Radionuclide Hysterosalpingography for Evaluation of Fallopian Tube Patency

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A prospective study was undertaken to evaluate the efficacy of radionuclide hysterosalpingography (RNHSG) using a technique with some modifications, that was described by Iturralde and Ventner (*1*). As these investigators demonstrated, technetium-labeled human albumin microspheres (HAM) will normally migrate spontaneously from the vagina to the ovaries. This study confirms that in the presence of fallopian tube obstruction, fibrosis and/or lack of motility, this migration does not take place, and that the presence or absence of migration of HAM can be imaged with a gamma camera. In the evaluation of 52 tubes we found that the efficiency of RNHSG for evaluation of fallopian tube patency when compared with contrast hysterosalpingography and/or direct observation of surgical pathology was over 94%. RNHSG is an essentially innocuous technique for assessing functional and mechanical fallopian tube obstruction that can be performed with conventional nuclear imaging equipment.

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In a study attempting to demonstrate a possible route of contamination of human ovaries with talc and asbestos particles which they postulated as being responsible for some ovarian carcinomas, Iturralde and Venter (*1*) described spontaneous migration and imaging of particulate radioactive tracer [technetium-99m (^{99m}Tc) human serum albumin microspheres (HAM)] from the vagina to the peritoneal cavity and ovaries. These physicians later indicated that such a technique could be used in the clinical evaluation of fallopian tube obstruction. However, the procedure described was fairly cumbersome and radionuclide hysterosalpingography (RNHSG) has not become a commonly used procedure. The purpose of this report is to describe and evaluate a simple technique for RNHSG and to discuss the efficacy of the procedure as compared to the results of contrast hysterosalpingography and/or direct observation of surgical pathology.

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MATERIALS AND METHODS

Human serum albumin microspheres labeled with 1 mCi of ^{99m}Tc were suspended in 1 cc of normal saline. After signing an approved consent, each patient volunteer was placed in the lithotomy position with a slight Trendelenberg. After a speculum had been placed into the vagina and the cervix exposed, the labeled microspheres were applied directly onto the cervical mucosa using a syringe with a blunt needle. This was done by gently flowing the liquid onto the anterior aspect of the cervix and allowing it to wash down along the cervical mucous. Some of the liquid was also squirted at, but not directly into, the cervical os. A nonabsorbing tampon of the type used routinely in artificial insemination was then placed into the vagina and the speculum carefully removed. The patient dressed and walked from the OB/GYN Department to the Department of Nuclear Medicine—a distance of ~200 yards. All procedures were performed in the late follicular phase and cervical mucous was described by the gynecologist administering the radiopharmaceutical as being normal.

Images were obtained soon after the patient arrived in the Department of Nuclear Medicine which was

usually about 15 to 30 min after application of the labeled microspheres to the cervical mucosa. Anterior images of the whole pelvic area were obtained with a gamma camera. A pinhole collimator was used for essentially all studies, this allowed for caudal angulation. Approximately 30° of caudal angulation was used in the initial acquisitions since it was found to be effective in visualizing the region posterior to the uterus. After the initial anterior images with caudal angulation, subsequent images were obtained if the initial image was not clearly normal. Varying degrees of caudal tilt were tailored with the help of the persistence scope. Occasionally, lateral-oblique images assisted in differentiation of a structure seen on the preceding images. Imaging was performed with delay for 1 hr or more for all patients whose initial images were read as other than clearly normal. Imaging of patients with normal studies was terminated as soon as the study was interpreted as being normal. Two hundred thousand counts for each image were generally accumulated in about 15 min when using the pinhole collimator. After completion of the study, the patient was instructed to remove the tampon and to wash the perineum to discourage further migration of the radionuclide from the vagina to the adnexae and to minimize external contamination. Douching has not been recommended because of the theoretical possibility of forcing additional radionuclide onto the ovaries.

Four patients were imaged serially for up to 4 hr following application of the microspheres. The other patients were imaged for 3 hr or less. Since there are no anatomic landmarks available to assist with determination of left and right on the images, it was found necessary to mark the right side of the patient on the images with a small amount of ^{99m}Tc in a syringe or with a cobalt-57 marker during accumulation.

