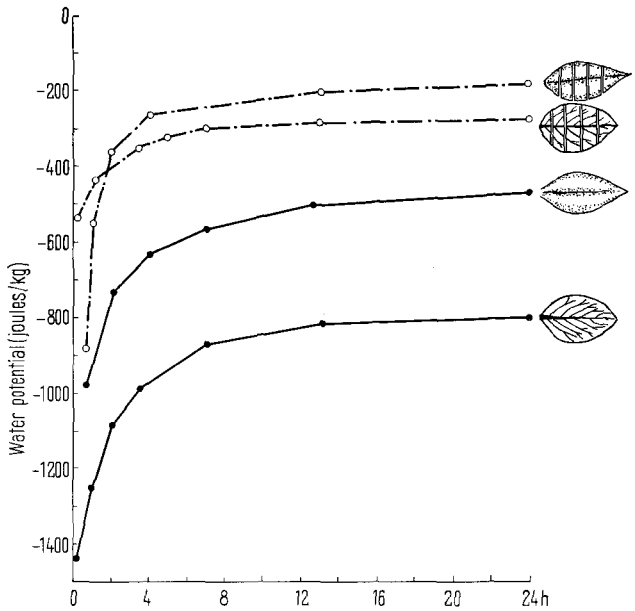

Effect of the excision of leaf tissues on the measurement of their water potential with thermocouple psychrometer 4–24 h after putting leaf material in constant temperature water bath.

were made throughout the period of equilibration and are presented in the Figure.

The results show that, in both the species, comparatively much higher water potential was recorded in the case of cut-leaf material than the uncut material and that the leaf-water potential of the two species, although growing under similar moisture conditions, were different from each other. These observed higher water potential values of the cut-leaf tissue were in contrast to the expected decrease since: (1) The excision of the leaf tissue results in the partial destruction of the cell turgor pressure. For water potential = osmotic potential + turgor pressure (where osmotic potential is negative and turgor pressure positive), the decrease in turgor pressure should obviously result in lower water potential of the excised leaf tissue. (2) The excision of the leaf material increases its rate of respiration. Increase in rate of respiration in turn should also deploy some extra energy from this leaf tissue, consequently further lowering its water potential. Although much further work is needed to explain these findings, it may be mentioned that the results assume special significance when using the thermocouple psychrometric technique for measuring the water potentials of leaf tissues.

Résumé. Le potentiel d'eau, mesuré dans un psychromètre à thermocouple, se révèle être plus haut dans les feuilles coupées que dans les feuilles intactes.

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Carcinogenesis and Regeneration in Newts

The concept of a definite relationship between neoplastic growth and organized development, as envisaged by WADDINGTON[1] and by NEEDHAM[2], has led several investigators to applying these ideas to the problem of regeneration in amphibians. Especially successful were the recent studies of SEILERN-ASPANG and KRATOCHWILL[3], who have shown that chemically induced epitheliomas often show regression and differentiation into non-malignant tissues when a regeneration process is initiated in the organism by amputating a limb or tail. The phenomenon seems to indicate that in periods of intensive secondary development, i.e. regeneration, the organism has an increased capacity to convey developmental information to its undifferentiated cells, converting those with malignant tendency to normal tissues.

We are in a position to contribute data to this concept. Experiments made at Fordham University to test the effect of carcinogenic hydrocarbons (1, 2, 5, 6-dibenzanthracene and 3-methylcholanthrene) on tail regeneration in the newt *Triturus* (*Diemictylus*) *viridescens* failed to produce typical tumours, either epitheliomas or sar-

