where λ is constant. But the data insist that λ is not constant: it changes by a factor of 3·5 during the course of the experiment. Singh and Koppelman[2] try to overcome the difficulty by approximating an exponential as a straight line. They do not succeed. Kinetic models based on erroneous assumptions are unacceptable. Any model which can satisfactorily fit the data of Harris and Watts must be rather more sophisticated than that of Singh and Koppelman.

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PATHOLOGY

Premalignant Cells in Tumorigenesis induced by Plastic Film

PLASTIC material inserted under the skin of mice and certain other laboratory animals frequently leads to the formation of sarcomatous transplantable tumours[1,2]. This finding deserves consideration in view of the use of plastics in human surgery. It also attracts theoretical interest as an example of "physical" carcinogenesis. (The role of chemical cofactors is still under dispute although evidence is mounting against it[3].)

Carcinogenic events are thought not to take place on the surface of the plastic insert but rather in connexion with the tissue capsule[3] which gradually builds up as a foreign body reaction. This communication presents evidence that 1–8 months before a tumour appears in mice, the premalignant cells are regularly found firmly attached to the insert itself where they seem to originate and mature. Premalignant cells could not be found in the capsule tissue except during the last 4 weeks before the appearance of palpable tumours.

Inbred mice (*CBA-T6*) at the age of 1·5–2 months received subcutaneous inserts in both flanks of double vinyl chloride acetate coverslips ('Dispo-slips') 15 × 22 mm in size. A control group (eighty animals) was left to itself. Tumours developed in 65 per cent of the male animals 9–12 months after operation, and in almost all the female animals after 7–12 months. In the experimental group, inserts and tissue capsules were cut in thirds after intervals of from 2 weeks to 12 months. One portion was left in the original animal. A second portion was used for histological, karyological and cultural examinations. The plastic and capsule pieces of the third portion were carefully separated and then individually transplanted into *CBA-H* recipient mice.

The results are shown in Table 1. No tumours developed in the original and the recipient animals when transplantation was carried out during the first 5 months after initial insertion of the plastic films. It is concluded that during this period premalignant cells either had not yet emerged or were unable to mature further outside the original film/capsule condition. The disturbance of the primary processes at this time caused by removing two-thirds of the film and tissue capsule apparently stops tumorigenesis even in the original animal. (A separate control experiment has shown that pieces of plastic film one-third the size of the original inserts, that is, 7 × 15 mm, no longer cause tumours within 15 months; they are obviously below the threshold size critical for tumorigenesis.)

Table 1. TUMOUR DEVELOPMENT FROM TRANSPLANTED PREMALIGNANT CELLS ON PLASTIC FILM AND IN CAPSULE TISSUE

Tumours simultaneous in original and recipient animals	Number and sex of animals	Insert carried in original animal (months)	Observed after transfer (months)
None	22 ♀ ♂	1/2–5	Up to 15
	6 ♀		
	12 ♂	6–10	Up to 13
From transferred film pieces only	2 ♂	7	6–8
	1 ♀	8	5
	2 ♀	6	4
	2 ♀, 1 ♂	6–12	3
	2 ♀	8–9	2
From transferred film and capsule	4 ♀	9–12	(<) 1
	1 ♂	8	(<) 1

Tumours developed at the expected rate in the original and also in the recipient animals when the transplantation was carried out 6 or more months after the initial insertion of the plastic films. The tumours appeared simultaneously in the original and the corresponding recipient animals. The origin and identity of the tumours were established on the basis of the T_6-marker chromosome. This indicates (1) that premalignant cells have emerged by the time of transplantation, (2) that premalignant cells are present in multiple foci, (3) that the population of premalignant cells is homogeneous with regard to the stage of development, and (4) that further maturation of premalignant cells towards the tumour occurs independently of the conditions of the film and capsule.

When the latent period (that is the time between transplantation and the appearance of the tumour) lasted 2–8 months, the tumours developed from transplanted film pieces only, not from capsule tissue. If the latent period happened to last 1 month or less, tumours developed in recipient animals from both the film piece and the capsule tissue. These results suggest that 2–8 months before the tumour appears the premalignant cells are firmly attached to the film and are not found in the surrounding capsule tissue. (It remains to be seen, however, whether premalignant cells in transplanted capsule tissue can be destroyed or returned to normality by the recipient animal in the absence of the piece of plastic film.) From the results available so far, it seems that tumorigenic cells detach from the plastic film and invade the capsule tissue only a few weeks before the growth of the tumour is recorded macroscopically. It can reasonably be assumed, therefore, that detachment of tumorigenic cells from the plastic film is actually one of the first manifestations of malignancy.

Apart from the experimental results described, it is suggested that this system allows the study of cell populations with a degree of premalignant maturation which can be determined accurately.

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BIOLOGY

Probable Instance of Genetic Polymorphism in the Graptolites

A SPECIES, in the biological sense, is a community of individuals with a similar genetic structure, drawing on a common gene pool and having the ability to interbreed. Individual variation within such a community can be accounted for, in large part, by the segregation and recombination of genes according to Mendelian rules. This variation may be continuous and capable of being