The initial phase of the study consisted of four patients scheduled for bilateral tubal ligations who were presumed to have normal fallopian tubes prior to surgery. The remaining cases were interpreted without knowledge of the individual patients' clinical status or of prior surgical or diagnostic procedures. However, these patients were all being worked up for infertility and were referred by the gynecologist because they had failed to conceive and either had recently been evaluated surgically or were scheduled for surgical evaluation of the genital tract. During the performance of the study, all consecutive patients fitting these clinical and procedural criteria were asked to participate. These general selection criteria were known to the interpreting physicians prior to review.

The protocol for imaging and criteria for interpretation of the images were evolved as the first ten cases were imaged and reviewed. The remaining cases were then interpreted in a standardized manner using the criteria developed. These criteria were as follows.

1. A fallopian tube was considered patent if a relatively intense focus of activity was imaged in the area of the adjacent adnexa, including outlining of ovary(ies) (*1*). The absence of such a focus of activity on images obtained 1 hr or more after administration of radiopharmaceutical was considered to be evidence of tubal obstruction. No study was terminated prior to 1 hr unless the earlier images showed bilateral tubal patency.

2. A "cornu cutoff sign" was developed, i.e., failure to image contiguity of activity from the region of a cornu into an ipsilateral fallopian tube (see Fig. 6). This sign is dealt with in more detail below.

Of the first ten patients studied, only one fallopian tube was reclassified. This was because of a "cornu cutoff" sign that was not recognized early in the series.

The time of termination of studies showing tubal obstruction was determined by the physician tailoring the study based upon (a) plethoric spillage of activity into the peritoneum from a contralateral tube which he considered would result in further delayed images of little diagnostic value (see Fig. 4); (b) no change in appearance of images obtained between 1 hr and 1½ to 2 hr, or (c) willingness of the patient to cooperate with long delayed (up to 4½ hr) images in an effort to see if the diagnostic impression would be altered. One of three different physicians tailored each of the patient studies. The interpretation of the study rendered by the tailoring physician is included as the data in this report, except for the one case mentioned above in which the initial reading was reclassified because of a "cornu cutoff sign." Since the final interpretation of a study depended somewhat upon the decisions made during tailoring of the study, an effort to evaluate for interobserver variability was not systematically made during this evaluation of the efficacy of the RNHSG technique described. All three observers had approximately the same diagnostic accuracy with their interpretations. About 50% of the studies were interpreted by one of the observers and about 25% interpreted by each of the others.

All nuclear interpretations after the initial four prebilateral tubal ligation patients were ultimately correlated with conventionally obtained data. Three patients (six tubes) were correlated with the findings on radiographic contrast hysterosalpingograms and 19 patients (38 tubes) were correlated with observation of spillage (or absence of spillage) of methylene blue dye from the fimbriated ends of the fallopian tubes into the peritoneum at peritonoscopy or surgery after the dye had been introduced into the cervical os under low pressure. Data has been included in this report only if the correlation study was performed within 6 mo of the radionuclide study and there had been no therapeutic intervention in the interim. The totally normal cases showed the easily interpretable pattern, demonstrated and described by

