COLLOIDAL RADIOGOLD IN MALIGNANT EFFUSIONS AND EARLY OVARIAN CARCINOMA

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Radiogold has the advantage over most other sources of ionizing radiation in that it can be used either as a solid gamma-ray emitter (radiogold seeds) or as a liquid beta-ray emitter (colloidal radiogold). Radiogold seeds can be used as substitutes for radon seeds. During the past decade colloidal radiogold has emerged as a therapeutic agent of great promise in certain malignant conditions. Owing to its short half-life, its chemical inertness and its availability in a chemically pure state, colloidal radiogold can be used intravenously, interstitially and intracavitarily.

Recurrent malignant fluid formation in the pleural or peritoneal cavities in advanced malignant disease is a troublesome problem requiring frequent paracentesis to relieve the embarrassed patient, but since the advent of colloidal radiogold a method of treatment is available that is simple and effective in controlling these recurrent effusions in the vast majority of cases. In using colloidal radiogold, however, strict precautions must be taken to protect the nursing staff and visitors from stray gamma radiation emitted by the radioactive patient.

We have used colloidal radiogold essentially as a palliative measure to control recurrent pleural and peritoneal effusions in advanced malignant disease. Recently, however, one of us (E.L.J.) has used colloidal radiogold intraperitoneally as a curative measure for early ovarian cancer and some other malignant abdominal lesions following radical surgery.

This article reviews the value of colloidal radiogold as used in intracavitary radiotherapy during the past 5 years (1953-57), (1) as a palliative measure in the treatment of 38 cases of advanced malignancy in which different primary cancers presented with recurrent troublesome malignant pleural or peritoneal effusions, (2) as a curative measure in 6 cases of early ovarian cancer following radical surgery, and (3) as a curative measure in 3 miscellaneous cases. We have treated in all 47 cases with colloidal radiogold.

REVIEW OF THE LITERATURE

Müller[1] of Zürich (1945) was the first to use suspensions of radio-isotopes in the control of malignant ascites. He first used radiozinc prepared in a cyclotron, which he injected into the abdominal cavity of a patient suffering from advanced malignancy with ascites, and was able to keep the patient free of fluid for 3 years. Later[2] he used colloidal radiogold prepared in a nuclear reactor and by 1950 he was able to report encouraging results in 8 cases following the intraperitoneal administration of colloidal radiogold.

Since 1950 numerous reports have attested to the value of this radio-isotope in the control of malignant effusions. Kent *et al.*[3] in an analysis of 51 cases of malignant ascites treated with colloidal radiogold reported improvement in 60% of their cases. Walter[4] was able to control malignant ascites effectively in 7 out of 15 patients, while Storaasli *et al.*[5] found a good response in 7 out of 13 cases. Simon *et al.*[6] obtained favourable results in 7 out of 14 cases of malignant pleural effusions. Colby[7] administered colloidal

radiogold intrapleurally in 41 patients and was able to record a good result in 40%.

Kligerman and Habif[8] treated 35 cases of malignant pleural and peritoneal effusions and found that colloidal radiogold proved to be of value in 50% of those patients who had survived 1 month or more after the injection. They concluded that for the limited purpose of controlling malignant fluid formation in the serous cavities, colloidal radiogold was superior to any form of external radiation.

Dennis, Workman and Bauer[9] analyzed 58 cases of malignant serous effusions treated by them with colloidal radiogold and found that of 17 cases of malignant ascites secondary to primary malignancy of the ovary, 7 cases (41%) revealed a definite palliative benefit with an average duration of 4·5 months. Of the 10 patients who showed no improvement, all had large palpable masses when treated and 7 died within 30 days of the treatment. In 19 cases with pleural effusion secondary to proved bronchogenic carcinoma, excellent results were obtained in 15 cases (80%) with an average improvement of 5 months. Of the 8 cases of breast cancer with secondary pleural effusion, 6 (75%) showed excellent palliative results, lasting up to 11 months with an average of 5 months. In pleural effusions following lymphoma, they state that the results were surprisingly poor; only 1 case out of 5 showing any palliative response and that for a period no longer than 2 months.

Lewis[10] reported that in the treatment of ovarian cancer, he had used colloidal radiogold both as part of radical and part of palliative methods of treatment. For radical treatment he used colloidal radiogold in cases where free fluid was found in the peritoneal cavity at operation, or spill of malignant cells was suspected, or where small peritoneal seedlings were actually present. For palliative treatment he used colloidal radiogold where recurrent malignant ascites was the presenting symptom and here it was used alone or in combination with other methods. Out of 45 cases, 15 were treated from a curative point of view. Of these 15 cases, 3 have died but only one with ascites; 4 are alive and symptom-free, 29, 26, 18 and 12 months after single doses of about 150 mc. of colloidal radiogold introduced into the peritoneal cavity; 8 others are alive and symptom-free, but all these have been treated less than 1 year ago, and 4 of them less than 6 months. Lewis found that the colloidal radiogold therapy had caused only slight constitutional disturbances in these patients; some nausea without actual vomiting for one or two days seemed to be the rule, but it had not interfered materially with the subsequent general condition or drastically limited the amount of other treatment it had been possible to give them.

