

MEDICAL PRACTICE

Clinical Problems

Starch Granulomatosis of the Peritoneum

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Summary

Starch glove powder is used extensively by surgeons in Britain and is generally considered innocuous so that precautions to prevent granuloma formation, previously taken when talc glove powder was in use, are now neglected. Reported here are five cases of starch granulomatosis of the peritoneum occurring over a period of a few months. This condition requires reoperation within a limited time for its diagnosis and may be confused macroscopically with disseminated malignant disease or tuberculosis or may simply cause adhesions. Recognition is dependent on a high degree of suspicion by both surgeon and histopathologist, as special histological techniques may be necessary. Consequently, it is only in a minority of the florid cases that a diagnosis is made, and the condition would appear to be much more common than is generally realized. A plea is made for scrupulous care to avoid starch powder contamination of the operative field.

Introduction

Since the introduction of dry surgical gloves the powder used on these gloves has been under some degree of suspicion, but because any ill effect it might produce was masked by other more obvious factors such as infection, trauma, or suture material it attracted comparatively little attention. The incrimi-

nation of lycopodium powder as the causative agent in many granulomatous lesions and intra-abdominal adhesions has been well documented,¹ and the use of this powder was rapidly abandoned in favour of magnesium silicate or talc, which was thought to be physiologically inert. The recognition of silicosis as an industrial disease aroused interest in the possibility that talc might not be entirely innocuous, and in 1933 Antopol² reported two cases of granuloma due to talc, one in the neck and one in the serosa of the appendix. Though scattered reports of talc granulomas subsequently appeared in the literature little attention was paid to them by clinical surgeons until 1943, when a comprehensive article by German³ emphasized the danger of granuloma formation.

In 1947 Lee and Lehman reported⁴ a non-irritative glove powder with excellent physical qualities of flow and fineness which were largely unaffected by autoclaving. They found that it was completely absorbant from the peritoneum of animals without inflammatory reaction and without the formation of adhesions. Their clinical experience with the powder also proved eminently satisfactory. MacQuiddy and Tollman,⁵ who investigated the possible allergic properties of this powder, were unable to find any sensitivity reactions in the subjects tested, nor was it possible to produce a state of sensitivity in animals. This powder consists of a mixture of amylose and amylopectin, derived from corn starch, which has been treated by physical and chemical means to improve its lubricating value and to prevent gelatinization when autoclaved. A small amount (2%) of magnesium oxide is included for the purpose of further improving the flow properties of the mixture.

Corn starch powder has been used as a glove lubricant since 1948 and is now in widespread use under the trade name, Bio-Sorb. In spite of an experimental study by Lee, Collins, and Largent⁶ which showed that adhesions or nodules may occur when relatively large clumps of corn starch powder are placed in the peritoneal cavity, remarkably few cases of starch granulomatosis of the peritoneum have been reported in Britain.⁷ Cox, however,⁸ has reported four cases occurring

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in Australia, together with two cases of starch granuloma occurring in surgical wounds, and Bates⁹ reviewed 15 cases in the world literature.

The peritoneal nodules in this condition have the macroscopical appearance of malignant seedlings and can be associated with ascites which may be blood-stained.¹⁰ Such an appearance may lead to mismanagement of a patient,^{7 8} and outlined below are the case histories of three patients in whom peritoneal nodules of starch granuloma were initially mistaken for disseminated malignant disease, misleading the surgeon. Two further cases are also presented.

Case 1

A woman aged 62 was admitted to Redhill General Hospital on 6 September 1970 with pain and tenderness in her right iliac fossa. Laparotomy showed torsion of part of the omentum with resulting infarction. The affected portion of the omentum was excised and she made a slow recovery, being discharged on 20 September. Histological examination confirmed the clinical diagnosis.

