EDITORIAL

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Use of Radioactive Dye in Localization of Brain Tumours

A promising new possibility of the application of isotopes to medical diagnosis has recently come from the U.S.A. In a preliminary report, Moore[1] of Minnesota described the successful localization of intracranial neoplasms in a small series of cases by a Geiger-Müller counter applied to the intact skull two to four hours after intravenous injection of radioactive di-iodofluorescein.

It is interesting to trace briefly the steps which led up to this endeavour. In an attempt to enhance the natural fluorescence of tumours in ultraviolet light, Moore[2] injected patients intravenously with 5 cc. of 20 per cent. sodium fluorescein. He found that after an interval of three to eight hours, tumours abutting on the surface of exposed viscera fluoresced a vivid yellow colour in contrast to their neutral surroundings when inspected in the light of an ultraviolet lamp emitting rays at about 3,600°. However, areas of oedema and cyst formation also retained the dye whereas a number of bulky tumours and areas of necrosis failed to fluoresce. The most consistent results were obtained with brain tumours including the examination of aspiration material from subcortical lesions. Moore[3] and his colleagues have reported the results of the fluorescein fluorescence technique in 46 patients operated upon because of a clinical diagnosis of a possible brain tumour. The presence or absence of tumour tissue aspirated by needle biopsy was correctly determined in 44 of the 46 cases. Of 52 actual needle biopsies, fluorescence results tallied with histology in 48 instances, was wrong twice and doubtful twice. Five patients were found correctly to have no tumour. Positive fluorescence was obtained with the following types of growth:—meningioma (ten cases), astrocytoma (seven), glioblastoma (five), astroblastoma (three), metastatic (three), acoustic neuroma (two), chromophobe adenoma (two), angioblastoma (two), ependymoblastoma (two), medulloblastoma (one), ependymoma (one). A tuberculoma and a cholesteatoma were found not to fluoresce. One angioblastoma, possibly due to excessive blood clot content, did not fluoresce whilst one biopsy fluoresced for no accountable reason proving histologically free of tumour. Next, with the help of Drs. G. Boyack and W. Armstrong, Moore[1] synthesized di-iodofluorescein containing the radioactive isotope I^{131}. Twelve patients with questionable intracranial neoplasms were each injected intravenously with an amount of dye calculated to contain 500-600 μc. radioactivity. Gamma ray counts were taken for three to five minute periods at several positions on the skull. Differential readings between areas over suspected tumour and symmetrical control areas did not become evident until two to four hours had elapsed. Of the four cases which showed no significant counts, operation proved one to have an internal carotid aneurysm, one to have no tumour and one to have an acoustic neuroma. The fourth gave a normal ventriculogram and was not further explored. The remaining eight all proved to have tumours roughly but correctly localized. The growths were meningioma, ependymoblastoma, glioblastoma and metastatic variously disposed in the occipital, parietal and frontal lobes. A meningioma in the right middle fossa gave counts suggesting an origin in the right temporal area. Moore concluded that the limitations of the technique were as yet unknown and its clinical usefulness still to be determined. It is clear that if this correlation is confirmed in a further series of cases Moore and his colleagues will have made a noteworthy advance in the technique of intracranial tumour localization, as well as in the means of ruling out the presence of an intracranial neoplasm. They obtained no toxic reactions and the technique is painless; it should prove a boon to the patients.

Among the questions which arise from these results are:—Why does the dye stain brain tumours selectively as compared with healthy brain? How long does it stay in the body and what

is its route of excretion? Can it be used therapeutically? Can it be used for the localization of other tumours? Fluorescein and its derivations are chemically related to the phenolphthalein dyes which are excreted chiefly and fairly rapidly via the bile into the intestine and partly via the kidneys. Moore[3] found delayed excretion of sodium fluorescein in patients with severe liver disease. It is likely that the incidental irradiation of the liver, gall-bladder and intestines during the excretion of radioactive di-iodofluorescein will limit its usage to tracer investigations. Moore[1] found di-iodofluorescein to reach a concentration in induced brain tumours in mice 80 times that in adjacent normal brain. He[3] considered the selective staining of brain tumours to confirm Broman's[4] postulate that their vessels lacked the special permeability function of the blood-brain-barrier. Such a selectivity is less likely to obtain in tumours outside the brain but more experimentation is needed to determine the facts. Moore's work has already stimulated cancer research. Shapiro and Landing[5] have recently published their findings that the uptake of sodium fluorescein in transplanted mouse sarcoma was not selective but that poorly vascularized non-viable portions of the tumour tended to take up the dye more slowly and retain it longer than viable tumour and the rest of the animal tissues. We can expect further developments.

I. DONIACH.

REFERENCES

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'The Development and Goal of Western Medicine in the Indian Sub-continent' was the title chosen by Lieut.-General Sir Bennet Hance, K.C.I.E., F.R.C.S., for his Sir George Birdwood Memorial Lecture to the Royal Society of Arts on January 13th, 1949. To a receptive audience he first defined *western medicine* as '*the application of proved scientific fact, ascertained by observation and experiment, to the prevention and treatment of human disease.*'

Before the advent of more recent influences to the Indian sub-continent there were two indigenous schools of the art of healing:—the Ayurvedic, derived from the four sacred books which embody the Hindu religion, reaching its zenith about 600 B.C., but after Alexander's invasion remaining static and concerning itself with herbs, charms, amulets and the like, in spite of efforts to revive the old vedic lore; and the more recent Arabic system deriving from the Greek schools of philosophy enriched by the Arab physicians, Avicenna, Rhazes and others, and coming to India with the Islamic conquest. It too made little advance and, coming into contact with the Ayurvedic system, exchanged science for ritual.

The earlier European medical adventurers were notable more for their courage and idiosyncrasies than for their scientific attainments. Some were of note however such as John Woodall who, before 1643, was insisting on fresh fruit juices for the prevention of scurvy, and John Holwell who, whilst surgeon to Calcutta Hospital (1740), also served as Mayor and was constantly pressing for sanitary reforms in that city. The earliest hospital was in the Portuguese settlement at Goa; others followed in Bombay, Madras and Calcutta, whilst the three Presidency Medical Services with fixed grades and rules for promotion were formed in the 1760's. These changes were soon reflected in the character and calibre of the medical men employed and in the reaction of the Indian people to them.

In 1835 the first Indian Medical College was founded in Calcutta, offering a comprehensive course including dissection. The first operation undertaken by an Indian qualifying from that school was in January 1836 and, being a high-caste Hindu, his action required great scientific enthusiasm and high moral courage.

From this beginning the Indian Medical profession had grown by the time of the transfer of power to include some 50,000 registered practitioners, qualified from 19 medical colleges. At first they were of two classes, *graduates* and *licentiates*, but this system has now been abolished except in Bengal.

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