Elkins and Keettel[11] record their experience in the treatment of 66 cases of ovarian malignancy with colloidal radiogold from a palliative as well as a curative point of view. In 25 of these cases they had used colloidal radiogold either alone[12] or in conjunction with deep X-ray therapy[13] as a curative measure following hysterectomy and bilateral salpingo-oöpherectomy. They conclude that it was still too soon to draw any conclusions, but they were of the opinion that surgery and external radiation were inadequate for the radical treatment of ovarian cancer, particularly in early cases, and that colloidal radiogold was not only of benefit as a palliative measure in advanced ovarian cancer with recurrent malignant ascites, but that it was perhaps the best curative measure to be used in early cases, alone or in conjunction with external radiation following radical surgery.

Gwen Hilton *et al.*[12] record that during the past 3 years they have treated 100 cases of malignant effusion by intracavitary injection of colloidal radiogold and that the results could be assessed in 94 with primary growths in bronchus, ovary, breast, lymph tissue, stomach, ampulla of Vater, uterine cervix, body of uterus and colon. Of these 94 cases (*a*) 40 showed a good response (i.e. they ceased to make further effusions for a period ranging from 2 to 30 months—a few of them required more than one aspiration before the formation of fluid stopped, and in 12 cases a second injection of colloidal radiogold was required after an interval of 6 weeks to stop the fluid formation); (*b*) 8 showed a moderate response (i.e. they ceased to make effusions rapidly, so that the interval between aspirations could be extended); (*c*) 25 did not respond to treatment (in these cases, numerous or large tumour masses were present, and the authors state that they would not now consider them for treatment with colloidal radiogold); and (*d*) 21 died under 6 weeks.

Our experiences with colloidal radiogold are similar to those of other workers in this field.

THE USE OF COLLOIDAL RADIOGOLD

Source and Transport

In South Africa colloidal radiogold is obtained by ordering it through the South African Atomic Energy Board who, by law, control the distribution of radioisotopes in the Union. The colloidal radiogold arrives 7—10 days after the order has been placed. It is prepared at the Radiochemical Centre in England and is dispatched by air either as air freight or in special wing-tip compartments which require no shielding. After its arrival at Jan Smuts Airport machinery exists for transporting it to any of the major centres of the Union.

Physics

Colloidal radiogold can be prepared with high specific activity and free from radio-active contaminants. It has a half-life of 2·69 days and emits beta- and gamma-rays. The beta-rays have a maximum energy of 0·96 m.e.v., an average energy of 0·39 m.e.v., a maximum range of 4·0 mm. in tissue and a half thickness in tissue of 0·4 mm. The gamma-rays are predominantly of energy of 0·411 m.e.v.

The physiological effects are caused almost entirely by the beta-rays, which give up all their energy to the serosal surface with consequent high dosage to this surface. The gamma-rays are absorbed throughout a much larger volume, producing a more widely distributed dose of lower intensity. They can be detected externally and serve as a check on the distribution of the radiogold in the serous cavities.

By using the theory of Hine and Brownell[13] an approximate calculation may be made by making assumptions as to the distribution of colloidal radiogold in the peritoneal cavity. Assume 100 mc. of colloidal radiogold has been administered and that 80% of this becomes uniformily fixed to the serosal surfaces in the form of a thin film. The serosal surfaces are assumed to have an area of 3 square meters. The beta dosage at various depths below the surface is given in the following table:

Depth in mm.	*Dose in r.e.p.**
0·01	3,500
0·1	1,750
0·5	560
1·0	180
2·0	28

* The r.e.p. in these circumstances is approximately equal to the r.

The gamma dosage may be calculated by assuming the cavity to be spherical and to have a diameter of 16 cm., and that the colloidal radiogold has been uniformily distributed throughout this volume. For 100 mc. administered the dose in roentgens at the centre of this volume will be 1,000 r and at the periphery it will be 500 r.

Protection of Nursing Staff

According to the recommendations of the International Committee on Radiological Protection (1954) an individual may receive a maximum of 300 mr. of stray gamma radiation per week, 3,000 mr. in any consecutive 13 weeks, and 5,000 mr. per year. If only the hands and forearms are exposed, a maximum of 1,500 mr. per week is permissible.

The radiation levels around a patient who has received 250 mc. of colloidal radiogold have been calculated by assuming that the radiogold is situated in the centre of the

abdomen. Dosage rate in mr. per hour at various distances from the patient and at various times after the placing of 250 mc. of colloidal radiogold in the peritoneal cavity are given in the following table.

