safeguarding the Protestant succession by the Act of Settlement of 1701, by which the crown was transferred from the Catholic House of Stuart to that of Hanover, and so brought George I and his descendants to the English throne.

We express our profound gratitude to his Royal Highness Prince Ernst August of Hanover, Duke of Brunswick and Luneburg, head of the House of Hanover, and to Her Royal Highness Princess Ortrud for their personal interest and invaluable help, and for permission to consult and quote from family papers in the Niedersächsische Staatsarchiv, Hanover.

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Endolymphatic Therapy for Malignant Melanoma

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Among those who have studied malignant melanoma there is general agreement that the primary tumour should be widely excised to prevent local recurrence. It is also agreed that regional lymph nodes should be excised if on clinical examination they seem to be involved. Where uncertainty and disagreement occur is in the management of patients in whom the regional nodes are clinically uninvolved. Fortner *et al.* (1964), who performed routine block dissections in such patients, found that in 38% of them the nodes contained microscopic metastases. Block dissection, inevitably and unfortunately, carries definite morbidity and mortality rates, and many surgeons prefer to avoid its routine use, waiting to see if nodes become enlarged before operating.

Endolymphatic therapy to nodes in such cases is largely free of the complications and disadvantages of block dissection. Earlier work (Edwards *et al.*, 1965, 1966; Edwards, 1966) has suggested that it might be effective in place of block dissection. Where the metastases are microscopic they might be destroyed, and over a greater anatomical range than by block dissection; and where there are no secondaries no harm would be done. We have used it routinely after excision of primary melanomas, as the sole initial treatment to the regional nodes when they were not enlarged, or after a suitable interval followed by block dissection if they appeared to be involved. The treatment is described in greater detail below.

Endolymphatic therapy consists of an injection into a lymph vessel near the primary site so that the lymph pathways, the vessels, and nodes draining the tumour area are filled. The material injected, usually a radioactive isotope, lodges in the nodes, where it delivers a heavy dose in close proximity to metastases should they exist. When the isotope is, for example, iodine in Lipiodol the nodes are opacified and radiographs may reveal metastases that might be undetected clinically. Further changes in nodes may be studied in subsequent radiographs, as the medium remains in the nodes for several months.

We report here observations on a group of patients given endolymphatic therapy and compare them with another group treated without its use.

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Clinical Staging and Management of Melanoma

Clinical staging of melanoma (stage I, primary alone; stage II, regional nodes involved, analogous to that used for carcinoma of the breast) has proved useful in prognosis and treatment, though other authors have not, so far as we can find, made use of it to any extent.

Clinical stage I melanoma is defined as primary melanoma with the regional nodes clinically negative, and clinical stage II melanoma as primary melanoma with the regional nodes clinically positive.

Treatment of Primary Lesion in Clinical Stage I Melanoma

Role of Biopsy.—Where the diagnosis of melanoma is highly probable on clinical grounds full definitive excision is performed without previous biopsy. Otherwise suspicious lesions are first excised with a clear margin of apparently healthy skin around the mole and further treatment given when indicated. Incisional biopsy—that is, actually cutting out parts of the tumour—is avoided.

Definitive Treatment of Primary Melanoma.—Many of the patients had primary melanoma situated on the lower limb. The description below relates largely to this site. The excision is wide in extent and a skin graft is necessary to cover the defect unless an amputation is done. The excision should be sufficient to exclude recurrence due to intradermal lymphatic permeation. This usually means excising an ellipse of skin some 6 by 4 in. (15 by 10 cm.) with its long axis in line with that of the limb. The depth of excision included the deep fascia in nearly all our earlier cases when the primary was treated in our own clinic. More recently we have taken the excision down to the deep fascia but left this layer intact following Olsen's (1964) report suggesting that this made recurrence less likely.

In most instances the lesion and surrounding skin have been gently washed with surgical spirit and covered with a layer of Nobecutane or Steridrape before excision. After complete excision the operation area is washed with clorpactin or distilled water to kill loose cells. The skin graft has always been taken from the opposite limb as a first separate operation in order to avoid possible contamination and implantation of tumour cells.

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Cade (1961) and Petersen *et al.* (1962) also advise using the opposite limb.

Endolymphatic Therapy in Clinical Stage I Melanoma

Therapeutic lymphography is done two to three weeks after excision of the primary. There are several reasons for this delay: (1) to be sure that the lesion excised proves to be melanoma on histological analysis, (2) to provide time to procure the isotope preparation from the Radiochemical Centre, and (3) to provide an interval for possible tumour metastases in transit to arrive at the regional nodes. This is an idea promulgated by Petersen *et al.* (1962) and by other workers.