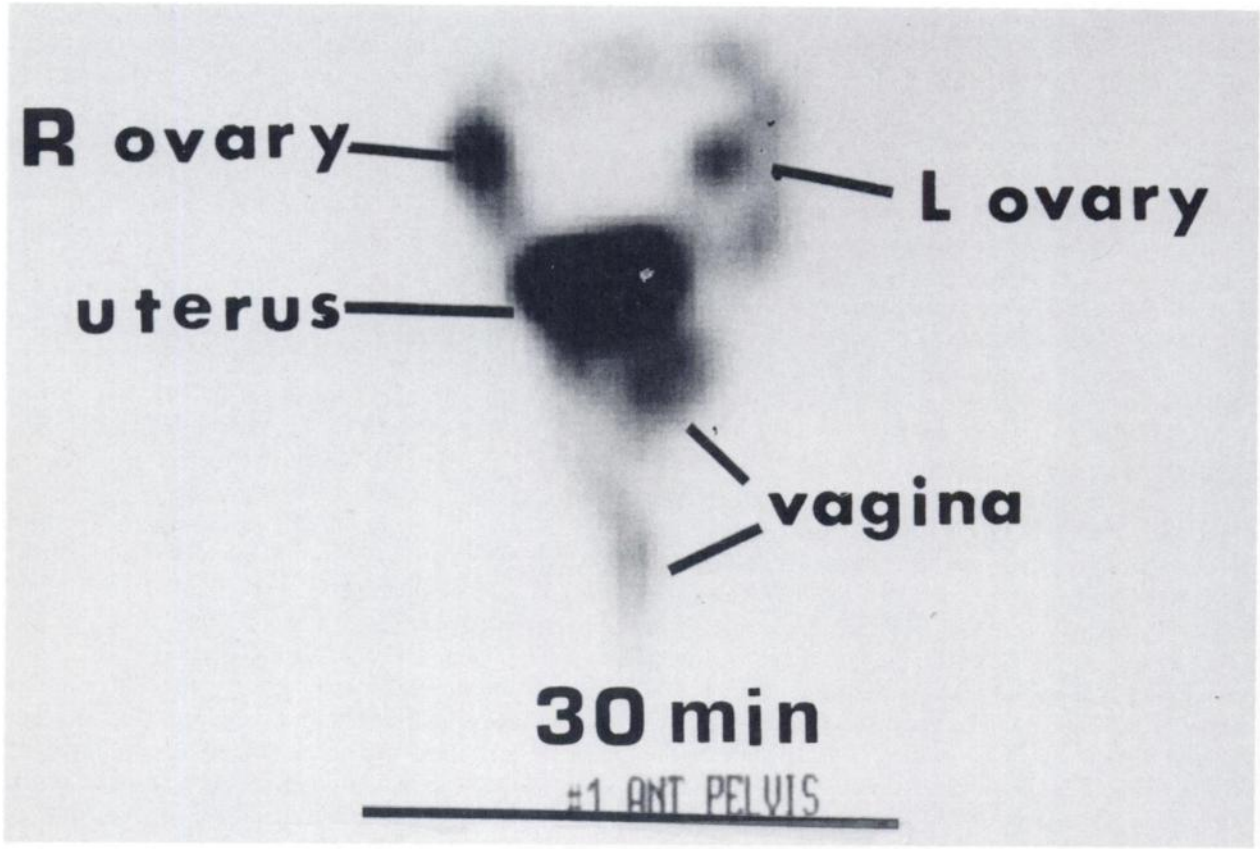

FIGURE 1
Normal radionuclide hysterosalpingogram (RNHSG)

TABLE 1
Correlation for 26 Patients (52 Tubes Studied)

Surgical and contrast hysterosalpingogram data			
	Item	Tube patent	Tube obstructed
RNHSG interpretation	Tube patent	34	1
	Tube obstructed	2	15

Iturralde and Ventner (*1*). The total study involved 26 patients, or 52 fallopian tubes.

RESULTS

In none of the four patients studied prior to bilateral tubal ligation were there any findings at surgery to suggest that the fallopian tubes were not patent, and the resected segments of these tubes were histologically normal.

The findings in all 26 patients (52 tubes = 100%) are presented in Table 1. Using results of contrast tubal patency studies (except in the four initial normal patients) for correlation in these 52 tubes, the sensitivity of the test for detection of tubal patency was calculated to be 92%, and the specificity 93%. For the detection of tubal obstruction, the calculated sensitivity was 93% and the specificity 92%. The overall predictive value of the test for tubal patency was 95% and the predictive value for tubal obstruction 88%. The overall efficiency (percent of tubes correctly classified) of radionuclide hysterosalpingography was 94%, when using the contrast studies as the "gold standard." Figure 1 shows a typical image in a normal patient with bilateral tubal patency. Figure 2 shows unilateral obstruction and Fig. 3 shows bilateral obstruction.

