voque, à doses plus élevées, une paralysie dont les caractéristiques sont essentiellement celles d'une curarisation compétitive survenant chez un animal dont les cholinestérases sont inhibées.

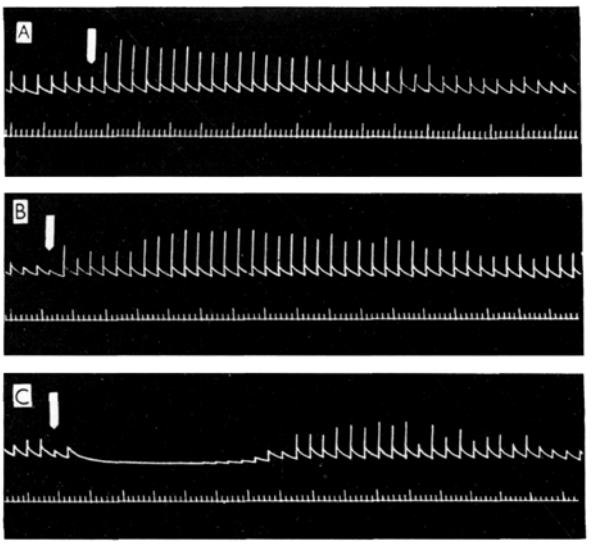

Fig. 4. *Action de l'acétylcholine sur la paralysie par le 3318 CT.* – Chat, 3,5 kg, chloralosé et atropinisé (expérience du 3 septembre 1953). L'animal a reçu deux injections successives de 0,7 mg/kg de 3318 CT qui ont déprimé les contractions de plus de 75%. En *A*: Chlorhydrate d'acétylcholine 0,1 mg/kg i.v.; en *B*: Chlorhydrate d'acétylcholine 0,2 mg/kg i.v.; en *C*: Chlorhydrate d'acétylcholine 0,5 mg/kg. i.v.

Ces observations attirent l'attention, une fois de plus, sur le fait qu'une paralysie neuromusculaire par un anticholinestérasique puissant ne résulte pas nécessairement d'une accumulation d'acétylcholine: le cas du 3318 CT pourrait paraître particulier parce que cette substance est caractérisée par la présence, dans la molécule, de deux fonctions ammonium quaternaire, c'est-à-dire par un facteur structural considéré comme favorable au développement d'une activité curarisante; on peut cependant en rapprocher le cas de l'ésérine, de structure très différente, et qui, selon FATT et KATZ[1], aurait une action curarisante indépendante d'une accumulation d'acétylcholine; au demeurant, il est loin d'être certain que l'inhibition de WEDENSKY provoquée par le T.E.P.P. ou le D.F.P. soit en relation avec l'inhibition des cholinestérases (BERRY et EVANS[2]).

D'autre part, l'inefficacité de la prostigmine sur la transmission neuromusculaire du chat traité par le 3318 CT contraste avec l'activité sensibilisante qu'exerce la prostigmine sur la transmission vagale du chien injecté de doses élevées (1 à 5 mg/kg i.v.) de 3318 CT; cette différence de comportement entre les deux transmissions est, certes, d'interprétation délicate; cependant, on ne peut s'empêcher de la rapprocher de l'opposition existant entre la faible teneur en XChE des muscles striés et la forte concentration en XChE des organes à innervation parasympathomimétique (ORD et THOMPSON[3]); on serait alors tenté d'attribuer l'activité sensibilisante vagale de la prostigmine après 3318 CT à l'inhibition des XChE.

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Laboratoire de pharmacologie, Service de chimie thérapeutique de l'Institut Pasteur, Paris, le 22 juillet 1954.