(a) Dosage

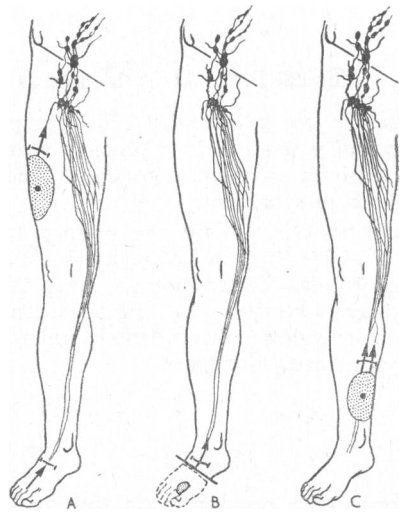
The dosage of radioactive ^{131}I in Lipiodol now aimed at is 40 to 45 mCi in 4 ml. of Lipiodol for the lower limb and 30 to 35 mCi in 2 ml. of Lipiodol for the upper limb. Occasionally bilateral pedal or brachial lymphograms were made with these dosages to each site, and in one instance all four limbs were infused for melanoma of the back. Most of the radiation effect due to ^{131}I is obtained from the β-particle emitted from the isotope. The penetration of these particles is to a maximum of 2 mm. in tissue, with a mean of 0.3 mm. The dosage was increased to the present level in order to produce higher concentration of the particle capable of penetrating 2 mm. and was correlated with histological analysis of block-dissection specimens. The radiation received by lymph nodes with this order of dosage was calculated by direct measurement of excised nodes, using the formulae of Hine and Brownell (1956), to be up to 100,000 rads per g. (Edwards *et al.*, 1966; Edwards, 1966).

The amount of ^{131}I Lipiodol used is important. It has been found that 4 ml. when infused from the lower limb is sufficient to fill ilio-inguinal and para-aortic lymph node groups of an adult patient without undue spillover to the lungs. This volume may need to be less in the elderly patient in whom the capacity of the lymph nodes is diminished. The average spillover to the lungs, measured by external scanning, has been about 12% of the dose. Repeated scans showed more rapid elimination from lungs than from nodes. The spillover can be still further reduced by keeping the lower-limb injection volume to 4 ml. or less. Long-term studies have shown no lung-radiation effects on clinical examination, radiology, or lung-function tests even in patients receiving multiple injections.

The dosage aimed at is based on studies with animal tumours and on increased experience with patients where it has been found that such doses are tolerated without complications. The amounts actually received by the patients in this series were lower. About one-third received doses to the regional nodes of the lower limb (inguino-ilio-lumbar) of less than 20 mCi. These were the earlier patients. With more experience and greater efficiency larger doses were achieved, and the later patients had node doses of 20 to 30 mCi, one receiving 35 mCi.

(b) Technique of Lymphography

The technique of lymphography was essentially that described by Kinmonth (1952, 1954), where lymph trunks are made visible by preliminary subcutaneous injection of a suitable dye such as patent blue violet, and after isolation one of them is injected with a needle. The only modifications made were those including protection during radioactive infusion. The patient was given Lugol's iodine (5 minims t.d.s. orally) for three days before the procedure in order to limit the uptake of free ^{131}I by the thyroid. Whenever possible injection of the radioisotope combination was made just proximal to the excision area representing the site of the primary melanoma and following lymphatic vessels draining the primary site. Occasionally infusion of the isotope was made from two sites as shown in the Diagram. The lymphangiogram set* (Rutt *et al.*, 1964) is primed with radioactive Lipiodol. Should plain Lipiodol be infused initially then some nodes may be filled with inert material which is not eliminated by the subsequent radioactive solution.



Melanoma at various sites on lower limb. Infusion is made proximal to the site of the melanoma whenever possible.

The syringe (made of strong polypropylene) is filled with the measured dose of ^{131}I Lipiodol and placed in an automatic injector and then connected with the lymphogram set. The syringe is handled with remote-control tongs of simple design and the machine is now completely screened by a casing of 2 cm. of lead.

The rate of injection is slow initially, about 10 minutes for each millilitre, to avoid extravasation around the nodes. Injection of the final 0.5 ml. is deliberately rapid, however, in order to achieve extravasation from the afferent lymphatics and thereby produce a perilymphatic dose.