DISCUSSION

Human serum albumin microspheres were felt to be appropriate for this procedure since they measure between 10 and 35 μm in diameter, with a mean diameter of 20 μm. This roughly approximates the size of a human sperm which measures ~8 μ in diam at the head and is 40 μ long. There is no reason to believe that other agents such as sulphur colloid would not be successful. Agents which could be absorbed into the bloodstream from the peritoneum and subsequently excreted into the urine would result in bladder activity that could confuse interpretation of the images.

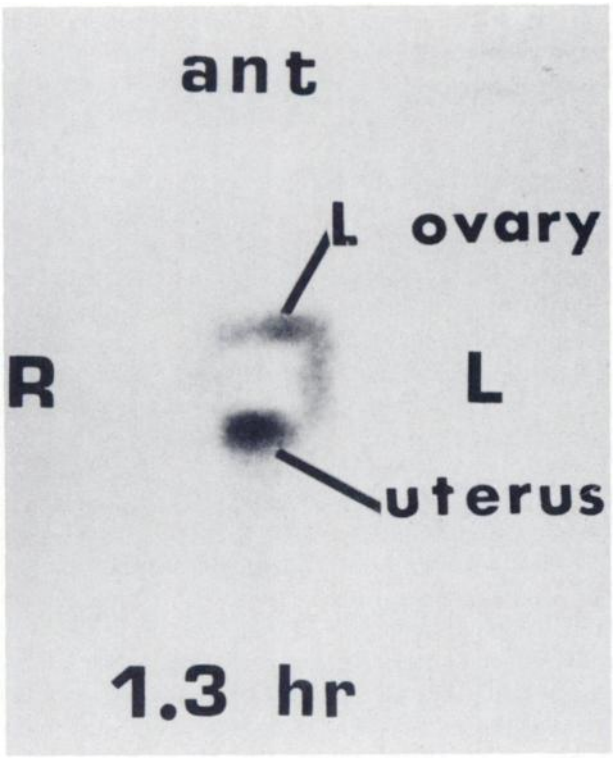

FIGURE 2
RNHSG showing patent tube on left but obstruction on right

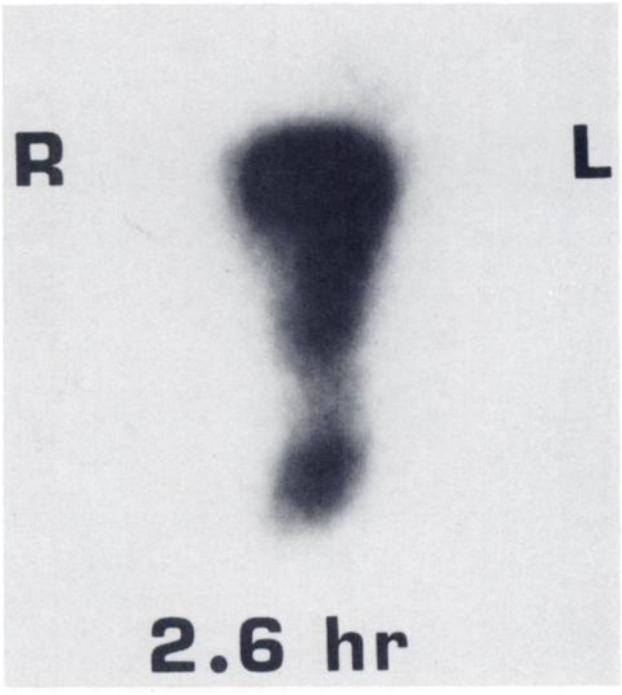

FIGURE 3
RNHSG showing bilateral fallopian tube obstruction

Copious spillage of activity into the peritoneum on delayed images (beyond 1 hr) occasionally rendered interpretation of such images difficult (Fig. 4). In only one fallopian tube out of 52 was information obtained on images delayed beyond 1 hr that was not clearly available on images obtained at or prior to 1 hr. The study of this patient demonstrated bilateral obstruction on earlier images, but suggested unilateral patency at 4 hr. She was found at surgery to have complete obstruction on one side and a patent but fibrosed and barely motile tube on the other. Thus this delayed finding was probably misleading rather than helpful since the tube was apparently subtotally functionally occluded and not likely to allow normal reproductive function.

