soc. Biol.*, **153**, 1180 (1959).
4 Harman, D., *J. Gerontol.*, **11**, 298 (1956).
5 Tappel, A. L., *Geriatrics*, **23**, 97 (1968).
6 Dormandy, T. L., *Lancet*, ii, 684 (1969).
7 Marco, G. J., Machlin, L. J., Emery, E., and Gordon, R. S., *Arch. Biochim. Biophys.*, **94**, 115 (1961).
8 Tappel, A. L., and Zalkin, H., *Arch. Biochim. Biophys.*, **80**, 333 (1959).
9 Gerschman, R., *Proc. XXI Intern. Cong. Cienc. Fisiol.*, Buenos Aires 1 (1959).
10 Gerschman, R., Gilbert, D. L., and Caccamise, D., *Amer. J. Physiol.*, **192**, 563 (1958).
11 Taylor, D. W., *J. Physiol.*, **140**, 37 (1958).
12 Gerschman, R., Gilbert, D. L., Nye, S. W., and Fenn, W. O., *Fed. Proc.*, **14**, 56 (1955).
13 Sobel, H., *Aerospace Med.*, **41**, 524 (1970).
14 Machlin, L. J., and Gordon, R. S., *Proc. Soc. Exp. Biol. Med.*, **103**, 659 (1960).
15 Machlin, L. J., *J. Amer. Oil Chem. Soc.*, **40**, 368 (1963).
16 Wilson, R. H., *J. Agric. Food Chem.*, **28**, 375 (1956).
17 Ross, M. H., *J. Nutrit.*, **97**, 565 (1969).
18 Harman, D., *J. Gerontol.*, **12**, 257 (1957).

Stimulation by Artificial Lighting of Calcium Absorption in Elderly Human Subjects

VITAMIN D, the "sunshine vitamin", is produced in the skin when ultraviolet radiation is absorbed by the pro-vitamin 7-dehydrocholesterol[1]. The endogenous vitamin, together with dietary vitamin D, is then apparently converted in the liver to 25-OH vitamin D, and this active metabolite facilitates the intestinal absorption of calcium and the uptake and release of calcium by the skeleton[2,3].

The amounts of vitamin D usually produced in the intact human skin are unknown. Ultraviolet irradiation of the skin cures childhood rickets[4–7]; in this case endogenous production must be at least equivalent to the minimum curative dietary dose of 200–400 IU daily[8]. Extrapolation of these results to adults is difficult, because their dietary requirement for vitamin D is not established[8]. But there is indirect evidence, summarized by Loomis[9], that the production of vitamin D induced by ultraviolet light is important in the skin.

Ordinary window glass absorbs essentially all radiation of the wavelength necessary for this *in vivo* synthesis—between 275 and 310 nm—of vitamin D[4–7]. Millions of people work behind glass, underground or in the extreme north, travel to and from work in closed vehicles, and venture outdoors only in the early morning or late evening, when ultraviolet radiation is minimal[10]. Incandescent bulbs emit little ultraviolet radiation; the small amount from ordinary fluorescent bulbs is usually absorbed by the fixtures in which they are mounted. We have examined changes in calcium absorption after exposure to 'Vita-Lite' (Duro-Test Corporation, North Bergen, New Jersey), a commercial fluorescent lamp of conventional geometry and loading, designed to duplicate Sun and sky radiation at a colour temperature of 5,500 K (CIE D-5500). About 5% of its total radiant power lies at wavelengths between 290 and 380 nm. Our data suggest that illumination which simulates natural light significantly increases the efficiency of intestinal calcium absorption in people who receive no ultraviolet light from the Sun.

Eighteen white, male residents of the Chelsea Massachusetts Soldiers' Home were selected on the basis of ability to cooperate, age (57–80) and freedom from significant disease. All studies were done with their voluntary consent.

From December 20, 1968, to April 25, 1969, subjects were asked to stay indoors and away from open windows during daylight. Men who normally took multivitamin preparations containing vitamin D were given a substitute lacking this vitamin. Their normal diet contained restricted types of seafoods. They were asked to maintain their habitual intakes