In view of these findings it was, therefore, accepted that the occurrence of these tumours was not the result of the experimental procedures.

It has been demonstrated that it is possible to produce tumours which appear to be arising from the mesothelial cells of the pleura by inoculating certain dusts into the pleural cavities of rats. One further tumour was obtained by exposing an animal to an asbestos dust cloud. The fact that these neoplasms were produced by silica and chrysotile asbestos as well as crocidolite fibre complicates the interpretation of these preliminary observations, and indicates the need for further investigations.

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An Early Test for Possible Skin Carcinogens in the Mouse: Effect of Different Doses of 3-Methylcholanthrene in Benzene Solution

AN early test for possible skin carcinogens in the mouse has been reported^{1,2}. The test is based on a tetrazolium reduction method. It was demonstrated that the test could reveal the carcinogens in a blind test of 21 substances of which 7 were carcinogens.

The present communication gives the values obtained with different doses of 3-methylcholanthrene in benzene solution applied to a circumscribed area of the skin of hairless mice. The results are given in Table 1.

Table 1. TETRAZOLIUM TEST WITH DIFFERENT DOSES OF 3-METHYLCHOLANTHRENE

μg applied	% solution in benzene	No. of mice	Test result
0.4	1/128	16	0.898
0.8	1/64	16	0.792
1.6	1/32	16	0.818
3.1	1/16	32	1.107
6.3	1/8	32	1.168
25.0	1/2	32	1.361
50.0	1/1	16	1.410

Terracini, Shubik and Della Porta³ found a step-like increase in the tumour yield after single applications to mouse skin of different doses of DMBA. Studies are in progress at our Institute to find out if such a step exists for hairless mice exposed to single applications of 3-methylcholanthrene. The preliminary results ten months after the single painting are shown in Table 2.

Table 2. SKIN PAPILOMATA OCCURRING TEN MONTHS AFTER A SINGLE SURFACE APPLICATION OF 3-METHYLCHOLANTHRENE IN BENZENE TO HAIRLESS MICE

% solution	No. of mice	Papillomata
1/64	30	1
1/32	30	1
1/16	30	20
1/8	30	22
1/1	30	34

These results demonstrate that such a well-known carcinogen as 3-methylcholanthrene gives negative results with the tetrazolium test when very small doses are given. The testing of unknown substances should therefore be performed with relatively strong, but non-ulcerative, doses. The possible specificity of the test, however, is given some further support by the preliminary results reported in Table 2. These seem to be in accordance with the conclusion of Terracini, Shubik and Della Porta³: "A critical dose level exists at which single application of carcinogens becomes fully effective".

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Mineral Phase in Osteoporotic Bone

IN a survey of the incidence of fractures¹, particularly those of the head and neck of the femur, expressed in terms of population at risk, the distribution found made it quite clear that some must be of pathological origin. Such bones appear osteoporotic, and there has been a widespread assumption that the tissue component at fault is the calcium phosphate.

Should a change occur in the mineral, or in the calcium- and phosphate-level of its surroundings, one would expect to find changes in composition. Traditional methods of chemical analysis for calcium and phosphate cannot be profitably used, because the main need is to distinguish between a number of closely related calcium phosphates which might be present as mixtures. A further complication is that the mineral crystallites in bone have a very large surface area, so that adsorbed ions could produce misleading results. At present the most sensitive method for demonstrating individual components, which can be interpreted unambiguously, is X-ray diffraction.

A satisfactory method for distinguishing the various calcium phosphates involves taking photographs at room temperature, and then after heating to 1,000° C (ref. 2). At room temperature possible compounds are hydroxyapatite, octacalcium phosphate, monetite, brushite and calcium carbonate. After heating: apatite remains as apatite; apatite mixed with the other calcium phosphates, or apatite with phosphate adsorbed on to the crystal surfaces, reacts to form β -tricalcium phosphate, the proportion depending on the amount of excess phosphate present; calcium carbonate is transformed into calcium oxide.

One example where a difference is known in the tissue fluids surrounding the mineral in bone is in infants. These children have a higher serum phosphate than older children and adults. X-ray diffraction examination of bone from infants gave the hydroxyapatite pattern when unheated, and hydroxyapatite mixed with a little β -tricalcium phosphate after heating. Bones from the older age-groups gave hydroxyapatite only. In this case the different ionic concentrations in the surrounding fluids have been mirrored in the mineral composition.

To investigate possible differences in the mineral composition in osteoporotic bone the upper ends of the femur were used. At least three separate sub-