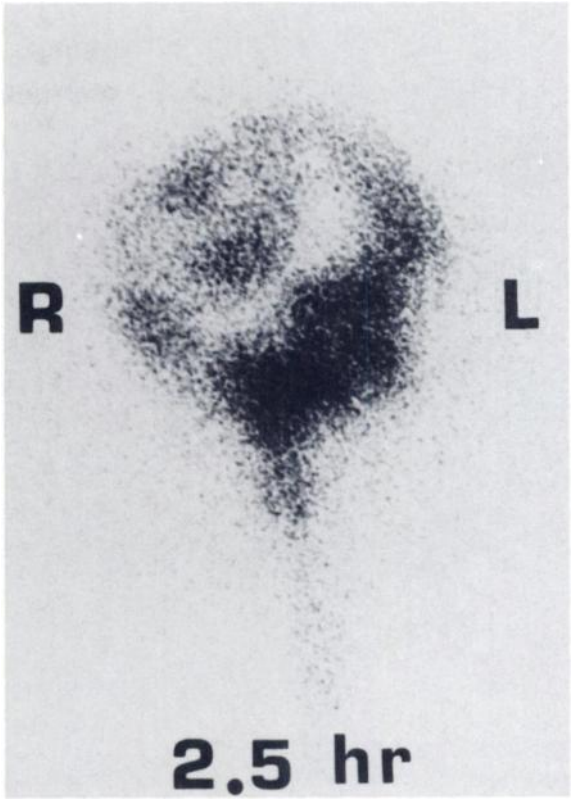

FIGURE 4
Copious spillage of activity into peritoneum renders interpretation difficult

A discussion of the three patients for whom the RNHSG results did not agree with contrast study datum is in order. In one patient, the RNHSG was interpreted as showing bilateral patency while the patient was found to be obstructed on one side at surgery. A collection of activity that had spilled from the patent tube may well have been misinterpreted as having accumulated on the contralateral ovary by way of a patent tube on that side. This study was performed near the beginning of the series. Careful attention to oblique views (which were obtained only when the frontal projections showed questionable findings) obtained on the selected subsequent patients probably enabled us to avoid this pitfall later in the series. The use of rotational single photon emission computed tomography

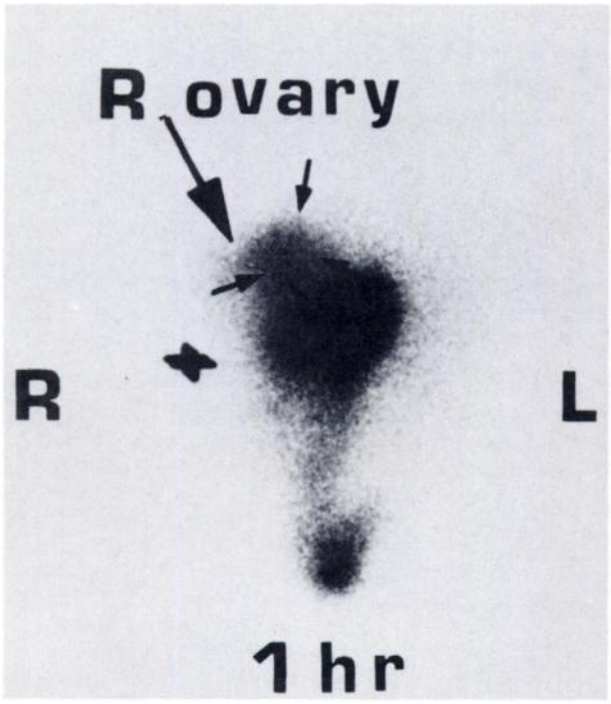

FIGURE 5
Activity on right ovary which is adjacent to posterolateral aspect of uterus (arrows). Left fallopian tube is obstructed

(SPECT) imaging should theoretically eliminate such problems.