Day	Distance from the centre of activity		
	12 *inches*	30 *inches*	72 *inches*
	mr./h.	mr./h.	mr./h.
1st	640	100	18
2nd	490	80	14
3rd	380	60	11
4th	320	50	8
5th	230	36	6
6th	180	28	5
7th	140	22	4

Measurements made at the bedside of a patient who had received 250 mc. of colloidal radiogold were about 15% lower than those given in this table.

The time spent by nurses close to patients after surgical administration of colloidal radiogold under a general anaesthetic will depend upon the extent of the operation, the condition of the patient, and any special nursing procedures that are adopted. It would be impracticable to lay down hard and fast rules for the maximum time nurses may remain at the bedside of such patients.

The next table illustrates the order of exposure to be expected under average conditions with no shielding, after surgical administration of colloidal radiogold under a general anaesthetic. We may assume that immediately after the operation the nurse would 'special' the patient until full consciousness had been regained (about 1½ hours). This could be carried out from the head end of the bed (a distance of 30 inches from the centre of activity). Subsequently, washing, changing of dressings, bed making and feeding would take about ¾ hour during the day and about ½ hour at night, with the nurses standing about 12 inches from the centre of activity. Under these circumstances the day and night nurses would receive the following amounts of stray gamma radiation (in mr.) during the first week of nursing:

Day	Time spent near patient (hours)	Distance from activity (inches)	Gamma-ray exposure (mr.)	
			Day nurse	Night nurse
1st	1½	30	150	—
	¾	12	480	—
	½	12	—	320
2nd	¾	12	360	—
	½	12	—	240
3rd	¾	12	290	—
	½	12	—	190
4th	¾	12	240	—
	½	12	—	150
5th	¾	12	170	—
	½	12	—	120
6th	¾	12	140	—
	½	12	—	90
7th	¾	12	110	—
	½	12	—	70
Total			.. 1,940 mr.	1,180 mr.

From the above table it is evident that some form of shielding is necessary to protect the nurses from the stray gamma radiation that is being emitted by the radio-active patient as a result of colloidal radiogold therapy. A lead shield ½ inch thick will reduce the radiation by about 19/20th i.e. to about 2% of the yearly maximum permissible amount.

We recommend that nurses attending closer than 3 feet to radio-active patients treated with colloidal radiogold should at all times work from behind a portable screen of ½ inch thickness of lead (Fig. 1). As the hands and forearms can

Fig. 1. Portable lead shield for nurses attending radio-active patients.

Fig. 2. Portable lead shield in use.

tolerate greater exposures of radiation, she can with safety wash and feed the patient, change the dressings, etc., provided she works from behind the lead screen, in the manner shown in Fig. 2. The portable lead screen is pushed snugly up against the bed so that the half-moon lead shield thoroughly protects the nurse attending to the patient. We also recommend that the attending nurse should wear a face mask, rubber gloves and an overall over her uniform when handling dressings that may have become contaminated with colloidal radiogold. A pocket dosimeter should be pinned to the overall and the sister in charge of the ward should keep a record of its readings, which should be consulted in assigning duties to the nurses.

Preferably all radio-active patients treated with colloidal radiogold should be nursed during the first 2 weeks in a single-bed ward, or at most a two-bed ward with maximum gamma activity per ward of 500 mc.

Young visitors should be allowed only a few minutes in the ward of a radio-active patient and during that time should not come closer than 6 feet to the patient. It would be unreasonable to restrict older visitors (past child-bearing age) in this way but, as a general rule, all visitors should abstain from sitting closer than 3 feet to the patient or staying longer than 1 hour per day during the first week.

Precautions at Post-mortem Examinations

If a patient should die soon after the administration of colloidal radiogold, the post-mortem examination should be delayed until the radio-activity had decayed to a level permitting the pathologist to work without excessive irradiation. The determination of the safe level is based upon a number of assumptions, but it should be sufficiently accurate to give the approximate order of exposure to stray gamma radiation from the radio-active body that is to be expected.

Assume: (1) Rubber gloves 0·5 mm. thick are worn, (2) time taken is 1 hour, (3) activity per unit area of the gloves is the same as that per unit area on the surface of the abdominal organs, (4) surface area of abdominal organs is 30,000 sq. cm. and (5) beta dose permitted is 750 mr.e.p. (approximately equivalent to 750 mr.).

Calculated by the method of Hine and Brownell[13] it was found that the activity in the abdomen should not exceed 10 mc. of colloidal radiogold, i.e. the post-mortem examination should not be performed until 12 days after the administration of 250 mc. of colloidal radiogold, or 9 days after the administration of 100 mc.

The radio-active body at a post-mortem examination should be placed on disposable plastic sheeting to prevent the spread of radio-active contamination, and the area should be surveyed for activity when the examination is over. All persons attending the post-mortem examination should wear rubber gloves, overall and a dosimeter pinned on the overall. A record of the readings should be kept.