She was readmitted to hospital on 14 October with generalized lower abdominal pain and increasing distension. On examination her abdominal wound was found to be indurated and tender and there was lower abdominal distension. Special investigations were unhelpful and she was submitted to a further laparotomy, when greenish free fluid was found together with many adhesions between the omentum, small bowel, and the previous abdominal wound. Multiple hard nodules were present in the mesentery and over the surface of the ileum and lower peritoneal cavity. A diagnosis of metastatic malignant disease was made but no primary tumour could be found. The nodules were biopsied and the incision was closed. She made another slow recovery and was discharged on 12 November.

Histopathological Examination.—Microscopy showed fibrous trabeculae enclosing granulomas composed of compact giant cells, lymphocytes, histiocytes, and fairly numerous eosinophils (Fig. 1).

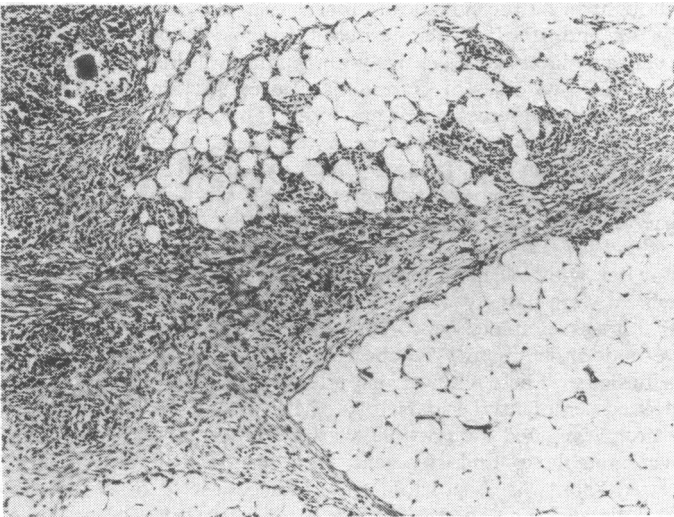


FIG. 1—Case 1. Fibrous trabeculae enclosing starch giant cell granuloma and leucocytic exudates. (H. and E. $\times 60$.)

No frank tissue necrosis was evident but there was some focal fibrin exudation, patchy oedema, and a few eosinophil-rich granulocytic microabscesses, which measured up to 350 μm in diameter. Many of the giant cells contained translucent, pale blue-green starch granules. These granules were slightly larger than those in the cases reported below, having a modal diameter of 8 μm . They stained dark blue with Lugol's iodine, magenta with periodic-acid Schiff, and were resistant to diastase digestion; they did not exhibit the acid-fast fuchsinophilia described by Ising.¹¹ In polarized light the starch granules displayed a variable degree of Maltese cross bire-

fringence which was much reduced or suppressed after treatment with Lugol's iodine or periodic-acid Schiff. The granules were compared with those of the glove powder and were found to be identical.

Case 2

A woman aged 39 underwent hysterectomy and left salpingo-oophorectomy on 1 January 1971 at another hospital. The operation was apparently conducted without difficulty and her postoperative course was uncomplicated. She was discharged on 17 January but admitted to Crawley Hospital as an emergency on 31 January with a three-day history of right hypochondrial pain radiating through to the back. Examination showed tenderness and guarding in the right hypochondrium, and a plain x-ray film of the abdomen showed multiple small radiopaque calculi in the region of the gall bladder. At laparotomy (J.N.) some bloodstained free fluid was found, with multiple small nodules scattered over the whole of the peritoneal cavity including the surface of the liver. Friable adhesions, incorporating these nodules, were attached to the previous abdominal incision and to the pelvic organs. As no primary tumour could be found a diagnosis of disseminated malignant disease was made, possibly of ovarian origin. A biopsy specimen of the peritoneal nodules was taken and cholecystectomy proceeded with as it was thought that the gall stones were responsible for her symptoms. Postoperative recovery was uneventful and she was discharged on 14 February. When seen in the outpatient department on 12 March she was well with no evidence of ascites.