The course of the infusion is monitored carefully by the following methods:

(1) External scanning with two collimated Geiger counters. One is fixed over the regional node area which is being treated, while the other is used to follow progress of the ^{131}I Lipiodol up the limb and also to scan the lung fields. Early high lung readings, which have rarely been found, may be caused by inadvertent venous injection or perhaps lymphovenous connexions in enlarged nodes. If high readings are obtained the infusion is stopped.

(2) Early radiography of the limb and regional areas after injecting 1 to 2 ml., particularly where any doubt of a satisfactory cannulation exists. The patient lies on a cassette tunnel modified to the operation table.

All radioactive waste is collected in a suitable screened container. It is estimated at the conclusion of the operation and is used in calculating the actual dosage received by the patient.

Radiographs taken of the limb, pelvis, and abdomen on completion of the injection are repeated 24 hours later (lymphadenograms). These films demonstrate the amount of extravasation in the limb, and assessment can be made of possible metastases in the regional lymph nodes.

Total scanning of the patient with a mobile scintillation counter is made 48 hours after the procedure, and in some cases repeated scans are carried out so as to study the rate of elimination of the isotope from the two main areas of uptake—lymph nodes and lungs. The body distribution of Lipiodol after direct intralymphatic injection has been studied in view of possible

* Obtainable from McCarthy Ltd., Seymer Road, Romford, Essex.

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clinical significance. In the experimental animal this has been followed in detail (Edwards *et al.*, 1965 ; Edwards *et al.*, 1966) and in man by scanning techniques.

The levels of radioactivity in blood and urine are routinely measured in the postoperative phase. In the successful procedure average blood levels of ^{131}I comprise 0.01% of the administered dose per litre whereas average urine excretion levels amount to 1% of administered dose in each 24 hours.

Clinical Stage II Melanoma

It is universally recognized that this group of patients presents an infinitely more serious problem than the stage I group, and the prognosis is correspondingly bad by all conventional methods of treatment.

The treatment has been the same as for stage I patients with the addition of block dissection of regional nodes about four weeks after the intralymphatic injection, when the isotope has had time to decay to a safe level. The operation is not much more difficult after endolymphatic therapy unless more than a month has been allowed to elapse.

Results

Our experience with endolymphatic therapy for melanoma extends over a period of nine years. During this time 82 patients have been treated with different isotopes via the endolymphatic route as part of their treatment for melanoma at various sites. This review does not include details of other malignant disease treated by endolymphatic therapy.

The first radioisotope used was radioactive colloidal gold (^{198}Au) and the first patient in a small group of 13 was treated in 1958. These patients were all of the stage I clinical group, and the initial results were presented elsewhere (Jantet, 1958, 1962 ; Jantet *et al.*, 1964). Ten of these patients were alive five to nine years after treatment.

Radioactive ^{131}I Lipiodol has been used instead of gold colloid since 1963, and 59 patients have been treated with it up to the present time.

The 50 patients under review were treated by a combination of surgery and endolymphatic ^{131}I Lipiodol. The first patient in this group was treated four years ago, the most recent 18 months ago. All these tumours were carefully examined by our pathologists and classified as invasive malignant melanoma.

Most of the lesions were on the lower limb (35). The other sites were trunk (8) and upper limb (7). Patients with melanomas on other anatomic sites, such as the face, have also been given endolymphatic therapy, but none of them for long enough to be included in this review.

The survival rates after treatment are presented in Table I. There is a marked disparity between stage I and II groups, with a much better prognosis for stage I patients.

Stage I Patients

In the stage I group the eventual survival rate over a period of one and a half to four years is 29 out of 31 (93.5%). The two patients who died in this group did so from recurrence within about 12 months of treatment.

TABLE I.—*Survival of Patients with Melanoma Treated with Endolymphatic Therapy and Surgery*

Clinical Stage	No. of Cases	Females	Males	Deaths	Survival
I	31	26	5	2	93·5%
II	19	11	8	9	52·6%
I and II	50	37	13	11	78%

The first patient, a woman aged 44, had a melanoma excised widely from the right thigh with infusion of a lymphatic leading from the excised area at the same time. This was technically unsatisfactory owing to extravasation, so a further dose was infused through a dorsal pedal lymphatic, with better filling of lymph nodes up to an estimated total of 15 mCi. Local recurrence was evident within a year. Re-excision was attempted but was incomplete because of deep extension into muscle planes. Continuous intra-arterial infusions of melphalan failed to control the disease and the patient died 15 months after inception of treatment. In the light of later experience two faults can be seen. The first excision was done without precautionary measures to prevent local implantation of malignant cells that we now employ, and hence recurrence. The second was in the dose of isotope. In similar circumstances we would now persist with injections until a larger amount, 30 or more mCi, had been successfully injected.