The Biological Response

There is no clear explanation of how the colloidal radiogold inhibits the formation of malignant effusions. Andrews *et al.*[14] observed the disappearance of free tumour cells from the fluid after colloidal radiogold therapy in humans, and Goldie and Hahn[15] demonstrated the lethal effect of intraperitoneal colloidal radiogold on free sarcoma cells in the peritoneal fluid in mice. There now appears to be sufficient evidence to show that provided the lesions on the serosal surfaces do not exceed 2·0 mm. in depth the colloidal radiogold has a lethal effect on these small tumours and on the free cancer cells in the serous effusions. Furthermore, the inflammatory reaction produced on the serosal surfaces by the beta-rays of the colloidal radiogold mobilizes the defence mechanism of the body and many of the malignant cells and in some cases tumour masses are disposed of in this way.

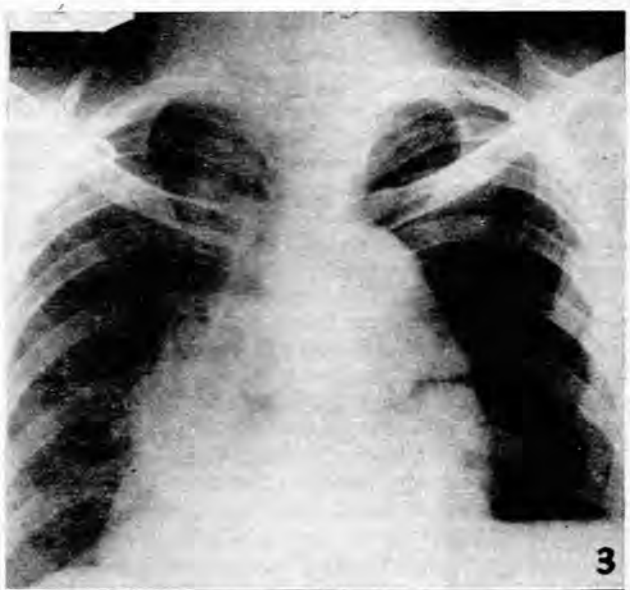
Selection of Patients

Dennis *et al.*[9] suggests as follows: 'In treating these malignant pleural and peritoneal effusions, the patients should be selected carefully for optimal results. Ideally, patients should be (1) those in whom the fluid formation has become a troublesome problem, (2) those in whom the metastases are small serosal seedlings rather than large tumour masses, and (3) those without severe constitutional effects, i.e. cachexia, anaemia, leukopenia, etc. Since the radiation effect is primarily a surface phenomenon, patients with large tumour masses are usually not effectively treated with radiogold as these large tumour masses are insufficiently irradiated. In those patients with severe constitutional effects the radiogold will often produce a rapid cessation of fluid formation but sometimes speed the downhill course.' We are in general agreement with this conception. We have, however, been surprised to see large secondary masses disappear from the pleural and peritoneal cavities after colloidal radiogold therapy administered ostensibly to inhibit recurrent fluid formation; but these cases are exceptional. (Figs. 3 and 4.)

Technique of Colloidal Radiogold Injection

Ingenious methods of protecting the staff from beta and gamma radiation during the injection of colloidal radiogold have been described by many authors, viz. Chamberlain *et al.*,[16] Andrews *et al.*,[14] Simon *et al.*,[6] Tabern *et al.*,[17] Tabern,[18] Shanks,[19] Karioris and Cowan,[20] and Gwen Hilton *et al.*,[12] to name but a few. Most departments of radiotherapy appear to have devised their own particular method of colloidal radiogold injection and protection after much trial and error. No method appears to have gained universal acceptance, except that most authorities favour the simple methods.

Lewis[10] voices the modern trend when he states: 'It is a simple matter to devise lead protection for the container; a lead bottle 2·5 cm. thick reduces the dose rate to tolerance at 7 inches (18 cm.) when holding 300 mc. Remote-control delivery devices, if they are to serve more than one case, have proved less satisfactory. The glass, however, of an ordinary Record or Luer syringe will stop all the beta radiation from the radiogold. A 20 c.c. syringe containing 150 mc. of radiogold will have a surface dose rate of about 300 mr. per minute,



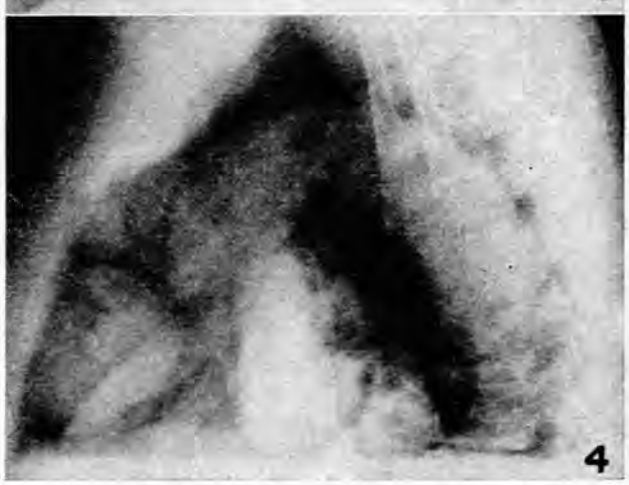


Fig. 3. Case of carcinoma of the kidney. Diagnostic pneumothorax to demonstrate, cannon-ball metastases to the pleura with malignant effusion.

