

sion of a nucleus of a third cell by amitosis. The times of total performance of the mitosis were 30 and 60 min; the division of the nucleus by amitosis takes about 2 h, but, at least during the time of our observation, it was not followed by division of the cytoplasm.

Discussion and conclusions. The reproduction of irradiated cells can be studied by integrating the observations that we obtained on fixed stained cultures and on living cultures observed by phase contrast with time cinematography. The relation between the number of cells that begin mitosis and the number that have nuclei dividing by amitosis (Table), established by observations on fixed stained cultures, was revised according to the value of the data provided by cinematography. The mechanism by which the nuclei divide by amitosis required, in some cases, more than twice the time necessary for a cell dividing by mitosis. Therefore the reported percentages can have only an indicative function, because they would be modified as a function of the time of evolution of each process.

Another consideration is that a notable percentage of cells which enter mitosis develop in irregular mitosis. The dislocation of the chromosomes is so atypical that it is not easy to say (and cinematography has not proved beneficial to us in this respect) if these irregular mitoses remain abortive, or if they evolve in cells with micronuclei by formation of these from dislocated chromosomes which do not return again into the common mass.

It has been reported³ that giant cells can begin mitosis but, owing to the damaged chromosomes, atypical anaphases may be derived, showing numerous chromosomal bridges. The authors do not say what the evolution of such cells attempting mitosis may be, and if, as a result of the chromosomal bridges, cells may be present in irradiated cultures, with the daughter nuclei joined together. We do not think that the cells showing the nuclei

dividing by amitosis, present in our preparations, are postmitotic figures of this type because of three considerations: (1) the percentage of mitosis is inversely proportional to the dose used, although irradiation causes an increase of the time of evolution of mitosis⁴⁻⁶; (2) very often we observed a direct division of the nucleus without any shape that reflects an attempt at mitosis; (3) at every dose level used, we have observed that nuclei are joined together or detached by one bridge only, and we have never observed images that could be the result of numerous chromosomal bridges⁷.

Riassunto. Colture primarie di rene di scimmia sono irradiate con 300, 600, 1000, 1500 e 3000 R. La riproduzione delle cellule irradiate è studiata con osservazioni su colture fissate e colorate e con cinematografia a contrasto di fase. In un certo numero di cellule irradiate i nuclei si dividono direttamente per amitosi; tale numero aumenta con l'aumentare della dose di irradiazione. La cinematografia a contrasto di fase ci permette di seguire i tempi di evoluzione della riproduzione cellulare.

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⁵ J. E. TILL, Ann. N.Y. Acad. Sci. 95, 911 (1961).

⁶ G. F. WHITMORE, C. P. STANNERS, J. E. TILL, and S. GULYAS, Biochem. biophys. Acta 47, 66 (1961).

⁷ The authors wish to express their appreciation to Prof. M. AGENO for the irradiations performed in the Department of Physics.

Probable Induction of Chondrogenesis by the Spinal Cord Tissue in the Ammocoetes

The present study was undertaken primarily to inquire if ablation of the spinal cord in the base of the tail in the ammocoete larvae of the lamprey would have any adverse effect on regeneration of the tail when the latter is amputated at the same time. While the results gave a negative reply to this inquiry, certain developments were noted in some cases which indicate the capacity of the spinal cord tissue to induce cartilage formation in these animals. These observations are reported below.

The material consisted of 15 ammocoetes of *Petromyzon marinus* and *Entosphenus lamottenii*, 72–105 mm in length. In each case, after anaesthetizing the animal in 1:4000 MS222 solution, an incision was made through the tail muscles alongside the base of the dorsal fin on the right side near the cloaca. The incision exposed the spinal cord, a small piece of which was cut out and removed. The caudal part of the spinal cord was thus separated from the same organ in the rest of the body. The distal portion of the tail was amputated immediately after this operation. All the animals survived; they were killed at various intervals and their tails sectioned for microscopic study.

Although attempts had been made to remove the severed segment of the spinal cord completely from the operated region, the sections showed that it was not successful in three cases, in which several small fragments of the spinal cord tissue were left behind in the area near the base of the dorsal fin. One of the three animals was killed and its tail sectioned 26 days after the operation. In this case many mesenchymal cells, together with numerous leucocytes, were found disposed around these fragments of the neural tissue.

The other two animals were killed and their tails sectioned 90 days after the operation. In both of them definite cartilaginous structures were found to have developed around the spinal cord fragments left behind in the area near the base of the dorsal fin. These structures were tubular with the spinal cord fragment occupying the lumen in each case. In one of the two animals there were two such tubes, more than 250 μ in length, situated parallel to the long axis of the tail. These cartilages had developed in entirely abnormal positions. The operation had caused quite extensive damage to the muscles in this region and much dedifferentiation of this tissue had occurred in this area. It is probable that the cells for the abnormal cartilages may have been derived from the dedifferentiating muscles in the operated region. That chon-

drogenesis of somitic cells does occur has been reported in various vertebrates¹⁻³. Moreover, the connective tissue of the tail in the lamprey larvae contains many undifferentiated cells which are utilized for the linear growth of the fin-rays throughout the larval life⁴. The cells for the abnormal cartilages may also have come from this source.