The second patient, a woman 38, was treated for melanoma of the right lower leg and died from recurrence of disease within 12 months of treatment. In this patient endolymphatic therapy had been given distal to the primary site and extravasation of radioactive material occurred round the graft, leading to radionecrosis. The lymph nodes in fact received only some 17 mCi and the procedure was regarded as a technical failure. As with the first patient, we would consider local or regional node treatment inadequate according to later standards.

Two other patients in this group developed recurrence of disease, which was subsequently treated satisfactorily.

One patient, a man aged 29, developed recurrent disease in the right iliac nodes a year after treatment for melanoma of the thigh. The nodes were excised and the patient remained well two years after initial treatment. On reviewing the original lymphadenograms, filling defects could be seen in these *x*-ray films that would have warranted treatment as for a stage II melanoma.

The other patient with recurrent disease was a woman aged 47. At another hospital in April 1964 a malignant melanoma had been excised from the right forearm, and this had been grafted. She was referred to us for endolymphatic therapy. Injection into a hand lymphatic resulted in extravasation in the forearm and unsatisfactory filling of axillary nodes. One year later nodes became enlarged in the axilla and a block dissection was done. The patient remained well two years after inception of treatment.

Stage II Patients

The prognosis in stage II patients, as already indicated, is much worse. The survival rate over a similar period to that of stage I was 10 out of 19 patients (52.6%).

The cases of the patients who died were analysed in more detail and are presented in Table II. An encouraging feature of these results was the success of the combination of endolymphatic therapy and surgery in treating sometimes gross

TABLE II.—*Analysis of Deaths in Clinical Stage II Patients (Nodes Involved When Seen) During Periods of One to Four Years After Treatment Began*

Case No.	Sex and Age	Site of Primary Melanoma	Recurrent Disease	Further Treatment
1	F 39	Left leg, with left ilio-inguinal nodes	Cerebral metastases	
2	F 59	Right leg, with right inguinal nodes	Cerebral metastases	
3	M 65	Right subungual axillary nodes	Lung metastases	
4	M 40	Left leg, with left inguinal nodes	Left leg, with right inguinal nodes	Re-excision. Gland dissection. Chemotherapy
5	M 52	Left scapular area, with left axillary nodes	Widespread metastases	Systemic chemotherapy
6	M 32	Right leg, with inguinal nodes	Right leg and beneath inguinal scar	Re-excision. Chemotherapy
7	F 72	Left arm. Recurrence, with left axillary nodes	Widespread metastases	Systemic chemotherapy
8	M 59	Left foot, with left ilio-inguinal nodes	Lymphovenous connexion. Systemic disease	
9	F 47	Left leg, with left inguinal nodes	Left leg at primary site. Multiple skin metas ases	Re-excision. Intra-arterial chemotherapy

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metastatic disease in lymph nodes. Deaths were due to systemic dissemination or to failure of the initial surgical treatment at the primary site. These aspects are discussed below.

Comparison with Results of Other Methods

It is difficult to compare the results with those obtained by other methods and may even be misleading because the series of other authors may have different sex distributions, different anatomical distribution, and, perhaps even more important, different proportions of patients with node involvement. A working party of the Medical Research Council has started a statistically controlled study for this reason, but it will be several years before assessment is possible.

In the meantime some comparison may be attempted. Bodenham has made excellent and careful studies, but his patients were "staged" on a histological basis not used by our pathologists. With his colleagues (Petersen *et al.*, 1962) he reported only 4 survivors out of 21 patients in a group which appears to correspond to our clinical stage II group at three years, most of them dying in the first year. Their patients were treated by excision and block dissection. The group reported here which had endolymphatic therapy, so far as it is comparable, shows 10 alive out of 19 (Table I).

Patients Given Surgical Treatment

As it proved difficult to find comparable published figures we reviewed a group of patients treated by conventional methods in other surgical services of our hospital. These were graded clinically in the same way—that is, stage I primary only, stage II regional nodes involved on clinical examination. They were also more comparable than other groups because they were drawn from the same population area and treated over an approximately similar period of time, and because the histological diagnoses of malignant melanoma were made by the same pathologists. The surgical treatment usually consisted of excision of the primary lesions followed by dissection of the regional nodes if these became clinically involved.