Fig. 4. Same case as Fig. 3. Lateral view showing the cannon-ball metastases. After colloidal radiogold therapy these disappeared completely and the malignant effusion was inhibited. The patient is alive and well 23 months after radiogold therapy.

which would be reduced to 100 mr. per hour by a combination of 0·5 cm. lead shielding and a pistol grip making a syringe-hand-distance of 10 cm. The simplest and quickest approach to serve our purpose thus seems to be a shield protecting a standard syringe to enable a rapid and reasonably accurate injection to be made into the drip tube.'

During the past 5 years we have tried many complicated methods of injecting colloidal radiogold, but they have all been discarded in favour of the shielded-syringe method as described by Lewis.

We have found that by using a Burrell's lipiodol syringe the hands of the operator need not come closer than 5 cm. to the 3-4 c.c. of colloidal radiogold required in the syringe. The dose rate to the fingers of the operator is 160 mr. per minute while the gold is in the syringe. To reduce this to negligible amounts, namely 1·0 mr. per minute we have devised a hollow lead 'candlestick' container for the 25 c.c. Burrell's lipiodol syringe. The thickness of the lead is 0·5 cm. This special lead 'candlestick' container with syringe in position, and a second syringe next to it is shown in Fig. 5 with the bottle containing the colloidal radiogold, along with its lead shield.

Fig. 5. Two 25 c.c. Burrell's lipiodol syringes, one placed in the lead candlestick container, with colloidal radiogold vial and lead container.

The technique that we employ for injecting colloidal radiogold into the serous cavities is as follows:

1. *For malignant pleural or peritoneal effusions as a palliative measure.* Under local anaesthesia a needle is introduced into the pleural or peritoneal cavities and as much fluid as possible is withdrawn; through the same needle, the colloidal radiogold, which is ready in a second similar syringe protected by the lead candlestick container, is introduced directly into the pleural or peritoneal cavity. The precaution is taken of withdrawing small amounts of fluid during the injection to make sure that the colloidal radiogold is reaching the pleural or peritoneal cavity and is not being injected into underlying organs or superficially into the wall of the chest or abdomen. A dose of 50-250 mc. of colloidal radiogold contained in from 3-10 c.c. of reddish-brown coloured fluid is quickly introduced and in a matter of minutes the whole operation is completed. We have found that the dose can safely be repeated in 4-6 weeks if required.

2. *For early ovarian cancer without effusion as a curative measure after radical surgery.* We follow, with some modification, the procedure described by Lewis. If at the time of the radical surgery colloidal radiogold is available, it is introduced through the same incision or preferably through a separate stab wound. If colloidal radiogold is not available at the time of operation, a small stab wound under a general or local anaesthetic is made at a later date. In the absence of ascites it is dangerous to use a puncture needle for fear of introducing the colloidal radiogold into the underlying intestines or abdominal wall. After the stab wound has been made a catheter is introduced and the peritoneum is gathered around the catheter by means of a purse string suture in readiness to close up the abdominal cavity when the catheter is withdrawn at the end of the injection. The catheter is connected to a vacolitre containing 1,000 c.c. of sterile water coloured with methelene blue. A small amount of the coloured sterile water is allowed to flow into the peritoneal cavity to make sure there is no leakage at the wound. Sterile water is preferred to normal saline, for the latter is believed to cause flocculation of the colloidal radiogold.

The colloidal radiogold is then withdrawn from the lead-protected vial and injected into the most distal part of the drip-tubing while the drip is running. Sterile water from the drip-tubing is withdrawn into the syringe at frequent interval