The RNHSG technique described two other patients as having unilateral tubal obstruction while methylene blue dye introduced into the cervical os under low pressure showed the tubes to be anatomically patent on both sides in both patients. One of these two patients was considered to have an "obstructed" tube on the basis of a "cornu cutoff" sign. The tubes in these two patients that were classified as obstructed by the RNHSG technique were described at surgery as being immotile with peritubal and periadnexal adhesions and attachment to bowel or pelvic wall. Based upon these observations, the surgeon's impression was that although these tubes were anatomically patent and able to allow passage of dye injected under pressure, they were probably unable to actively transport particles and presumably sperm. Iturralde and Ventner have also described five patients in whom RNHSG seemed to demonstrate functional tubal obstruction in immotile but anatomically patent tubes (*1*).

If the hypothesis supported by our limited data as well as that of Iturralde and Ventner (*1*) that anatomically patent but "functionally obstructed" fallopian tubes are identified by RNHSG is correct, actually only one fallopian tube out of 52 studied was incorrectly classified by radionuclide hysterosalpingography in this study. This would increase the overall efficiency of the test in our study from 94 to 98%.

Some of the images obtained were more difficult to interpret than those shown in Figs. 2, 3, and 4. Figure 5 shows such a case in which the left tube is obstructed but activity on the right ovary is evidence for right tubal patency. The right ovary is positioned adjacent to the posterolateral aspect of the uterus making it difficult to separate the two structures as distinct entities. Figure 6 shows a "cutoff" of activity in the area of the right cornu of the uterus and no activity emanating from this area. The "cornu cutoff" sign was seen in studies of four fallopian tubes and led to a correct diagnosis of tubal obstruction three times, the fourth case showed patency on a methylene blue procedure but was judged to be functionally obstructed at surgery. Figure 7 shows two well-defined collections of activity in the areas of the two ovaries suggesting bilateral tubal patency. However, the presence of a "cornu cutoff" sign on the right enabled the observers to correctly classify this patient as having unilateral obstruction. The extra focus of activity may be a convolution of the patent fallopian tube. SPECT imaging using rotational acquisition has the potential to minimize geometrical problems by viewing the images either in cine format or after reconstruction in various tomographic planes which might alleviate some of the difficulties in imaging interpreta-

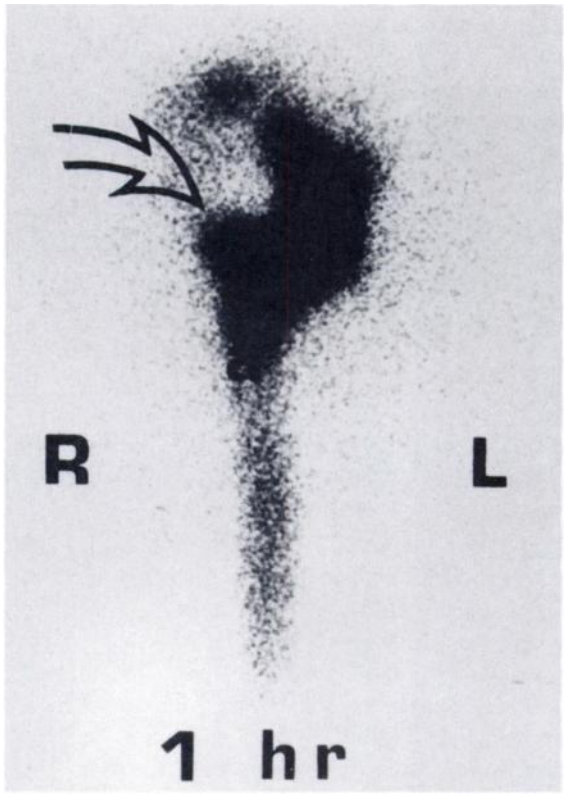

FIGURE 6
Note abrupt cutoff of activity in area of right cornu of uterus (arrow). Patient had obstruction on right with patent hydrosalpinx on left at surgery