The figures for this "surgery alone" group are set out in Table III. There were 52 patients in this group, of whom 24 survived three years—that is, 46%, compared with 78% in the "surgery and ^{131}I" group. The figures for the stages are: stage I, 55% and 93%; stage II, 10% and 52.6%. In both stages and in the groups as a whole the figures are better for the patients who had ^{131}I. There are some ways in which the groups are not similar. For example, the ^{131}I patients were followed one and a half to four years, the others at three years. This might perhaps favour the ^{131}I groups, though analysis showed that most of the deaths in the other group, particularly in stage I patients, occurred during the first two years of treatment. There are more stage II patients—19 in the ^{131}I group, compared with only 10 in the surgery alone group. This might favour the latter.

TABLE III.—*Survival of Patients with Melanoma Treated by Surgery Alone*

Clinical Stage	No. of Cases	Females	Males	Deaths	Survival
I	42	28	14	19	55%
II	10	8	2	9	10%
I and II	52	36	16	28	46%

Comparison of Morbidity

It is much easier to compare the morbidity and complications of treatment because they often arise early and are almost uninfluenced by differences in the length of follow-up studies, staging, sex composition, and other factors which might differ in various series. Fortner *et al.* (1964) described the results of groin dissection for melanoma. They adopted regional node dissection as a routine procedure after treatment of the primary. Of their patients 3% had operative complications, which included one cardiac arrest with death, severed ureter, bladder laceration, and laceration of a major vein. Postoperative complications included necrosis of the skin flaps to a varying degree in 64.5%. Secondary skin grafting was needed in 23% of these, while healing by second intention occurred in others.

Apart from the effect on the patient of a complication of therapy the period in hospital for all patients is known to be appreciable after lymph node clearance, and even longer for the complicated cases.

The complication rate of endolymphatic therapy has been low. Failure to administer a therapeutic dose to the lymph node area occurred in two patients in the group of 50. In one patient a radionecrotic ulcer developed which needed excision and skin grafting. There has been no mortality from therapy or any undesirable after-effects. Occasionally there was a transitory pyrexia of 1 to 2° C. in the early postoperative phase. Long-term studies have failed to show any lung damage arising from overflow of radioactive contrast material to the lungs. Chiappa (1966) and other workers with this technique also report freedom from such complications. Hypothyroidism as a result of thyroid uptake of ^{131}I has not occurred.

Lymphoedema of the infused limb is not unusual but is of mild degree. Oedema requiring elastic support and other conservative measures is quite rare. Indeed it has been difficult to distinguish lymphoedema due to endolymphatic therapy from that which would have been expected to occur below the area of wide excision and skin grafting of the primary lesion. The explanation for this appears to lie in the resistance of lymph channels to radiation compared with the cellular contents of the lymph nodes. It appears that the parenchyma and its contents may be destroyed and still leave pathways, perhaps in cortical sinuses or vessels overrunning the node, to conduct lymph. Our observations in clinical and animal studies support this. Wiljasalo and Perttala (1966) published studies describing this resistance of lymph vessels to radiation. The absence of lymphoedema probably also accounts for the low incidence of satellite seeding in limbs. The incidence of this is high after block dissection, as Ariel and Resnick have described.

Discussion

Possible advantages of endolymphatic therapy for stage I patients over block dissection are decreased morbidity and increased effectiveness in treatment of nodal secondaries. There is no doubt about the decreased morbidity. The effectiveness, however, needs careful examination. Four out of 31 stage I patients developed nodal metastases despite endolymphatic therapy. This is probably a lower figure than might be expected had the nodes been left untreated. If the work of Fortner *et al.* is representative then 38%—that is, about 12—might have been expected to show subsequent evidence of node metastases. The four cases are described under Results. For various reasons the treatment of the nodes or of the primary lesion had been inadequate. It seems fair to conclude that endolymphatic therapy for stage I patients is as good as, if not better than, surgery alone.

The nodes in stage II melanoma cannot be treated by endolymphatic therapy without surgery as they contain metastases too large for the β-particle of ^{131}I or indeed of more energetic isotopes, such as ^{90}Y or ^{32}P, to reach. These nodes often contain tumour areas deficient in lymph and blood circulation and are therefore inaccessible. The combination of endolymphatic therapy with surgery presents certain advantages:

(1) It could reduce the viability of cells which might be split during the dissection, thus reducing the incidence of recurrence at the site of surgery.