It is significant that these cartilages developed only in those cases in which fragments of the spinal cord were left behind in the operated area. This fact, together with the close morphological association of these structures with the pieces of the spinal cord, indicates that the latter played an active role in the formation of the former. It seems that the fragments of the neural tissue became the centres around which the undifferentiated cells present in the area accumulated and later differentiated into cartilage. The spinal cord has been found to induce chondrogenesis in all the major classes of vertebrates¹⁻³. The present observations, although made on numerically very

few cases, suggest that this may also be true for the cyclostomes.

Zusammenfassung. Einige Fälle werden berichtet, die vermuten lassen, dass das Rückenmark in den Ammonoeteslarven der Neunaugen die Fähigkeit besitzt, Knorpelbildung hervorzurufen.

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Beitrag zur Homotransplantation der Menschenhaut

Wir konnten zeigen, dass ϵ -Aminocapronsäure (ϵ -ACS) die Erhaltung der Homotransplantate der Ratten verlängert und dass die Kombination des ϵ -ACS mit einem Histaminliberator in einem grossen Prozentsatz der Fälle zu dauernder Erhaltung des Transplantates führt¹. Als unsere Mitteilung in Satz ging, publizierten BERTELLI und FRONTINO² eine Arbeit in der sie zeigten, dass ϵ -ACS zu einer Verlängerung der Erhaltung des Homotransplantates führt. BERTELLI und FRONTINO arbeiteten nur mit ϵ -ACS, ohne einen Histaminliberator. Es ist bekannt, dass ϵ -ACS die Fibrinolyse hemmt, aber sie wirkt auch antinekrotisch.

Es interessierte uns, die Wirkung des ϵ -ACS auf Homotransplantate der Haut des Menschen zu untersuchen.

In dieser vorläufigen Mitteilung berichten wir über 5 Fälle mit schweren Verbrennungen, in denen wir ϵ -ACS prinzipiell in gleicher Weise wie in früheren Experimenten gaben. Donator und Akzeptor erhielten ϵ -ACS zwei Tage vor der Operation, und dann täglich bis die Abstossung erfolgte.

Die Präparate Epsamon³ und Capramol³ wurden in Dosen von 2,5 g i.v. injiziert. Die beiden Präparate enthalten reine ϵ -ACS; es besteht kein Unterschied zwischen ihnen.

Man muss betonen, dass ein prinzipieller Unterschied zwischen den Bedingungen der Transplantationen in unseren Tierversuchen und den klinischen Bedingungen besteht: in der Klinik kommt das Homotransplantat auf mehr oder weniger infizierte Granulationen, die auf eine antibiotische Therapie resistent sind.

Nach den Angaben der Literatur⁴ und auf Grund unserer Erfahrung bleibt ein Homotransplantat ungefähr 4 Tage bis 4 Wochen erhalten. Die durchschnittliche Dauer der Homotransplantate der Patienten, die wir mit ϵ -ACS behandelten, betrug 7 Wochen. Die Fälle Nr. 1 und 3 sind interessant, weil die Homotransplantation mit Erfolg wiederholt wurde, und sich lange hielt, obwohl wegen der entstandenen Antikörper eine frühere Abstossung zu erwarten war.

Der Allgemeinzustand unserer Patienten war auffallend gut und die Granulationen, die günstig für die Plastik waren, zeigten sich schon früh nach der Abstossung des Homotransplantates an.

Wir denken, dass diese Untersuchungen ermutigend sind und die Experimente weiter verfolgt werden sollten.

Summary. It has been shown that homologous skin grafts made with simultaneous application of ϵ -aminocaproic acid survive longer than in non-treated patients.

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| Zahl | Fälle | Alter | Geschlecht | % der erfassten Körperoberfläche | Intensitätsgrad | Überlebenszeit in Tagen |
|------|-------|-------|------------|----------------------------------|-----------------|-------------------------|
| 1. | S.J. | 5 | ♀ | 20% | III° | 58 T/II/46 T |
| 2. | S.M. | 51 | ♀ | 21% | III° | 50 T |
| 3. | N.M. | 3,5 | ♂ | 36% | III° | 62 T/II/39 T |
| 4. | M.J. | 4 | ♀ | 30% | III° | 43 T |
| 5. | L.L. | 6 | ♀ | 9% | III° | 50 T |

¹ P. STERN und E. VAJS, *Vojno-sanit. Pregled* **20**, 141 (1963).

² BERTELLI und FRONTINI, *Nature* **197**, 510 (1963).

³ Wir danken für «Epsamon» der Firma Emser-Werke AG, Zürich und für «Capramol» dem Laboratoire CHOAY, Paris.

⁴ F. ZDRAVIČ, *Vojno-sanit. Pregled* **13**, 175 (1956).