Production of Lesions in Guinea Pig Brain by Radon Seeds. (25598)

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Radioactive seeds have been used for experimental production of lesions deep within the central nervous system in dogs(1,2,3) and monkeys(4). The present work deals with the feasibility of extending this technic to a smaller animal, the guinea pig, and in particular with the tolerance of this animal to implantation of gold and glass radon seeds in the brain.

Method. Single implantations were made with glass-encapsulated radon seeds in 61, and with gold-shielded seeds in 17 adult guinea pigs. Under ether anesthesia and sterile conditions, a small hole was bored in the calvarium, and the dura was incised at a site which permitted placement of the seed in the center of one hemisphere, 5 mm back of the frontal pole. The seed was expressed from the tip of a lumbar puncture needle by insertion of a stylet, the needle being withdrawn 3 mm from its maximum depth to form a short channel. Glass seeds were 2 to 4 mm in length and 0.5 mm in external diameter, with walls of 0.1 mm thickness. Gold seeds had walls 0.25 mm thick, a diameter of 0.7 mm and a length of 2-5 mm. Strengths of seeds as measured initially by the commercial supplier* ranged to 7.0 mc for glass seeds and 12.0 mc for gold ones. Each seed was used in several animals, strengths at implantation being calculated from initial values on the basis of a half-life for radon of 3.8 days. No examination of the emission was made, but the values are probably similar to those given by others showing that about 90% of total radiant energy emitted by gold radon seeds is gamma radiation and the rest is beta emanation, whereas 96% of the emission from glass seeds are beta rays(5). Per mc of radon total radiant energy from a gold seed is roughly only 3% of that of a glass one. Calculation from these values indicates that a gold seed of 1.5 mc emits approximately the same amount of gamma radiation as a 1.0 mc glass seed.

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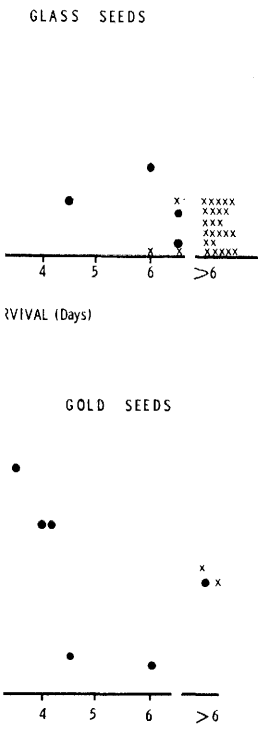
Fatalities were noted to the nearest 12-hour period and survivors sacrificed at one week. Lesions were measured at the equator of the seed emplacement on Weil-stained sections.

Results. All but one animal which had received glass seeds of more than 1.5 mc died within 2 days, and about half of those animals in which seeds of approximately 1 mc were placed died within one week (Fig. 1). Seventeen of 18 guinea pigs with glass seeds having less than 0.75 mc survived beyond 6 days. Deaths were particularly plentiful during the 6 to 18 hours after implantation, and 23 animals died during this period. These deaths cannot be attributed to causes unrelated to irradiation injury, since none of 23 guinea pigs which received seeds of less than 0.75 mc died in this early period.

Only 3 of 17 animals receiving gold seeds were alive at one week, the seeds in these 2 having initial values of about 4 mc (Fig. 2). Deaths were more scattered in time than following glass-seed implantation and, though animals with stronger seeds tended to die within 2 days, only 2 guinea pigs died at the 12-hour period.

Discussion. The basic advantage afforded by radioactive seeds in making experimental lesions in the brain lies in the gentle and gradual nature of the destruction, which permits functional compensations vital to the animal to be established. Ability of the animal to endure the seeds will, of course, depend on site of placement. The dog may, for example, survive implantation of glass seeds of 1 mc if the site is in the cerebrum(4), while in the medulla bilateral insertion of seeds exceeding 0.015 mc (each) will bring on death (3). In the guinea pig, cerebral implantations show that doses produced by glass seeds of more than 1 mc are not tolerated, and for insurance of survival beyond one week the seed strength should be reduced below 0.5 mc. In this respect it may be noted that, in terms of general susceptibility to ionizing irradiation,



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il under implantation ds differ in the high in- glass seeds within the ence of such early le- This contrast is prob- ture of the radiations. penetrating beta rays nse lesion concentrated early deaths primarily radiation and not the , judging from the fact gamma emission equal of even the strongest ıot cause early death.

