PREPARATION OF \textsuperscript{113m}In-ALBUMIN SOLUTION

Our recent abstract in the \textit{Journal of Nuclear Medicine} described the usefulness of radioaerosol inhalation lung scanning in the diagnosis of pulmonary embolism when perfusion scans show areas of ischemia (\textit{J Nucl Med} 11: 330, 1970). When the inhalation scans rule out obstructive airways disease as a cause of regional ischemia, the diagnosis of pulmonary embolism is further substantiated. Indium-113m is an ideal agent for inhalation scans in those institutions using \textsuperscript{99m}Tc-tagged MAA for perfusion lung scans, since the logical sequence of screening first with \textsuperscript{99m}Tc-MAA perfusion scans can be followed by inhalation scanning using the higher energy \textsuperscript{113m}In-albumin aerosol. This communication is in response to many requests for our method of preparation of the \textsuperscript{113m}In-albumin solution.

Four milliliters of \textsuperscript{113m}InCl\textsubscript{3} eluate (pH 1.2–1.3) are mixed with 0.25 ml of 1% human serum albumin solution. Then 0.75 ml of 0.2 N NaOH is added to elevate the pH to about 4. Finally 1.0 ml of 0.1 M phosphate buffer (pH 7.8) is added. The preparation is carried out at room temperature with gentle agitation. The pH of the final product ranges from 6.5 to 7.5. The exact identity of the final product has not been determined but is assumed to be a complex of \textsuperscript{113m}In(OH)\textsubscript{3} and albumin. No particulate matter is observed by light microscope. The aerosolized product is tasteless and nonirritating when inhaled. Total preparation time is less than 5 min. After the reagents have been checked with trial runs, a pH meter is not necessary, and the entire preparation may be carried out in a closed sterile pyrogen-free vial.

For aerosol inhalation lung scanning this solution is aerosolized by an ultrasonic nebulizer. The patient inhales radioaerosol during normal tidal volume breathing through a mouthpiece, and scanning is done at the completion of the inhalation procedure.

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UNSUCCESSFUL IMMUNOSUPPRESSION WITH RADIOACTIVE GOLD COLLOID

IN CANINE LIVER ALLOTRANSPLANTATION

Intravenously administered \textsuperscript{198}Au-gold colloid is rapidly phagocytosed by the body’s reticuloendothelial cells which subsequently act as sites of beta and gamma radiation (1). Approximately 70–90\% of the administered gold localizes in the sinusoidal (Kupffer) cells of the liver and remains there during radioactive decay (2). This organ therefore receives continuous selective internal irradiation mainly by short-ranged beta rays, a fact that would seem to lend itself to useful application in hepatic allotransplantation as a form of immunosuppression. This hypothesis was tested in dogs with liver allografts. Preliminary results suggest that the radiocolloid is ineffective at least as a sole immunosuppressive agent for liver allografts in this species.

Mongrel dogs weighing 17–23 kg were used. Three animals served as nontransplant controls while five received orthotopic allografts. The operative technique was similar to that described by Starzl (3). The radioactive gold colloid (Aureotope, Squibb) was administered intravenously at regular intervals of 72 hr. Repeated injections of the radiocolloid were adjusted to compensate for the physical decay of the isotope previously administered, so as to maintain a reasonably constant millicurie amount of radiogold in the liver (physical half-life of \textsuperscript{198}Au = 2.7 days). The first injection of radiocolloid to the transplanted dogs was given within 20 min of closure of the surgical incision. Table 1 summarizes the amounts of radiogold administered, the calculated beta dose to the liver (4), gamma irradiation to the whole body (4), pre- and post-treatment lymphocyte counts, and the results.

The three control dogs showed no signs of radiation sickness. Appetite and body weight remained unchanged over the 3-week period of radiogold treat-
ment. Biochemical determinations of hepatic function (serum glutamic-oxaloacetic transaminase, alkaline phosphatase, bilirubin, total protein, and albumin) were unaffected. Mild lymphopenia was achieved, which was more evident in the dogs receiving the higher radiation doses. The animals were sacrificed at the end of 3 weeks. Histological examination of the liver revealed no abnormality.