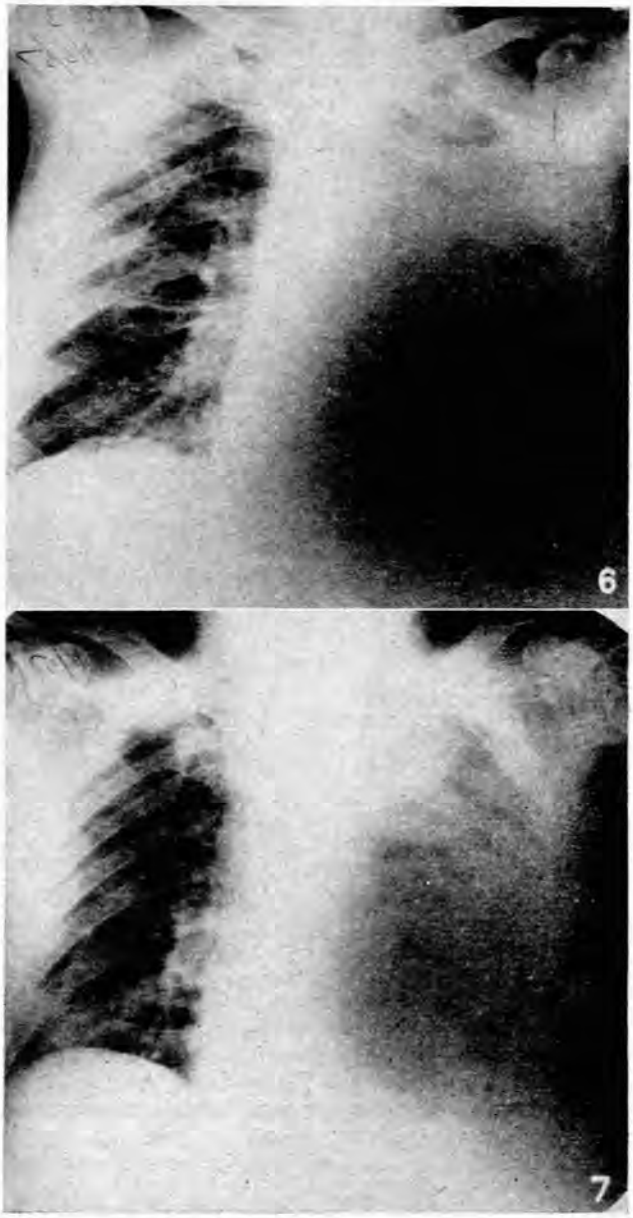


Fig. 6. Radiograph of the chest 24 hours after injection of 100 mc. of colloidal radiogold.

Fig. 7. Radiograph of the chest 120 hours after injection of 100 mc. of colloidal radiogold.

to clear the syringe completely of all the colloidal radiogold. In all, about 500-1,000 c.c. of sterile water is allowed to flow into the abdominal cavity along with 200 mc. of colloidal radiogold contained in about 5 c.c. of fluid, which is injected into the distal end of the drip-tubing in an operation time of not more than 2 minutes from the time the colloidal radiogold is withdrawn from the vial and injected into the abdominal cavity and the catheter is withdrawn and the stab wound closed.

The patient is then returned to the ward and made to lie first on one side and then on the other to obtain a good distribution of the radiogold in the abdominal cavity. The distribution can be checked, as shown by the accompanying radiographs of the chest following upon colloidal radiogold injection (Figs. 6 and 7) or by a gammagram of the abdominal cavity, which is more accurate (Fig. 8).

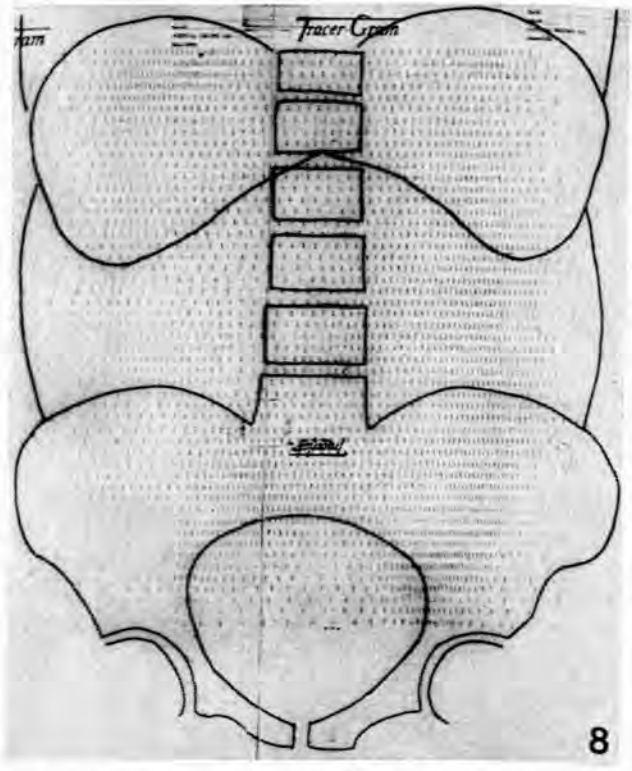


Fig. 8. Gammagram showing distribution of colloidal radiogold in the peritoneal cavity 24 hours after administration. Greater concentration on left side. There was a stab wound on the right side, and the patient preferred to lie on the left side owing to the wound pain on the right side.

