Session 3

Oncology 1976;33:89

Discussion Session 3, March 26th, 1976 – Summary

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(1) Is the original concept still valid of carcinogenesis being a unique phenomenon resulting from the accumulation of irreversible changes?

Consideration of the existence of DNA excision and postreplication repair mechanisms, of enzyme induction, of syncarcinogenesis and cocarcinogenesis may point towards some possible reversibility. Other results point to irreversibility, hence no definite answer is yet possible.

(2) What is the difference between a strong carcinogen, a weak carcinogen and a cocarcinogen?

From a pragmatic point of view, a strong carcinogen induces a high incidence of tumors within a short induction period in relatively low dosage. A weak carcinogen however produces a low yield of tumors after a long induction period in relatively high dosage. In practice it may be difficult to distinguish experimentally between a weak carcinogen and a cocarcinogen but this should be done in theory because a cocarcinogen by definition does not produce tumors if administered alone. Even more problematic are the questions of incomplete and secondary carcinogens.

(3) Can the postulated role of DNA repair in carcinogenesis, investigated in special models, be generalised to all processes of chemical carcinogenesis?

For alkylating carcinogenic agents this appears to be valid but for certain tissues with a high susceptibility to tumor production, i. e. the liver, this is still under investigation. Furthermore, there are no data as yet on non-alkylating carcinogens. The role of enzyme induction and of enzyme activation also requires further consideration. The need for more research into basic toxicological mechanisms was stressed by many participants.

(4) Is there any human epidemiological evidence for threshold effects?

The only apparent evidence to date comes from the transplacental induction of adenocarcinoma of the vagina following high dose administration of DES to the pregnant mother.

(5) What is the role of micropollutants in water and food for human carcinogenesis?

Examples are asbestos, nickel, chromium, polybrominated biphenyls and related compounds. The epidemiological evidence is not yet available to answer this question.

(6) At the end of the discussion the following conclusions were drawn which could stimulate future research:

an inability to state at present whether a threshold dose for carcinogenesis exists;

the carcinogenic potential of every compound has to be evaluated individually;

the present mathematical models for estimating risks of cancer have insufficient biological background;

strong carcinogens should be removed from the human environment;

there is not enough information to consider the existence of so-called “secondary” carcinogens and to evaluate their role in carcinogenesis;
the available statistics are not sufficiently sophisticated to extrapolate the experimental data on dose-response relationships of carcinogens.