STARCH GRANULOMATA

BY

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During the years 1933 to 1941 attention was drawn in a number of publications to the irritative effect of talc, the introduction of which into tissues, particularly the peritoneal cavity, led to the formation of granulomata and chronic inflammatory adhesions (Haythorn, 1933; Antopol, 1933; Owen, 1936; Fienberg, 1937). The work of Ramsey and Douglass (1940), Byron and Welch (1941), and others made it clear that the use of talc as a glove powder lubricant was largely responsible for such lesions, which developed as a sequel to previous operative procedures, when glove powder had inadvertently been introduced. Postlethwait, Howard, and Schanher (1949) considered that the implantation of surgical glove lubricant could occur from unwashed or perforated gloves, spill on to instruments and suture material, and by direct airborne route. It is probable, as will be shown below, that the introduction of glove powder into the peritoneal cavity of women is not limited to these routes.

The rejection of talc as a glove lubricant led to the search for substitutes, and experimental work, mainly upon dogs and rabbits, indicated that suitable starch preparations could act as serviceable lubricants, and that they produced minimal lesions within tissues (Lee and Lehman, 1947; MacQuiddy and Tolman, 1948; Postlethwait *et al.*, 1949).

In the above hospital starch powder was substituted for talc as a glove lubricant in 1952, since when starch-containing lesions have been found at laparotomy on three occasions. In respect of talc granulomata there is often a lapse of many years between the introduction of the powder and the recognition of talc lesions; in these the spicules of talc remain apparently unabsorbed, but are enveloped by foreign body and fibrous tissue reactions of varying magnitude. It was difficult to believe that starch particles could be similarly unabsorbable, and therefore inquiries were made to determine the method by which these particles had been introduced into the peritoneal cavity, the nature of the tissue response, and the

probable duration and pathological significance of the lesions produced. An account of these investigations forms the subject of this communication.

Case Reports

Case 1.—Mrs. Br., aged 39 years, gave a two-day history of lower abdominal pain. On examination a large tender cystic mass was felt arising from the pelvis. There had been no previous operations, and she had two normal deliveries, her children being aged 16 and 10 years respectively. The duration of time from pelvic examination on admission to laparotomy was two days. A panhysterectomy and double salpingo-oophorectomy was performed. The specimen showed a papillary erosion of the cervix; the endometrium was of normal secretory pattern; old fibrous adhesions were present on the posterior aspect of the uterus and on the tubes; both ovaries contained areas of endometriosis. In a crypt of the right ovary there was a proliferation of recent granulation tissue containing starch granules and infiltrated by polymorphonuclear leucocytes, monocytes, and macrophage cells (Figs. 1 and 2).

Case 2.—Mrs. Ba., aged 65 years, an emaciated old woman, complained of loss of weight and of a bearing-down sensation on walking. A painless mass was felt in the right iliac fossa. A vaginal examination confirmed the presence of this mass, and a similar but smaller mass was felt on the left side. The masses were considered to be ovarian or intestinal, but a barium enema did not show any interference with the bowel lumen. The patient gave a past history of pulmonary tuberculosis at age 31 years. There had been no previous operations. The duration in time from pelvic examination on admission to laparotomy was nine days. At laparotomy the genital tract appeared normal. The masses were found to involve the bowel, there being two masses in the small intestine 5 and 18 in. from the ileo-caecal valve, and a further mass in the sigmoid colon. The lesions presented as soft diffuse thickenings of the intestinal wall without any appreciable narrowing of the gut lumen. No lymph node enlargement was found and the liver felt normal; at the reflection of the peritoneum from the mesentery on to the small intestine, two small nodules were seen. These were removed for biopsy and the abdomen closed. The patient sub-

FIG. 1.—Case 1: section through ovarian crypt showing starch granuloma. Haematoxylin and eosin, $\times 90$.

FIG. 2.—Case 1: section through ovarian starch granuloma. Haematoxylin and eosin, polarized light, $\times 90$.

FIG. 3.—Case 2: section of peritoneal starch granuloma. Haematoxylin and eosin, $\times 90$.