Histopathological Examination.—Microscopy of the peritoneal nodules showed granulomas composed of giant and epithelioid cells, lymphocytes, histiocytes, fibroblasts, numerous eosinophils, and a few neutrophil granulocytes. Around the granulomata there was prominent pavementation of venules by granulocytes and mononuclear cells but there was no organized peripheral fibrosis (Fig. 2). Some loose interstitial and subserosal fibrin exudation and patchy oedema were present but there was no necrosis. Almost all the starch granules were located within giant cells.

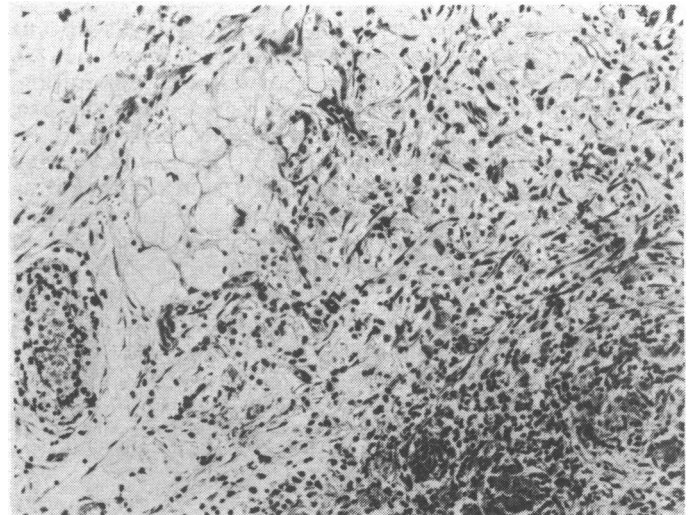


FIG. 2—Case 2. Mononuclear exudate and disorderly fibroblastic proliferation surrounding starch giant cell granulomas (bottom right) (H. and E. $\times 150$.)

Case 3

A man aged 42 was admitted to Crawley Hospital as an emergency on 4 January 1971 having collapsed after passing a melaena stool. Four months previously he had undergone vagotomy and pyloroplasty elsewhere for duodenal ulceration. He responded to conservative treatment, and as a barium-meal examination did not show a definite ulcer an insulin test meal was given. This suggested incomplete vagotomy, and after a period of observation as an outpatient he was submitted to laparotomy on 1 March—that is, about six months after vagotomy. At operation a high posterior gastric ulcer was found, together with some nodules around the origin of

the left gastric artery. A Billroth I type of partial gastrectomy was performed and the nodules were excised for examination. He made an uneventful postoperative recovery, and when seen as an out-patient six weeks later was in excellent health.

Histopathological Examination.—Sections of the stomach showed a simple peptic ulcer with sinus catarrh and reactive changes in two lymph nodes. There was no evidence of malignancy. The granulomas in the left gastric pedicle were of two kinds. Some incorporated both suture threads and starch granules and some starch granules alone. All were more circumscribed than those in the above cases and principally featured compact giant cells and histiocytes, with only a few small round cells resembling lymphocytes and extremely scanty granulocytes. Focal fat necrosis was present. A few starch granules were also present in adjacent small vessels, which appeared to be lymphatic channels, and in the sinusoids and sinus-lining histiocytes of a local lymph node (Fig. 3).

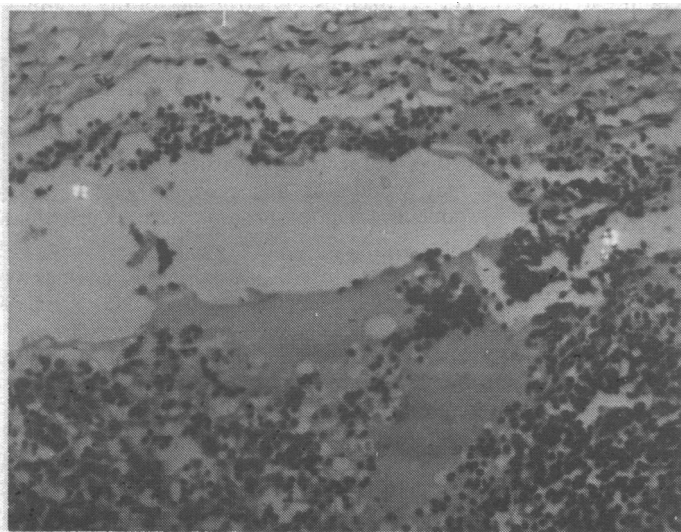


FIG. 3—Case 3. Starch granules exhibiting Maltese cross birefringence in peripheral sinus of lymph node. (Polarized light. H. and E. $\times 200$.)