[1] C. H. WADDINGTON, Nature *135*, 606 (1935).
[2] J. NEEDHAM, Proc. R. Soc. London *B 29*, 1577 (1936).
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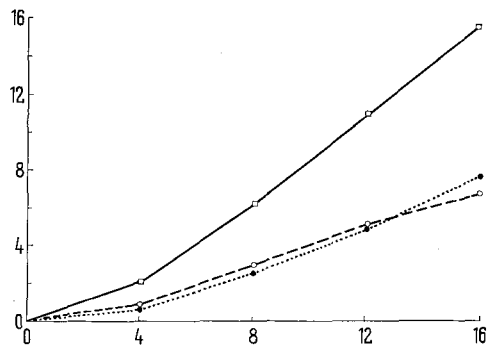
comas, in a great number of specimens, the tail of which was partly removed a week before the administration of the carcinogens. There were occasional temporary thickenings of the epidermis at the site, where the carcinogens were injected but they did not persist or grow. Such local proliferations of the epidermis without spreading cannot be considered as a sure sign of incipient carcinogenesis in newts since this tissue is known to show excessive growth when and where it is injured. This, in fact, plays a role in regeneration processes and in tissue transplantation. We have never observed the characteristic cell proliferation in the epidermal mucus glands, described by SEILERN-ASPANG and KRATOCHWILL as a sign of invasive neoplastic growth. Our negative results were disappointing at the time since by then several investigators have reported successful carcinogenesis with the same chemicals, which we have employed[4]. But in the light of the findings of the Austrian investigators the negative results become understandable, especially because in our experiments the crystals of the carcinogens were administered in oil deposits in the vicinity of the amputation. It seems that by eliciting a regeneration process prior to the administration of the carcinogens we have successfully prevented carcinogenesis in the experimental animals.

However, it would be erroneous to assume that the cellular material, which the carcinogens presumably stimulated to active growth, contributed in a constructive manner to the process of regeneration. It is a tempting idea that potentially neoplastic material, when converted to normally differentiating tissue, might become incorporated – because of the vicinity – into a regeneration blastema and enhance the process of regeneration. But there is no evidence for such a process. On the contrary, the presence of carcinogenic substances in the organism definitely retards the process of regeneration. Comparing the growth of the regenerates in carcinogen-treated specimens (1 mg methylcholanthrene or dibenzanthracene in 1 ml corn oil) with controls (injected with 1 ml corn oil or glycerin) we have observed a marked inhibition of regeneration. The length of the regenerates was measured at weekly intervals for 18 weeks and it was found that the growth rate of the carcinogen-treated specimens is less than half of the control rate, while the methylcholanthrene and dibenzanthracene series hardly differ from each other (Figure).



Growth of tail regenerates of *Triturus (Diemictylus) viridescens*, with and without carcinogen treatment. Abscissa, time in weeks; ordinate, length of regenerates in millimetres. Squares and full line, controls; empty circles and broken line, newts treated with dibenzanthracene; full circles and dotted line, newts treated with methylcholanthrene. Treatment was one week after tail amputation (controls injected with 1 ml corn oil or glycerin, experimental animals with 1 mg carcinogen in 1 ml corn oil). Each point in the graph is based on 10 data, which showed less than 10% standard deviation.

It thus seems evident that regeneration and carcinogenesis are antagonistic processes in the newts. Regeneration inhibits to a gratifying degree malignant growth but the opposite is also true: the presence of carcinogenic tendencies in the organism during regeneration retards considerably the reconstruction of an organ lost through amputation. Similar conclusions were reported already in the literature[5] but other investigators reported an adjuvant effect of carcinogens on regeneration[6] and the controversy remained unresolved. We believe that our results, both in their negative aspect (no carcinogenesis by hydrocarbons in regenerating newts) and on their positive side (reduced regeneration in carcinogen-treated specimens) strongly support the view that carcinogenesis and regeneration are, in spite of their superficial similarity (both represent a rapid growth of dedifferentiated cells in an adult organism) antagonistic rather than synergistic processes.

The negative interference of carcinogens with regeneration poses some further problems. It seems to contradict experimental evidence, which shows that a regeneration blastema removed from an organ stump and transplanted to the flank of the body stimulates a second regeneration of the organ[7]. It seems that in these cases an additional supply of dedifferentiated cells was present in the body, possessing the same morphogenetic tendency as the regeneration blastema. These cells, in some unknown manner, increased the rate of regeneration. On the other hand, when neoplastic tissue – or its precursor – is present in the body during regeneration this additional 'embryonic' material has other morphogenetic tendencies than the regeneration blastema and the two systems mutually weaken rather than reinforce each other. It will be a challenging task to clarify the molecular-biological mechanism of these interactions.

Zusammenfassung. Bei Untersuchungen an Molchen *Triturus (Diemictylus) viridescens* über Carcinogenese und Regeneration ergibt sich, dass während Schwanzregeneration die mit Dibenzanthracen oder Methylcholanthren behandelten Tiere im Unterschied zu nicht regenerierenden keine Geschwulstbildung zeigen. Andererseits hemmen aber carcinogene Stoffe den Regenerationsprozess bedeutend. Carcinogenese und Regeneration sind also verwandte, aber antagonistische Prozesse.

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January 6, 1966.

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