

Comparison of experiments on the effect of antibiotics, cysteamine and bone-marrow transplantation on oral lesions and mortality

Number of animals	Doses (rad)	Antibiotics	Cysteamine	Bone-marrow	% of oral lesions	% of healing	% of mortality
22	800	x			0	—	0
10	1000	x			0	—	0
10	1500	x			0	—	100
10	1000		x		30	100	0
9	1000			x	89	75	22
22	800	control	control	control	86	5	82
10	1000	control	control	control	100	0	100
10	1500	control	control	control	100	0	100

with 20 mg daily of chlortetracycline and chloramphenicol. This combination of antibiotics was selected by means of an antibiotic sensitivity test of the bacterial flora found in ulceronecrotic lesions of whole-body irradiated hamsters. Irradiation with 800, 1000 and 1500 rad in antibiotic-treated animals did not produce oral lesions. Similar doses in control animals produced oral lesions in 86 to 100% of the animals. Mortality 30 days post-irradiation was 0% in antibiotic-covered animals irradiated with 800 and 1000 rad; over 80% of non-treated controls irradiated with the same doses died within 30 days. 100% of both groups (antibiotic-covered and non-treated controls) irradiated with 1500 rad died within 30 days. This seems to indicate that over a certain dose the antibiotic is no longer effective in reducing mortality produced by irradiation but it still protects against oral lesions, even in lethal doses of irradiation.

β -Mercaptoethylamine (cysteamine) in doses of 150 mg/kg body weight, by intraperitoneal injection, reduces oral lesions resulting from total body irradiation by 70% (100% of control group presented lesions). All lesions in protected animals healed, whereas none healed in the control group. No mortality was observed in protected animals; control group mortality was 100%.

Transplantation of homologous bone marrow was done by injecting intravenously $12.5 \cdot 10^6$ cells 24 h after irradiation. Oral lesions appeared in 89% of the animals but a great tendency to healing (75% of cases) and low mortality after 30 days (22%) were noted.

In summary, analysis of the above-mentioned experiments indicates that the use of antibiotics is the most effective means of controlling ulceronecrotic oral lesions induced by irradiation as well as of obtaining a greater survival time. Less effective results were obtained with cysteamine. Bone marrow transplantation in the doses used does not impede oral lesions but does seem to accelerate healing. These data appear to point to a major role of the bacterial factor in the lesions studied⁴.

Zusammenfassung. Es wurde der Einfluss von Antibiotica, von homologem Knochenmark und von Cysteamin in der Entwicklung der im Munde des *Mesocricetus aureatus* durch totale Bestrahlung des Körpers produzierten nekrotischen Ulcera studiert. Es ergibt sich, dass bei den untersuchten Läsionen der bakterielle Faktor eine wichtige Rolle spielt.

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⁴ The authors wish to acknowledge the generosity of Lepetit Argentina S.A., who provided an ample supply of the antibiotic used.

Gametes and Senescence

We have been able to observe, tentatively, since 1957¹⁻³ that the male gamete seems to be capable of elaborating one or more biologically active substances, which, in some, cases, appear to exert some effects on the dysfunctions normally occurring – at an individually variable age – in the second half of mammalian life (so-called 'senescence' phenomena).

Since each species has its characteristic signs of senility, and in view of the individual variability and the well-known heterochronia of such alterations, it seemed preferable to analyse only one of the more frequent structurally 'irreversible changes', in a suitable experimental animal.

We have chosen for this purpose the senile cataract of the dog. It is well known that this 'irreversible' alteration

of the lens is among the significantly prevalent (usually after dental decay) signs of senility for this particular species, and in which therapeutic or spontaneous reversions are uncommon.

Crystalline opacity can easily be recorded by means of slit-lamp photography. We have adopted the method and apparatus of DUGNANI⁴.

¹ G. FACHINI, Riv. Idrobiol. 2, 11 (1960).

² G. FACHINI and G. GIANFRANCESCHI, Atti Acc. Med. Piacenza, Meeting of December 13 (1961).

³ G. FACHINI et al., Nature 199, 195 (1963).

⁴ E. DUGNANI, Klin. Monatsbl. Augenheilk. 134, 674 (1959). Photos have been kindly prepared by Dr. E. DUGNANI, Ophthalmological Division, Civil Hospital, Varese.

Our trials were carried out with (A) whole dog's semen or homogenates of centrifuged nemasperm; (B) concentrated extracts of bovine nemasperm (partially obtained by the technique described previously³).

Results, which must be considered approximate, are summarized in the Table. It is important to underline the fact that the effects are far from being constant. No explanation can be given of these inconsistencies at this time.

Effects of nemasperm homogenate or extracts on lens opacity in cataracta senilis of the dog, expressed as % reduction of the opaque surface

Type of extracts	Approximate % reduction of the opaque surface of the lens, roughly evaluated by projection on the frontal plane of the lens (average of 8 eyes each)
(A)	10-20
(B)	30-40

Slit-lamp photographs of the opaque lens, before and after the administration of the extracts, are presented in Figures 1 and 2 (see legend). The mean single dose is equivalent to 3 ml for (A) and 80-100 ml for (B), expressed in terms of whole seminal fluid. Each dose was usually administered daily, for 3 consecutive days.