Case 4

A boy aged 3½ years presented with insidious tiredness and haematuria. Investigations showed a tumour of the left kidney, and transabdominal nephrectomy was performed on 17 March 1971. Postoperative recovery was uneventful and he was transferred to St. Bartholomew's Hospital for radiotherapy. Four days after starting radiotherapy and 16 days after nephrectomy an asymptomatic pyrexia (100° - 101° F; 37.8° - 38.3° C) developed which persisted despite the use of penicillin and ampicillin. Twenty-one days after nephrectomy he complained of epigastric pain, which moved to the right iliac fossa during the next two days. Laparotomy for suspected appendicitis 24 days after nephrectomy showed serous ascites, adhesion of the omentum to the caecum, and a thickened appendix with a fibrinous serous exudate. Cultures were taken from the appendix and the ascitic fluid and appendicectomy was performed. The cultures were sterile and he made a satisfactory postoperative recovery.

Five days after his discharge from hospital on 13 May he was readmitted complaining of colicky abdominal pains, but these settled with conservative management and he was sent home on the 22nd. He was readmitted again within a few hours with a recrudescence of abdominal pain. A further laparotomy the next day showed a diffuse plastic peritonitis with dilated proximal jejunum.

Histopathological Examination.—The appendix (6 cm long) and mesoappendix displayed extensive injection of their serosal surfaces and a focal fibrinous adherent exudate. The subserosal layer of the appendix was thickened, particularly towards the tip, and cream-coloured. The deeper layers of the wall were macroscopically normal. Microscopically pathological changes were limited to the serosal and subserosal regions of the appendix and mesoappendix.

Here there was an exuberant inflammatory infiltrate composed of epithelioid and giant cell granulomas admixed with lymphocytes and eosinophil granulocytes (Fig. 4). Several small eosinophilic necroses (up to $250\ \mu\text{m}$ long) lay in apposition to the giant cell granulomas (Fig. 5). These necroses were of two types. Some were irregular and lacked sharp margins and some were oval, circumscribed, and

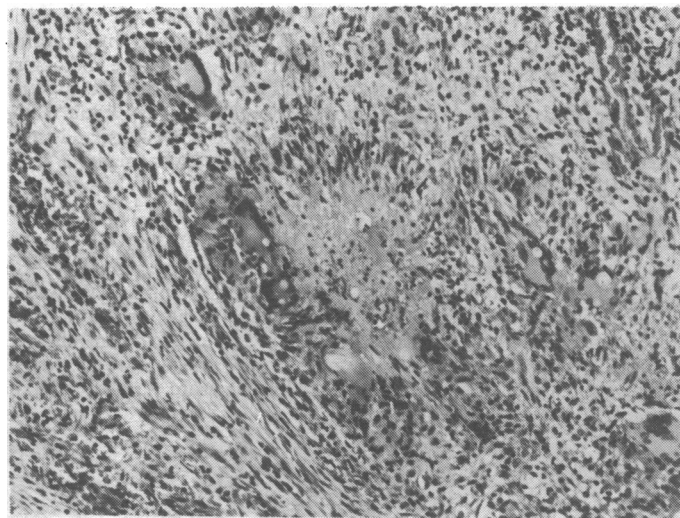


FIG. 4—Case 4. Necrotizing granuloma in appendix bounded by radial histiocytes and giant cells. Starch granules (clear oval spaces) within necrosis and giant cells. (H. and E. $\times 150$.)