Emanation from gold seeds on the other hand is comprised largely of gamma rays which may produce more diffuse injury and at greater distances, including in these small brains vital brain stem centers. Although the few observations on gold seeds of low strength do not permit delineation of the threshold for 6-day survival with gold seeds, the fact that most animals survived with glass seeds of 1 mc or less indicates that gold seeds of equal gamma emission, that is, 1.5 mc and less, should not produce death. This value is a minimal one as the threshold strength for the glass seeds is presumably dependent upon the beta radiation, and, in fact, survival of several animals with 4 mc gold seeds points to a median lethal threshold at about that strength. Neither the early deaths with glass seeds nor the delayed ones with gold seeds, incidentally, correspond necessarily to deaths in dogs following implantation in the medulla, for these occurred only after 6 days(3).

Glass seeds of strengths permitting survival (0.4 to 0.6 mc) were found to produce lesions up to 5 mm in diameter in one week. Only minor enlargement of the lesion is to be expected at longer periods as the effective half-life of a radon seed is 3.8 days. Borison and Wang, for example, found that 80% of ultimate size of the lesion was attained by 7 days (3). Thus, it appears that glass seeds can be used to make rather extensive lesions in animals which will survive for at least one week. All animals with gold-seed induced lesions of significant size, however, died within the first week.

Summary. Gold and glass radon seeds of varying strength were inserted into one cerebral hemisphere of mature guinea pigs and duration of survival up to one week observed. Animals having glass seeds of greater initial strength than 1.5 mc died within 2 days, whereas those with seeds of less than 0.7 mc survived. As glass seeds of about 0.5 mc produce lesions several millimeters in diameter, they may be used for short-term experimental production of lesions in this small animal. Gold seeds, however, cannot be used for this purpose.

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Comparative Passage of Sr^{85} and Ca^{45} from Plasma into Body Fluids in Man.* (25599)

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In vitro studies on comparative ultrafiltration of strontium and calcium(1) have shown that a lower percentage of strontium than of calcium is bound to plasma proteins. However, the passage of the 2 elements from plasma into cerebrospinal fluid in man occurred at similar rates(2), indicating that the membranes through which the ions pass discriminate in favor of calcium. In an extension of these investigations, transfer of calcium and strontium across membranes of other body cavities was studied and passage of both ions from plasma into peritoneal, pleural and interstitial fluid was investigated.

Materials and methods. Transfer of either Sr^{85} alone or of Sr^{85} and Ca^{45} from plasma into various body fluids was studied in 9 patients. The diagnoses of the patients and types of studies performed are listed in Table I. In patients with ascites in whom a paracentesis was indicated, a polyethylene catheter was inserted into the peritoneal cavity through a No. 14 needle after anesthetizing the skin. Ascitic fluid was obtained for analyses of protein and calcium by aspiration from the polyethylene catheter, the open end of the tubing being clamped afterwards. A tracer dose of either Sr^{85} or of Sr^{85} and Ca^{45} as the chloride was injected intravenously and samples of plasma and peritoneal fluid were then obtained serially. The patients were kept on a slowly oscillating bed for 4-8 hours in an attempt to obtain thorough mixing of peritoneal fluid with the radioisotopes. The peritoneal fluid was withdrawn 24 hours after injection of the tracers, to measure the fluid volume. Transfer of calcium and strontium from peritoneal fluid into the blood stream was studied in one patient by injecting the tracers into the peritoneal cavity and obtaining samples of ascites and plasma as indicated above. Transfer of the 2 elements from plasma into pleural fluid was also studied in 2 patients in a similar manner. Comparative concentration of radiocalcium and radiostrontium in plasma and interstitial fluid was studied in a patient with massive edema of the lower extremities (Patient 5) following intravenous injection of the tracers. Interstitial fluid was obtained by Southey tubes inserted into the subcutaneous tissue. Samples of plasma, peritoneal, pleural and interstitial fluid were analyzed for Sr^{85}, Ca^{45}, calcium, phosphorus and total protein. Sr^{85} was counted in a well-type scintillation counter and Ca^{45} was counted after precipitation with carrier calcium as the oxalate in a gas flow counter(3). Stable calcium was determined by the method of Kramer and Tisdall as modified by Clark and Collip(4), inorganic phosphorus by the method of Fiske and SubbaRow (5), and protein in serum and fluid by the Kjeldahl method, a small correction being made for non-protein nitrogen. Rates of flow

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