Reactions and Complications

Elkins and Keettel[11] record the following reactions and complications following intraperitoneal colloidal radiogold therapy:

Nausea for a few days, sometimes associated with vomiting. A slight rise in temperature. Pain that varied from a mild discomfort relieved with aspirin to a rather severe peritoneal reaction necessitating the use of morphine. A faecal fistula occurred in one case, which they ascribed to a probable perforation of the intestine at the time of injection; it closed spontaneously without ill-effects. In one instance the entire amount of colloidal radiogold was by mischance injected into the abdominal wall. This resulted in a severe subcutaneous and skin reaction necessitating two excisions of the involved area. In 9 of their cases they had occasion to reopen the abdomen up to 14 months after the intraperitoneal injection of colloidal radiogold; in some cases they found no changes that could be attributed to the colloidal radiogold, whereas in others the peritoneum was thickened rather like that seen in chronic peritonitis. Adhesions were present with some loops of intestine adherent to other loops, but in no case did these adhesions cause obstruction. They noted that a gold discolouration of the peritoneum and outer serosal surfaces of the intestines was present in most cases. They conclude that colloidal radiogold is not an entirely innocuous agent and that intestinal changes may occur months or even years after the injection of colloidal radiogold.

On one of our cases in which a post-mortem was performed on the 10th day after the injection of a 100 mc. of colloidal radiogold into the peritoneal cavity, there was no evidence of gold discolouration of the serosal surfaces. In this case colloidal radiogold had been administered for recurrent fluid in which malignant cells had been found, but no primary lesion had been discovered. At the post-mortem there was no evidence of malignancy; the patient had died of cirrhosis of the liver. In another case, where the colloidal radiogold had been given as a curative measure after hemicolectomy for cancer of the caecum, the patient returned 21 months later and was operated on for obstruction due to adhesions. At the operation there was no evidence of gold discolouration of the serosal surfaces nor was there any evidence of metasteses. The patient made an uneventful recovery.

Excretion of the Colloidal Radiogold

If colloidal radiogold is introduced into the serous cavities, it either remains in the ascitic fluid or it is deposited on the serosal surfaces, where it decays. Only a small proportion is absorbed into the blood-stream or lymphatics. In intracavitary colloidal radiogold therapy the blood level of radioactivity remains low in contrast to the high blood level following interstitial colloidal radiogold therapy. Excretion of colloidal radiogold introduced into the serous cavities is therefore negligible and no special precautions for disposal of urine and faeces are necessary (Gwen Hilton *et al.*,[12] Andrews *et al.*[21]).

RESULTS OF COLLOIDAL RADIOGOLD THERAPY

During the past 5 years (1953-57) we have treated 47 cases of cancer either palliatively or curatively with colloidal radiogold. The colloidal radiogold was introduced into the pleural cavity in 14 cases with 5 repeats, and into the peritoneal cavity in 33 cases with 5 repeats.

Of the 47, 38 were cases of advanced malignant disease with recurrent pleural or peritoneal effusions which were treated palliatively, 6 were cases of early ovarian cancer which were treated curatively following radical surgery, and 3 do not fall into either of these categories.

1. *Advanced Malignant Disease*

In an analysis of the 38 cases the primary growth was located in the thyroid, breast, bronchus, lymph tissue, ovary or kidney, and in 5 cases the site of the primary lesion could not be established. One of the 5 died of cirrhosis of the liver with no post-mortem evidence of malignancy. Of 38, 14 presented with recurrent pleural effusion and 24 with recurrent peritoneal effusion; the results of colloidal radiogold therapy have been grouped together. A good response is recorded where the colloidal radiogold therapy produced complete inhibition of fluid formation; a fair response where fluid formation was retarded and after a second course ceased to form; and a poor response where the patient died within 2 months of receiving the colloidal radiogold therapy.

The results in the 38 cases were as follows:

(*a*) 8 (21%) died within the 2 months, some, however, in the absence of fluid.

(*b*) 16 (42%) showed a good response, some even dramatic, and in one case, the patient remained fluid-free for 31 months before death. These cases remained fluid-free for an average period of 7·5 months before death.

(*c*) 10 (26%) had recurrent effusions requiring a second course of colloidal radiogold therapy 4-6 weeks after the first course. These cases had required frequent tapping before the colloidal radiogold therapy. After the first injection fluid formation was reduced but not completely stopped, and although tapping was less frequent it still caused embarrassment. After the second injection they remained fluid-free until they died. These patients lived on an average about 4 months after the first injection and during this period fluid formation was greatly reduced and usually ceased after the second injection of colloidal radiogold. 4 (11%) are still alive, 8 months, 4 months (2) and 3 months after a single injection of colloidal radiogold, and there is no evidence of recurrent fluid formation.