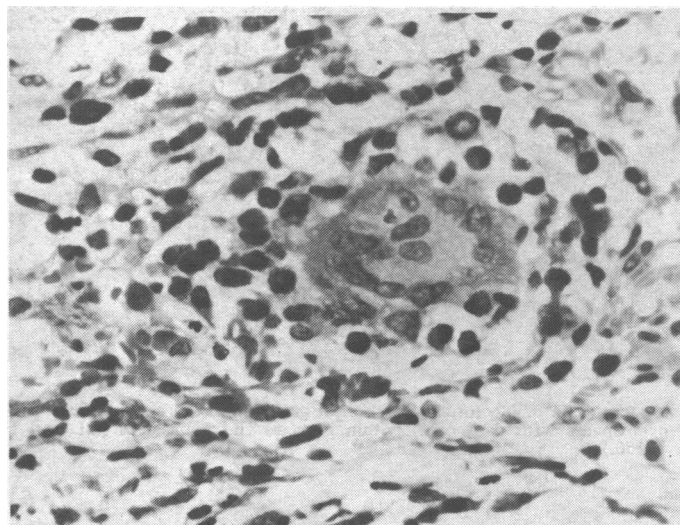


FIG. 5—Case 4. Eosinophil microabscess around starch-containing giant cell. (H. and E. $\times 600$.)

bounded by a radially arranged histiocytic palisade. In addition to these necroses focal fibrinous exudation was present on the serosa of the appendix. The starch granules were largely situated within the giant cells and the necroses. Some giant cells contained a second kind of foreign body which was made up of colourless polygonal or conchoidal fragments measuring up to $16\ \mu\text{m}$ long. These particles were anisotropic but displayed no Maltese cross birefringence and were unstained by Lugol's iodine and periodic-acid Schiff. No Gram-positive bacteria, alcohol-acid-fast bacilli, or fungal elements were detected in the lesions.

Case 5

A man aged 66 underwent partial gastrectomy at St. Bartholomew's Hospital on 24 March 1971 for an adenocarcinoma of the stomach which had metastasized to lymph nodes along the lesser curvature. His postoperative course was uneventful apart from a transient

pyrexia on the third evening. An episode of vomiting occurred three weeks postoperatively but he was otherwise well until 3 May when he complained of epigastric pain which was accompanied by a low grade pyrexia and some epigastric tenderness. This pain lasted about a week, resolving spontaneously, but recurred on 2 June accompanied by vomiting, dehydration, and radiological evidence of small-bowel distension with fluid levels. Despite nasogastric suction and intravenous fluids the pain continued, and exploratory laparotomy was proceeded with on 7 June (11 weeks after the initial surgery). At operation there was free peritoneal fluid, with multiple small nodules scattered over the parietal peritoneum, the mesentery, and the pelvic organs. Loops of small bowel were matted together by numerous adhesions. The clinical diagnosis of metastatic malignant disease was made and tissue from the adhesions and some seedlings was taken for examination. The patient made a satisfactory postoperative recovery.

Histopathological Examination.—Microscopically all four peritoneal nodules examined showed numerous starch granules within giant cell granulomata which had undergone central eosinophilic necrosis. Only a few small round cells, plasma cells, and eosinophils were present in the circumscribed fibroblastic perimeter of these lesions (Fig. 6). The fibrous tissue from the small-bowel adhesions contained anisotropic material resembling suture threads, but no starch granules were demonstrable.