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Summary

3318 CT [bis (piperidinomethylcoumaranyl-5) cetone dimethiodide], a specific inhibitor of acetylcholinesterase, antagonizes, in small dosages, the neuromuscular block induced by Flaxedil in the cat; in larger dosages, 3318 CT blocks the transmission: this paralysing action is not related to an accumulation of acetylcholine, as acetylcholine itself antagonizes it; decamethonium also restores, partially at least, the indirect contractions. Prostigmine and m-hydroxyphenyltrimethylammonium have no action. The neuromuscular block by 3318 CT thus appears as a competitive curarization in an animal with inhibited acetylcholinesterases. There was no indication that pseudo-cholinesterase can play a part in the neuromuscular transmission; whereas in the case of the vagal transmission such a possibility could not be ruled out.

L'acide borique, inhibiteur de la copulation gamétique chez *Allomyces*[1]

Lors de nos précédentes recherches sur la relation carotène-sexualité chez *Euallomyces javanicus* KNIEP[2], nous avions éprouvé quelque difficulté à maintenir le champignon dans sa phase gamétophytique pure. En effet, la moindre eau de condensation à la surface de l'agar nutritif favorise la libération des gamètes mâles et femelles, leur copulation subséquente et, ainsi, l'apparition de plages de nature sporophytique. Pour tourner cette difficulté, nous avons recherché un inhibiteur chimique de la copulation gamétique, de toxicité faible, voire nulle, à l'égard de la croissance gamétophytique.

Nous avons trouvé que l'adjonction d'un minuscule cristal d'acide borique à une suspension de gamètes mâles et femelles dans une goutte de solution tampon phosphate neutre diluée empêche toute copulation des gamètes. Dans un tel milieu, les gamètes femelles présentent un curieux phénomène d'agglutination en groupes compacts animés d'un constant mouvement vibratoire. Les gamètes mâles, par contre, conservent une autonomie relative. Après 4 h de séjour en chambre humide, les gouttes témoins présentent de nombreux zygotes alors qu'aucune cellule biflagellée et caroténifère ne peut être repérée dans les gouttes boriquées. Après 12 h, les groupes de gamètes femelles manifestent encore leur vibration caractéristique.

Nous avons mis à profit ces observations sur l'action anticopulatrice de l'acide borique en cultivant la phase gamétophytique d'*Allomyces javanicus* sur milieu gélosé à base d'amidon et d'extrait de levure[3] additionné de diverses concentrations d'acide borique. A la dose de 1/15 000, cet acide ne perturbe ni la croissance, ni la pigmentation normales d'*Allomyces* et permet le développement d'une phase gamétophytique exempte de sporophyte. Nos recherches se poursuivent en vue d'adapter cette méthode d'inhibition à la culture en milieu liquide de la phase sexuée d'*Allomyces*.

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Institut de botanique générale, Université de Genève, le 8 août 1954.

[1] Communication annoncée mais non présentée au VIII[e] Congrès international de Botanique, Paris 1954.
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Summary

Addition of a tiny crystal of boric acid to a drop of buffered water containing male and female gametes of *Euallomyces javanicus* completely inhibits copulation in this water mold.

Pure gametophytic growth can thus be secured by addition of 1/15,000 boric acid to the starch-yeast extract medium.

The Experimental Induction of Pseudogamy in Early Mouse Embryos

Pre-fertilisation treatments which eliminate the sperm or the egg chromosomes have long been known to produce gynogenetic or androgenetic development respectively in Amphibian embryos[1]. Treatment of the sperm is of two kinds: by irradiation[1] using radium, ultra-violet, or X-rays; or by chemicals[2], e.g. trypaflavine and toluidine blue[3]. Few attempts to reproduce the Amphibian results in the Mammalia have as yet been made. Ultra-violet irradiation of rabbit sperm by PINCUS and ENZMANN[4] and by BEATTY and SELMAN (unpublished), and X-irradiation of similar material by AMOROSO and PARKES[5], severely affected fertilisation and early cleavage. Both PINCUS and ENZMANN[4] and AMOROSO and PARKES[5] inferred the induction of gynogenesis from their histological examination of the fertilized eggs. In addition, haploid blastocysts are known to occur in the mouse both spontaneously in stocks giving a high incidence of heteroploid (chiefly triploid) embryos[6], and also following colchicine treatment at fertilisation designed to induce triploids[7].