Up to this time, the maximum duration of the remission recorded (i.e. the delay between treatment and reappearance of the opacity) is about 13 months.

Similarly, the active principle (s) from the gamete seems to possess an inconstant activity in causing something that may be described as temporary reversion in some other structures or functions which are also subject to senescent changes in the same animal (dental apparatus, muscles responsible for maintaining postural tonus, hair, vascular system, etc.). The exact evaluation of such effects, however, is obviously difficult since, as mentioned above, they are inconstant.

It may be of interest to recall that the homogenate, or active fractions, display a constant pituitary-inhibiting

action - perhaps due, at least partially, to the natural steroid content of the semen⁸.

Reference may also be made, for the purpose of analogy, to the data of STEINACH (1904-1920) and VORONOFF (1916-1925), relating to the effects of vasoligature, or testicular grafts, respectively, on senescent changes, including ocular signs. We wish to recall, on this latter point, the critical review of SIEGRIST⁵, where he stated that 'slit-lamp observations were never performed'.

From a general point of view, it seems not unfeasible to describe the effects as a partial homeostatic action directed towards maintaining the stable phase of a dynamic equilibrium, having temporarily converted it from a metastable phase.

Other preliminary data^{1,2,6} have led us to suspect that such an apparent action on the chronological sequence of the biological events may be, among others, one of the very complex non-sexual, para-gamic functions of the gamete, considered as a storage of information^{7,8}.

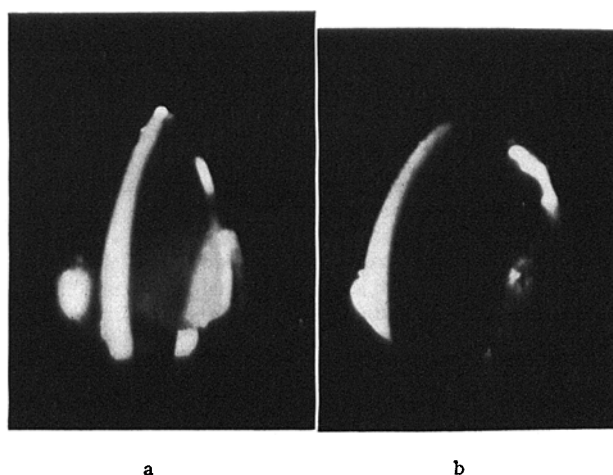


Fig. 2. Same type of photo as in Figure 1; dog aged 15 years. Cataracta senilis of about 12 months' standing; less severe than case 1. One day before (a) and 4 days after (b) the administration of the same type and dose of extracts as in case 1 (Dr. E. DUGNANI).

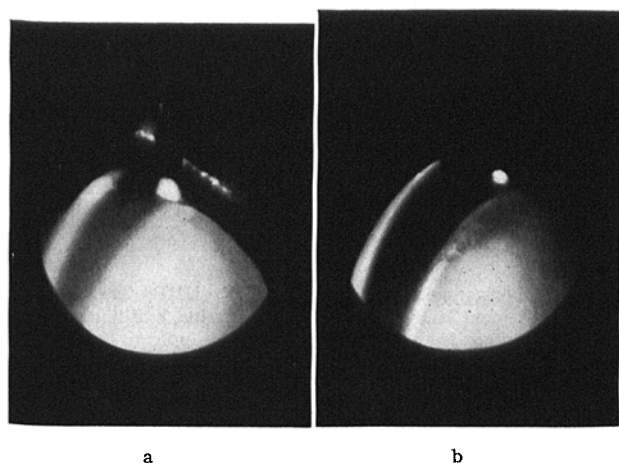


Fig. 1. Slit-lamp photographs of the opaque lens (cataracta senilis) in a dog 16 years old. Bilateral cataract, of at least two years' standing. Dog is practically blind. One day before (a) and 4 days after (b) the administration of the type B extracts; 3 ml for 3 consecutive (see text) (single slit lamp) (Dr. E. DUGNANI).

Riassunto. La somministrazione parenterale di materiale seminale intero omologo, o di omogenati di nemasperma; o di estratti deproteinizzati di omogenati di nemasperm eterologhi sembra poter indurre, in taluni casi, reversioni di variabile entità e durata nella cataratta senile del cane, per quanto concerne almeno la opacizzazione corticale.

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⁵ A. SIEGRIST, *Der Altersstar* (Urban und Schwarzenberg, Berlin 1928).

⁶ G. FACHINI and G. GIANFRANCESCHI, in press.

⁷ Some preliminary data seem to suggest that the same action can be expected from the female gamete.

⁸ We are deeply indebted to Prof. F. TOFFOLI, Istituto Superiore di Sanità, Roma, and Dr. M. MARABELLI for their collaboration in the preparation of the extracts. We also thank Drs. LEGORI, Melegnano, and LORETI, Luino, and Mr. G. F. NERI, Milano, for their valuable help in the collection of bovine semen.