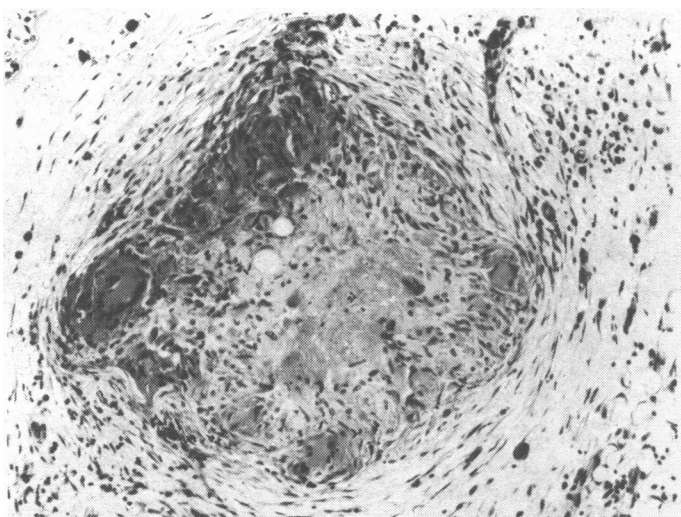


FIG. 6—Case 5. Necrotizing peritoneal granuloma. Starch granules (small oval spaces with dark core) within necrosis and giant cells. (H. and E. $\times 150$.)

Discussion

A widespread impression seems to have developed that starch powder is completely safe, and there has been a tendency to discard entirely the scrupulous efforts to minimize powder contamination of the operative field which were encouraged when talcum powder was in general use. Though early studies⁴ suggested that starch powder was completely absorbed from the peritoneal cavity and was thus benign, further experimental work,^{1,2} including some by one of the original authors,⁶ clearly reproduced granulomatous peritonitis in a variety of animals. Provided all other factors conducive to inflammatory reaction and adhesion or granuloma formation are excluded, starch powder would appear to be completely absorbed in most patients, leaving the serosal surfaces and soft tissues undamaged. When a complicating factor such as an infection is added to a foreign body reaction the process is much more violent and the extent of permanent scar formation is increased.

Evidence points to the starch granules themselves as the primary factor, though the 2% concentration of magnesium oxide has also been blamed,¹³ and the degree of reaction is

related to the total amount of corn starch to which the tissues are exposed.⁹ Myers *et al.*¹² produced intraperitoneal reactions in rabbits with one gramme of starch powder, estimated to be equivalent to the washings from one pair of surgical gloves, and after a single washing gloves have still been found to be abundantly covered with a fine coating of powder.⁴

The true incidence of tissue lesions attributable to starch powder is difficult to estimate, and no method is at present available for definitive diagnosis short of re-exploration. Minor lesions and even definite adhesions do not always lead to biopsy; even if they do the true causative agent may be overlooked by the pathologist. The commonest cause of misinterpretation is that the pathologist never gives a thought to foreign body irritation;¹⁴ thus he does not use polarized light but interprets the lesion as a non-specific granulation. Even examination in polarized light does not always disclose the presence of the typical granules. The other reason for failure to make the correct diagnosis is a true lack of the granules as a result of their complete absorption, which may take a variable time. In some older lesions only a thorough examination of the whole sample has led to a detection of the granules, which are further frequently seen in a partially disintegrated, hardly recognizable form.¹⁴ The major proportion of patients recover without further surgery and without the diagnosis being made. One may wonder if this type of reaction may commonly be producing vague postoperative abdominal complaints.⁹

In view of the widespread use of corn starch powder it seems likely that only some patients respond in this manner. When adhesions occur they may do so as the result of "clumps" of the powder which defy complete absorption for some time.¹⁵ The longer absorption is delayed the greater is the likelihood that the foreign body reaction will be irreversible and that adhesions will be permanent. Granuloma formation is unlikely to be due to "clumping," as the occurrence of peritoneal granulomas has been reported after vaginal examination,⁹ and powder from the same batch used in three of the reported cases was found to be entirely satisfactory by the manufacturers. The possibility of a hypersensitivity state has been thoroughly investigated by MacQuiddy and Tollman,⁵ who were unable to demonstrate any allergic properties of the powder, and though several patients with starch granulomatosis have subsequently been skin-tested, in only one was there a suggestion of a hypersensitivity reaction.⁹

Though the clinical picture is fairly constant the preoperative diagnosis of starch peritonitis is almost never made.⁹ The typical case will probably have a normal though perhaps slow recovery from the initial operation and will present between two and six weeks from the date of that operation with abdominal pain and tenderness, low-grade fever, nausea, vomiting, and distension. The pain is usually more severe than the abdominal signs would suggest¹⁰ and may be more intense in one area, suggesting localized disease. The white cell count may be normal despite the suggestion of intra-abdominal inflammation. Ileus, which may be confirmed radiographically, may also be present. The surgeon will initially believe the cause to be an acute inflammation or bowel obstruction and may well proceed to laparotomy, which is the only means of making a certain diagnosis.