The five transplanted dogs showed an initially satisfactory course. An immediate liver scan after the first injection of gold showed that there was uniform uptake within the transplanted liver of all the animals. Mild lymphopenia comparable to the control dogs was also observed. However, all five animals succumbed in 5–9 days. Death was preceded by pronounced elevation of the serum transaminase, alkaline phosphatase, and bilirubin concentrations. Occlusion of the hepatic arterial anastomosis contributed to graft failure in one animal, but histological evidence of acute homograft rejection was present in every case upon light microscopy. This was characterized by sinusoidal congestion, hepatocyte necrosis, and mononuclear cell infiltration of the portal tracts (5). The gallbladder and extrahepatic bile ducts showed especially prominent changes. The epithelium was denuded in many areas, and large accumulations of round cells with areas of necrosis were present.

The mean survival time after total hepatectomy and orthotopic liver allotransplantation in nonrelated mongrel dogs receiving no immunosuppression is 7.1 ± 2.2 days (5). Treatment with radioactive gold colloid in the present study has therefore not given any improvement in survival in this small series of dogs.

Intravenous radioactive gold colloid has induced lymphopenia in lymphocytic leukemia, with clinical remission and disappearance of blast forms from the peripheral blood (6). Selective lymphopenia with immunosuppressive effects has also been observed after renal allotransplantation in dogs which received the radiocolloid by intralymphatic injection (7). In the present study, despite the achievement of lymphopenia and selective continuous irradiation of the liver allograft, unabated graft rejection occurred. This probably reflects the inefficacy of this method of local allograft irradiation as a sole immunosuppressive agent for hepatic transplantation. The short-ranged beta radiation from the isotope lying within the Kupffer cells would have provided a significant radiation field only within the liver lobule because of the intralobular distribution of these cells. Inadequate radiation of the gallbladder, bile ducts and blood vessels, as suggested by the abundance of round cell aggregates around these structures at autopsy, might be the reason for failure. Radioactive gold colloid perhaps can still be valuable as an adjunctive immunosuppressant in liver allotransplantation, but further work is required to ascertain its possible effects in such a role.

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REFERENCES


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STERILIZATION BY FILTRATION

Although the use of filtration for sterilization is well established, some reluctance has been shown by potential users because of the difficulty of being certain of the integrity of the filter. This is especially so when the material to be sterilized, such as a short-lived isotope, is to be used before the sterility of the product can be checked. We have been in the practice of visually examining the filter after use, but this is somewhat unsatisfactory since small defects might easily be missed. If the user was doubtful about any particular filter, a second and third opinion was often sought with the usual result that to “be on the safe side” the material was filtered again, probably unnecessarily in many cases.

Following a suggestion by Millipore (U.K.) Ltd.,* a simple apparatus to test the “bubble point” of filters has been constructed. This test depends on the fact that filters saturated with liquid will not permit the passage of a gas until a limiting pressure, which depends on the pore size, is reached. The pressure also depends on whether the solution is aqueous or not, but for a 0.22-micron filter and an aqueous solution the pressure is 55 lb/in.² and for a 0.45-micron filter 32 lb/in.² However, we have found that after autoclaving the necessary pressure is somewhat less—about 50 lb/in.² for the smaller pore size.

A general view of the apparatus is shown in Fig. 1. An oxygen cylinder is used in our case because this was easily available, but nitrogen is probably preferable for safety reasons.

It has been suggested that the filter should be tested after autoclaving and before use but this is not considered worthwhile in our case since very few filters are in fact rejected. Hence after sterilization is complete and while the filter is still wet, the filter holder (A) is placed in the device and the holder tightened by turning the ring B until a gas-tight seal is obtained (Fig. 2). Then the gas cylinder tap is slowly turned on until bubbles are observed in the beaker which should not occur until the given pressure is reached (hence the term bubble point). If premature bubbling is observed, the material must of course be refiltered. We have checked the method with a filter pricked with the tip of a fine needle when the defect was immediately obvious. One must take

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