These 38 patients were given from 50-100 mc. of colloidal radiogold intrapleurally or 150-250 mc. intraperitoneally. Nausea was frequently complained of after the injection, and in some cases it was followed by vomiting. The severest constitutional reactions seemed to follow intraperitoneal therapy. The reactions were never so severe as to contra-indicate colloidal radiogold therapy for advanced malignant disease.

We are of the opinion that all these advanced cases of malignant disease suffered no unjustifiable ill-effects following colloidal radiogold therapy. Although 21% must be classed as failures as far as the inhibition of fluid formation was concerned, the patients' state of health was not aggravated by the therapy. We are satisfied that 79% derived great benefit. This is most gratifying when one considers that there is no other method of treatment available (other than the less satisfactory method of using nitrogen mustard) that can bring about the inhibition of recurrent malignant fluid formation. There was never any hope of bringing about a cure in any of these cases of advanced malignant disease; nevertheless, the results have been most dramatic in a large proportion, and the patients have been able to carry on with their work right up to the very end.

2. *Early Ovarian Cancer*

The following is an analysis of the 6 proved cases of early ovarian cancer. These cases were treated with colloidal radiogold introduced intraperitoneally by one of us (E.L.J.). The colloidal radiogold was employed as a curative measure following radical surgery and in the absence of any known malignant spread. The dose administered varied from 150 to 250 mc. Each case received one dose only. They were all seen as follow-ups during the month of July 1957 and the results are tabulated as follows:

Case number	*Radiogold given*	*Dose in mc.*	*Alive and symptom-free in months after therapy*
1	9.12.53	150	43
2	10.9.54	250	34
3	24.8.55	200	23
4	6.10.55	150	21
5	29.2.56	250	17
6	26.1.57	200	6

The method of using colloidal radiogold therapy as a curative measure following radical surgery in early ovarian cancer is put on record in this article, but it is still too soon to analyse these cases any further. They are at present all in excellent health with no signs of any recurrence or other complications.

3. *The 3 cases in other categories*

(i) *Ovarian cancer with peritoneal spread.* A woman aged 45 who was diagnosed as suffering from malignant ascites was operated upon on 15 September 1954 and a primary papillary adenocarcinoma of the ovary was found, which had ruptured through the capsule and had invaded the peritoneum and omentum. There were adhesions between coils of intestine and to the peritoneal wall in the region of the splenic flexure, with a considerable amount of free fluid. A hysterectomy and bilateral salpingo-oöpherectomy was performed. The patient had a stormy convalescence after an ileus from which she recovered. On account of the presence of known residual malignancy, deep X-ray therapy was given from 12 October to 10 November. A tumour dose of 3,600r was administered in 4 weeks to the pelvic area. On 16 November 1954 150 mc. of colloidal radiogold was injected into the peritoneal cavity with the object of obtaining a good dose over the whole peritoneal cavity. This patient is alive and symptom-free 33 months later.

(ii) *Uterine cancer with peritoneal spread.* A woman aged 55 had a hysterectomy performed for carcinoma of the uterus in 1953. In 1955 she had an operation for a ventral hernia, and at operation it was discovered that she had a solitary peritoneal nodule which on microscopic examination was found to be a metastasis from the uterine cancer. On 15 August 1955 colloidal radiogold was administered intraperitoneally. She suffered a severe reaction after the gold therapy but made an uneventful recovery and is alive and symptom-free, now 24 months after colloidal radiogold therapy.

(iii) *Caecal cancer with no obvious spread.* A man aged 55 had a hemi-colectomy performed on 16 August 1955 for carcinoma of the caecum. The carcinoma had penetrated the caecum to the peritoneal covering but had not extended through the peritoneum, nor was there any evidence of peritoneal spread. In October 1955 colloidal radiogold was administered intraperitoneally. The patient made an uneventful recovery, but returned 21 months later and was operated on on 16 June 1957 for intestinal obstruction due to adhesions. There was no evidence of metastases at the operation. The patient is alive and symptom-free, now 23 months after radiogold therapy.

CONCLUSION

We are of the opinion after reviewing the literature and analysing 47 of our own cases of malignant disease treated with colloidal radiogold that this method of treatment has (1) a decided place in the treatment of troublesome recurrent malignant fluid formation in the serous cavities in advanced malignant disease, (2) that, to improve the 5 year results, it should be seriously considered as a curative measure in the treatment of early ovarian cancer following radical surgery, either, alone in the absence of any obvious malignant spread, or in conjunction with deep X-ray therapy in the presence of known residual malignancy, and (3) that it should be recommended as a curative measure in cases of possible spread in the pleural and peritoneal cavities after radical operation for cancer in these areas.

We should like to emphasize that the administration of colloidal radiogold is quite simple and safe from the patient's point of view, but that it carries a heavy hazard for the nursing and medical staffs if strict precautions are not taken in the administration, in the subsequent nursing and, if the patient dies soon after colloidal radiogold therapy, in the post-mortem examination.

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