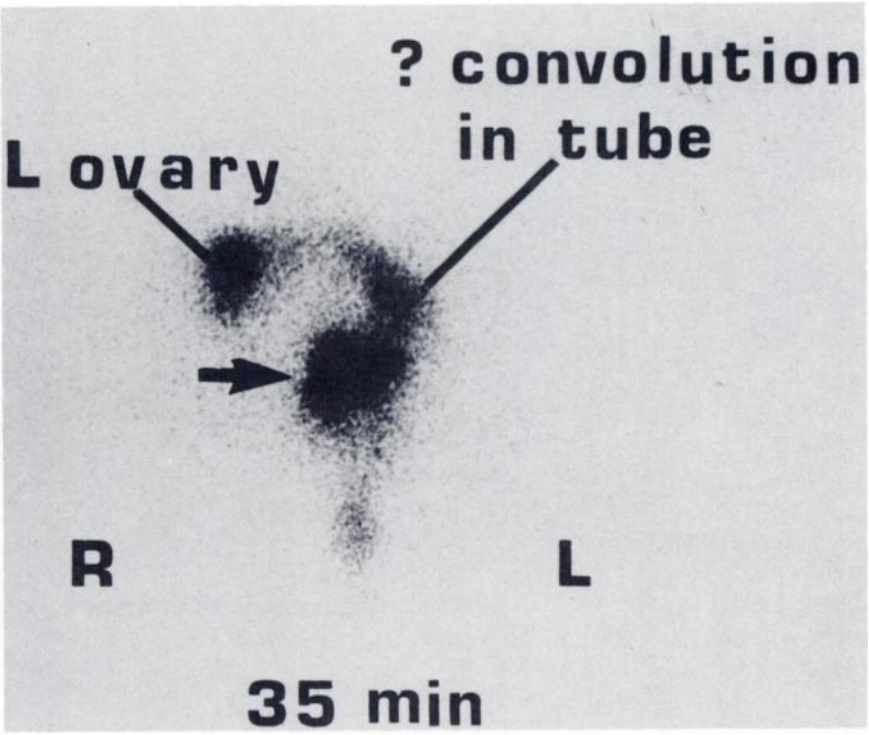

FIGURE 7
RNHSG showing patent fallopian tube on left with obstruction on the right. Note "cornu cutoff" at right adnexa (arrow). Concentration of activity in area of proximal left fallopian tube is probably convolution of tube (see text)

tion described above and thus improve reliability and ease of interpretation and performance of studies.

Although no attempt was made to describe morphological differences of the genital tract from RNHSG images, some of the images suggested the presence of a hydrosalpinx and these impressions correlated well with findings at surgery. Figure 6 represents such a case.

DOSE ESTIMATION

In two normal patients data was acquired onto a computer from anterior images of the pelvis obtained using a parallel-hole collimator at 30 and 60 min following vaginal administration of the ^{99m}Tc-labeled microspheres. Regions of interest were chosen over each ovary, the uterus, vagina, and the area between the uterus and ovaries (which presumably includes the fallopian tubes and activity that has spilled into the peritoneum). Analysis of this data indicated that between 5 and 7% of the total administered dose was present on each ovary at both time intervals. Assuming that 5% of the administered dose resides on each ovary for the duration of decay of ^{99m}Tc and taking into account radiation from adjacent areas (including vagina and uterus), the total absorbed dose to each ovary is 1.8 rad per administered mCi of ^{99m}Tc as calculated using S values from MIRD Pamphlet No. 11 (*2*). The Oak Ridge Radiopharmaceutical Internal Dose Information Center assumed a more conservative value of 7.5% of administered activity finding its way to each ovary (personal communication, June 1984). Based on this assumption, they calculated a total dose of 2.8 rad/mCi to each ovary.

