tion of clinical experience in the use of radiation, the advent of antibiotics, and the introduction of improved X-ray and gamma ray apparatus giving more penetrating beams. There is now a general feeling, however, that little further advance is to be expected along these lines. Patients with remote metastases at the time of treatment are not curable by radiotherapy alone. And there are still some patients whose local disease cannot be controlled, even with the most modern apparatus.

One possible reason for this failure of local control may be the protection against radiation given by anoxia. Some tumours probably contain viable cells which are severely hypoxic because of their distance from a capillary, and these would be radioresistant compared with normal cells. Tumours of this type might be treated more effectively if the patient were breathing oxygen at high pressure during treatment. The radiosensitivity of normal tissues would hardly be affected by this procedure because radiosensitivity reaches a plateau at quite low oxygen tensions.

This form of treatment has now been in use at a number of centres for several years. At a meeting held on January 18 at the British Institute of Radiology, an account was given of two clinical trials in which patients were randomly divided into two groups, one treated with and the other without high pressure oxygen. In both trials the regime of fractionation was kept identical in the two groups.

In one trial, concerned with carcinoma of the lung and bladder, treatments were given daily. No difference in survival was observed in the lung cancer series, while the bladder series suggested that the patients treated in high pressure oxygen were faring rather worse than those treated conventionally, although the difference was not statistically significant. At another centre the trial concerned cancer in various sites in the head and neck, and the patients were treated three times per week. These results suggested that treatment in high pressure oxygen improved the prospects for patients with secondary deposits in lymph nodes, but made no difference to those without involved nodes, but the differences were again not statistically significant.

Treatment under high pressure oxygen greatly increases the burden both to the patient and to the staff, and scientific attempts to decide whether the use of oxygen leads to any improvement in results are to be welcomed. In view of the meagre results of the trials made so far, it is important that future trials should have the maximum chance of success. Carcinoma of the lung is a bad choice for such a trial because failure to control the primary is seldom the cause of death. There is a high rate of metastasis, and increasing the radiation dose actually reduces life expectancy because it causes greater damage to the lungs (Deeley, *Brit. J. Radiol.*, **40**, 801; 1967). A more general point concerns the regime of fractionation. Daily treatment is customary, but treatment under high pressure oxygen is usually given once or twice a week, because of technical difficulties. If daily treatment is dropped in a comparative trial because of difficulties in the oxygen series, the conventionally treated patients may be receiving a treatment that is less than the optimum. A trial of two methods of treatment would ideally compare the best that can be done with each, without reducing the efficiency of one method for the sake of equalizing other factors.

Frog Haemoglobins and Metamorphosis

from our Cell Biology Correspondent

At metamorphosis and the transition from a purely aquatic to semiterrestrial life, frog tadpoles undergo profound biochemical changes. Regulation of these events appears to be under hormonal control, and the most clear-cut and familiar example is the induction of adult haemoglobin synthesis by the thyroid hormone thyroxine. Herner and Frieden (1961) found that in the bullfrog (*Rana catesbiana*), replacement of tadpole by adult haemoglobins begins abruptly after administering thyroxine to tadpoles. Moss and Ingram's work (1965) suggests that the thyroxine induces *de novo* synthesis of adult haemoglobin polypeptide chains and simultaneously represses synthesis of tadpole haemoglobin. In two papers in the current issue of the *Journal of Molecular Biology* (**32**, 481 and 493; 1968) Moss and Ingram now report analyses of the tadpole and adult haemoglobins of *R. catesbiana*.

Tadpole haemoglobin is resolved into five components, one major (60–70 per cent of the total) and four minor, by polyacrylamide gel electrophoresis. The amount of the minor components, which are not artefacts, varies among individual tadpoles, but it is impossible to determine the genetic basis of this variation because inbred stocks are not available. Moss and Ingram isolated enough of the major components and of one of the minor components to do fingerprint analyses. The two haemoglobins each have two distinct polypeptide chains and, moreover, the two chains of the major tadpole haemoglobin (N-terminal valine) are different from the two polypeptide chains (N-terminal glycine) of the major adult haemoglobin. The heterogeneity of the tadpole haemoglobins indicates there are at least four or five different polypeptide chains. There are at least three distinct polypeptide chains in the adult haemoglobins, so that in the bullfrog there are at least seven or eight structural genes specifying haemoglobins.

In the second paper, Moss and Ingram report that haemoglobin synthesized *in vitro* by erythrocytes from tadpoles treated with thyroxine is identical with the major haemoglobin in adult frogs. In natural metamorphosis, the transition from tadpole to adult haemoglobins is complete in froglets which still have small tail stumps. Autoradiography with Fe^{59} shows that the cells which synthesize adult haemoglobin after thyroxine treatment are immature judged by morphological criteria. Apparently the thyroxine stimulates synthesis of adult haemoglobins in young cells rather than in mature cells full of tadpole haemoglobins. This may well mean that the hormone does not act directly on the structural genes for haemoglobin but that, instead, it stimulates proliferation of an adult cell line while simultaneously repressing proliferation of the larval cell line. As yet, however, it is impossible to know whether thyroxine stimulates a clonal selection mechanism. It is not known whether or not the stem cells which give rise to the adult cell line are clonally distinct from those which give rise to the larval cell line.