At laparotomy ascites, adhesions, and granulomata may all be found and the condition may be confused with tuberculosis or disseminated malignant disease. This may well lead to incorrect management. Prompt diagnosis at the time of a second laparotomy is particularly important when further radical surgery is contemplated. Exclusion of carcinomatosis by rapid frozen section of the peritoneal nodules is usually possible. It should be emphasized that the use of polarized light will facilitate the identification of starch granules in frozen sections of a granuloma of otherwise obscure nature. While care is necessary to distinguish extraneously-introduced starch granules from those responsible for granulomas, the major

factor in establishing an early diagnosis of starch granuloma is awareness of the condition by both the surgeon and the histopathologist. Once the diagnosis has been made corticosteroids may be of value.¹⁰

There has not been any recent change in the manufacture of starch glove powder, and as starch granulomatosis would appear to be a relatively common condition animal studies are now being undertaken to re-evaluate the tissue reaction to this powder.

Conclusion

Starch granulomatosis of the peritoneum is a much more common condition than is generally realized. The majority of cases go unrecognized either because the clinical picture is not severe enough to warrant surgical intervention or because the features are missed either at laparotomy or under the microscope. Many so-called postoperative adhesions are also undoubtedly due to starch granulomas.¹⁶ In those patients submitted to re-exploration the condition may be confused with either tuberculosis or disseminated malignant disease and lead to errors of management.

It has been well established that starch powder is vastly superior to and less hazardous than talcum powder, but the same precautions which were employed when talcum powder was in general use are still important. In some hospitals surgeons do not take the precaution of washing the powder from their gloves before operating, but even this manoeuvre will leave a residue on the gloves, and it has been recommended that the outer surfaces of the gloves should be wiped with a moist towel to remove every trace of residual powder.¹⁷ Though starch powder is innocuous under ordinary conditions it is still a tissue irritant, and it acts for the duration of its presence in the tissue as a foreign body.

The reported cases were originally operated on in five different

hospitals but recognized over a few months in two centres which have recently developed an interest in this subject. Only a minority of cases are submitted to re-exploration, and of these some will escape diagnosis by the histopathologist either because the condition is not considered or because of the lapse of time between the two operations. The recognition of these five cases over a short period suggests that starch granulomatosis is a widespread and common condition, and every precaution should be taken to minimize starch contamination of the operative field.

We are greatly indebted to our colleagues, especially Mr. D. F. Ellison Nash, for access to case notes of patients under their care, and also to Dr. T. J. Wickham for access to pathological material. Mr. P. Crocker produced the excellent photomicrographs.

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Outside Europe

Independent Hospital Dialysis in Brunei

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Summary

In establishing a chronic haemodialysis unit in Brunei the difficulties encountered were less insuperable than had been expected. Quite unsophisticated patients successfully dialysed unattended in some cases, or with minimal supervision in others.

Introduction

Brunei is an oil-rich state under British protection which is in the position to provide free medical care for its citizens. It is an

enclave on the northern shore of Borneo which is in process of rapid development, lies in the equatorial rain forest belt and has a climate which varies little from one season to another, such seasonal variations as do occur being largely unpredictable. It is hot and humid, the mean air temperature being between 76° and 86°F (24.4° and 30.0°C). The annual rainfall is between 100 and 200 in (254 and 508 cm). The population numbers about 150,000. The predominant races are Malays (about half of the total) and Chinese (30%), with smaller numbers of Ibans, Kedayans, and Dusuns, and also expatriate Indians and Europeans.

Communications and Staffing

Towards the end of 1967 a Government decision was taken to establish a small renal unit. Both the consultant in charge and the first patient received initial training in the nephrology depart-

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