Experiments have been carried out using the mouse (*Mus musculus*) to investigate further the possibilities of causing haploid gynogenetic development in a mammal. Treatment of the mouse sperm was made on the lines previously successful in the Amphibia[8]: two being chemical treatments using trypaflavine and toluidine blue, and two irradiations by ultra-violet or X-rays. Three and a half days after artificial insemination with treated sperm, the developing embryos and the unfertilised eggs were washed from the uterus of the inseminated females. The embryos were squashed and stained, and chromosome counts made (to an accuracy of $\pm$ 5% of the total chromosomes) on the mitotic figures found. Typically the untreated mouse embryo is a blastocyst at three and a half days development.

Irradiation of the sperm by ultra-violet or X-rays produced a series of abnormal embryos. Three criteria were used to judge these embryos: their stage of development as shown by their nuclear number, their chromosome count, and their cytological appearance. With both irradiations nuclear number was inversely correlated with dosage up to the highest used (1·6 Joules per cm^2 between wavelengths 2100–3200 A°, and 50,000r respectively on the surface of the sperm suspension), though the X-rays gave a more uniform effect than the ultra-violet. The high dosages restricted development to the first cleavage division. Chromosomally, the X-rays produced a series of embryos which showed a gradual reduction from the diploid (i.e. 40) to the haploid complement with increasing dosage, this reduction being probably the result of an increasing inactivation of the sperm chromosomes by the X-rays. The ultra-violet, on the other hand, produced two different kinds of development over a wide range of dosages, one being diploid or near-diploid and the other haploid or near-haploid; a result which suggested an all-or-none response to the ultra-violet by the sperm chromatin. Most of the near-diploids were hypo-diploid by a few chromosomes. Cytologically, in addition to apparently normal nuclei, many embryos contained very small nuclei which, together with evidence of contracted and lagging chromatids, indicated mitotic irregularities during development. These cytological defects were probably the result of damage to the division centre or chromosomes of the sperm by the irradiations, and may be the cause of the hypo-diploid embryos obtained from the ultra-violet.

Trypaflavine treatment of the sperm at first suggested a HERTWIG effect[1], for at a concentration of 1/10,000 one haploid blastocyst and one triploid embryo were obtained among several diploids. But the haploid, taken from a female possibly heterozygous for the silver factor, could have been of spontaneous origin[2]. With both trypaflavine and toluidine blue two distinct kinds of development were induced; one kind was similar to controls in the stage of development reached, the other was highly retarded. All the classifiable normal embryos were diploid with the exception of the haploid and triploid mentioned previously.

The haploid and near-haploid embryos obtained from the irradiations were presumably gynogenetic in origin. All had low cell numbers when compared to controls, and were developing with difficulty. The retarded embryos from the chemical series were similar to those produced by the high irradiation dosages and by analogy with them are probably also gynogenetic. It is evident that haploid gynogenetic development in the mouse produced by these treatments is qualitatively different from that induced in the Amphibia[3] where gynogones often develop to metamorphosis; and as the results given here are closely comparable to the previous results from the rabbit[4], it appears that haploid gynogenesis in the Mammalia is highly abnormal and probably confined to the early cleavage stages.

In contrast to the retarded appearance of the haploids obtained from the irradiation series, the single haploid blastocyst obtained from the trypaflavine treatment, the haploids obtained from the colchicine treatment[5], and the spontaneous haploids[6] all appeared healthy and had cell numbers closely comparable to their diploid sibs. The contrast between the two types of haploid is even more marked when the other classes of heteroploid embryos accompanying the haploids are examined. The trypaflavine, colchicine, and spontaneous haploids occur often with triploids, whereas no triploids occur in the irradia-

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