Nearly all patient studies performed in this series were obtained using a pinhole collimator, this is relatively inefficient. Decreasing the administered dose will, of course, lengthen the acquisition time of the images. Rotational acquisition of data using a gamma camera with a far more efficient parallel hole collimator for SPECT should allow for obtaining excellent quality diagnostic information in a reasonable time (20–30 min per study), but with a marked decrease in administered activity. The dose to the patient would be reduced linearly as the administered dose of radiopharmaceutical is decreased.

The dose to the ovaries from diagnostic radiologic contrast hysterosalpingography is difficult to determine since fluoroscopy time and number of overhead and spot films will vary from institution to institution. The National Council on Radiation Protection and Measurements (NCRP) (Report No. 54) (*3*) reports the absorbed dose to the ovaries from x-ray hysterosalpingography to be as high as 6.7 rad not including the dose due to fluoroscopy. Using a freshly calibrated radiography and fluoroscopy room at our institution, dose to the ovaries for each spot film was calculated to be 225 mrad plus an additional 600 mrad for each minute of fluoroscopy. Other authors have reported the potential for lowering the gonadal radiation burden from contrast hysterosalpingography with the use of 100 mm fluorography (*4*).

The NCRP states that the risk to a fetus is considered to be negligible with an absorbed ovarian dose of 5 rad or less when compared to the other risks of pregnancy to the fetus. The risk of fetal malformation is significantly increased above control levels only at doses above 15 rad. This data indicates that the RNHSG technique reported here is within the limits of safety as it is currently performed, giving an ovarian dose approximately in the median range of the x-ray hysterosalpingography. Lowering the dose by 50% or more using SPECT technology would obviously be desirable and in accordance with the "as low as reasonably allowable" (ALARA) concept.

CONCLUSION

Our work confirms the observation of Iturralde and Ventner that inert particles are easily and spontaneously transported from the vagina through the genital tract to the ovaries. This implies that sperm motility, although possibly essential, e.g., for penetration of the ovum, may not be the basic factor in sperm transport. It also confirms that pathogenic materials deposited in the vagina can be transported onto the ovary and may play a role in the etiology of some ovarian carcinomas. This point becomes especially significant when one considers that talc, which is sometimes applied directly to the perineum or used as a lubricant in prophylactics, can contain as much as 30% asbestos.

As a diagnostic imaging modality, the procedure for radionuclide hysterosalpingography described produced images which the authors learned to interpret in a relatively straightforward way. RNHSG appears to be very accurate when correlated with anatomic criteria. The apparent ability of this technique to detect functional (adynamic) tubal obstruction in the face of anatomic patency suggests that it may provide not only a more acceptable but also a more valid approach for the evaluation of the status of the fallopian tubes in assessing the etiology of infertility. This information is not available from any modality other than direct observation of tubal motility at surgery. RNHSG is a suitable study for the evaluation of tubal function in most clinical circumstances in the investigation of failure to conceive. There are some additional circumstances in which it seems particularly attractive.

For example, patients who have had a surgical reanastomosis or tuboplasty for previously ligated or fibrosed tubes are at an unacceptable risk (3.3%) of developing a tubo-ovarian abscess as a complication of contrast hysterosalpingography performed during the first few weeks following surgery (*5*). Thus for this patient population, RNHSG procedure becomes a particularly attractive method for follow-up of the success of the surgery initially and then in the face of failure to conceive. RNHSG is also a simple, noninvasive way to confirm the success of a tubal ligation, which is a practical problem with potential legal implications for the surgeon.

The radionuclide hysterosalpingogram is a simple, accurate, noninvasive procedure. It uses a radiopharmaceutical and imaging equipment that is available in most nuclear imaging laboratories. The technique is relatively innocuous to the patient since it involves neither injection of contrast material into the cervical os under pressure nor direct intra-abdominal inspection. All of the patient volunteers in the study accepted the procedure readily and no noteworthy complications were anticipated or found. The radiation burden to the ovaries in RNHSG is comparable to that of contrast hysterosalpingography. It is likely that the administered dose could be decreased when imaging with a planar collimator during rotational acquisition of data for a SPECT imaging system (instead of using a pinhole collimator). The use of SPECT also promises to minimize geometrical imaging problems and potential interobserver error.

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