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(2) It might extend the effective limit of the treatment by destroying microscopic metastases in more proximal tissue than could be included in the dissection.

(3) Should any lymph nodes be inadvertently left behind they would be less likely to contain viable tumour cells. Radiographs taken during the operation would occasionally be of benefit in detecting lymph nodes overlooked during the dissection.

(4) It might give diagnostic information about metastases not clinically detectable.

The survival rates for the stage II patients was 52.6% compared with 10% for patients treated by operation alone. So far as such small numbers are comparable they suggest that the theoretical advantages may be fulfilled.

This has been a study of endolymphatic therapy, aimed chiefly at the nodes and to a less extent at lymph pathways leading to them from the primary lesion. It is, however, impossible to leave the discussion without comment on the initial treatment of the primary lesion. Many of our patients have undoubtedly lost their lives through inadequate initial treatment. Despite almost universal agreement in the literature about the need for wide excision and grafting or local amputation, we still see patients in whom the primary has been cut into, partly excised, or excised with little or no margin. Despite further excisions recurrence is very likely or has indeed taken place, and is then highly dangerous.

Summary

A group of 50 patients with malignant melanoma of the skin followed for periods up to four years after treatment are reviewed.

Clinical staging analogous to that used for other forms of malignancy, such as breast carcinoma, has proved useful in prognosis and management. All patients had excision of the primary followed by intralymphatic injection of ^{131}I in ultrafluid Lipiodol in dosages up to 35 mCi for each ilio-inguinal or 30 mCi for each axillary route. Clinical stage II patients whose nodes were palpably involved were treated four weeks later by block dissection.

Comparison with a group of patients clinically staged in the same way but treated without ^{131}I injection suggested that endolymphatic therapy may have beneficially influenced the early survival rate.

There were no deaths due to treatment. Complications were few and were of a minor nature.

We are grateful to many colleagues at St. Thomas's Hospital and elsewhere who have referred patients for treatment, and to other members of the staff of our department who have helped in this study. We are particularly indebted to Dr. T. M. Gimlette, of the isotope laboratory, Dr. J. A. Fleming, of the radiotherapy department, and Dr. W. F. Clapham, of the physics department, for their assistance. Dr. W. Charlton, of the Radiochemical Centre, has helped us particularly by perfecting the isotope preparation. We are also grateful for financial support in the study from the Endowment Funds of St. Thomas's Hospital, the Medical Research Council, and Messrs. McCarthy Ltd.

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Microembolic Pulmonary Hypertension in Pyogenic Cholangitis

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The purpose of this paper is to report the development of pulmonary hypertension as a complication of recurrent pyogenic cholangitis (Cook, Hou, Ho, and McFadzean, 1954; Ong, 1962). Evidence is presented which is consistent with the complication being due to repeated "silent" pulmonary microembolism and with the emboli having their origin within the liver. So far as we are aware this complication of cholangitis has not been described previously.

Case Reports

During periods of observation ranging from 2 to 12 years 14 patients with recurrent pyogenic cholangitis developed clinical, radiological, and electrocardiographic evidence of pulmonary hypertension. Males and females were equal in number, and their ages ranged from 29 to 49 years. All but two had a history of frequent exacerbations of pyogenic cholangitis of varying severity over periods ranging from 8 to 15 years. In the two exceptions the exacerbations occurred at most twice a year for 12 and 15 years respectively. An additional patient who presented with pulmonary hypertension was a man aged 21 who had had irregular attacks of fever, commonly associated with distending discomfort over the liver, since the age of 16. In that time there had been three attacks of lancinating right upper quadrant pain associated with repeated vomiting, high fever, and jaundice. He was first seen in the third attack. Six of the 15 patients gave a history of haemoptysis during one or more of the acute exacerbations, and four, three of whom had haemoptysis, had a history of recurrent attacks of pleuritic pain. None had experienced acute dyspnoea. In all cases the majority of the exacerbations had been treated with an antibiotic or antibiotics.

The radiological findings were similar in all. There was right ventricular enlargement. The pulmonary artery and its main branches were dilated, but the peripheral branches showed abrupt tapering. In none was the left atrium enlarged, and there was no evidence of intrinsic disease of the lungs. The electrocardiograms showed prominent pulmonary P waves and

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