FIG. 4.—Case 2: section of peritoneal starch granuloma. Haematoxylin and eosin, polarized light, $\times 90$.

sequently developed enlarged axillary lymph nodes, one of which was excised for diagnosis; after 18 months she died with extensive lymphosarcomatosis. The excised peritoneal nodules consisted of rather loose areolar connective tissue, containing small zones of lymphoid tissue. There was an indolent chronic inflammatory reaction with marked dilatation of the blood vessels. In one part there had been an extravasation of blood, wherein organization was in process. This area, which contained the largest number of starch particles, was infiltrated with polymorphonuclears, monocytes, and macrophage cells (Figs. 3 and 4).

Case 3.—Mrs. D., aged 47 years, was admitted to hospital with a history of heavy and irregular periods for two years. A diagnosis of multiple fibroids was made. There had been no previous operations. The interval between the first pelvic examination at the Out-patient Department and admission to hospital was six weeks: the interval between admission and laparotomy was two days. The specimen obtained after panhysterectomy and bilateral salpingo-oophor-

ectomy showed chronic cervicitis, a regenerating endometrium, multiple submucous and intramural fibroids and bilateral mild chronic salpingitis. The left ovary contained a very recently ruptured follicle and in one of the ovarian crypts there was a granulomatous mass containing starch particles. The appearance of this did not differ appreciably from that shown in Case 1.

In addition to these, a further case (Mrs. S.) has been seen in which a perineal sinus developed following a plastic vaginal operation. The sinus was due to a nylon suture, but in the wall both talc crystals and starch particles were visible.

Identification of Starch Particles

The recognition of starch particles in sections is facilitated by the use of polaroids, and a comparison was made between the appearance of starch in the lesions, that of glove powder in current use, and samples of the commonly available starch powders, potato, maize, rice, and

FIG. 5.—A comparison of maximum, mean, and minimum particle diameters of starch samples with those of starch in granulomata.

wheat. Not only was there a considerable variation in size and shape of starch particles from different sources, but a wide range of size variation in individual starches was noted. All the starches examined showed a Maltese cross configuration with polarized light, and it was found that the identification of a source of starch was best accomplished by determining the total range of particle size and the mean diameter. Accordingly 400 particles were measured in respect of each starch sample and of the glove powder, and the sizes of as many particles as possible (60 to 230) in sections of starch lesions. The results of these examinations, set out in Fig. 5, show that the particle size of the starch in the lesions corresponded closely to that of maize starch and of glove powder, which, according to the manufacturers, was prepared from maize starch. None of the particles in the lesions showed the oval forms and contours characteristic of potato starch, and it was therefore concluded that the lesions formed as a response to the introduction of glove powder containing maize starch.

Fate of Starch Suspensions Injected Intraperitoneally into Mice

Attempts were made to produce starch granulomata within the peritoneal cavities of mice. Animals killed one week after the intraperitoneal injection of each of the four starch samples, suspended either in saline or in citrated mouse blood, failed to show peritoneal lesions, nor was there histological evidence from studies of the omentum,

liver, spleen, and lungs of any starch survival or transportation.

In a second series, 24 mice were given intraperitoneal injections of 0.5 ml. 4% maize starch suspensions in saline. The mice were killed in pairs at intervals after inoculation, the peritoneal cavity of one of each pair being injected with 1.0 ml. Lugol's iodine immediately after death and before the peritoneal cavity was opened. At one and two hours there was a generalized darkening of the peritoneal wash in the iodine-treated animals, and polymorphonuclears with free starch particles were visible microscopically. No localization of the starch was noted, and histological examination of the omentum, intestines, liver, spleen, and lungs confirmed these findings. Mice killed at four hours showed small aggregations of starch surrounded by polymorphonuclears lying free within the peritoneal cavity; the omentum was stained black with iodine. After eight hours the starch no longer remained free within the peritoneum, but it was all immobilized in the omentum. Mice were then killed at 12, 18, 24 hours, and daily up to six days; iodine tests failed to show any gross aggregations of starch either free in the peritoneal cavity or within the omentum. Histological studies were made of the omentum, intestines, liver, spleen, and lungs; in no case was starch found in organs other than the omentum, in which it could be detected up to four days. The omental lesions are shown in Figs. 6 and 7.

It was noted that in the omentum of animals killed at 96 hours, although doubly refractile bodies were still evident, the proportion showing the Maltese cross configuration was appreciably smaller than in mice killed earlier. A further study of particle size in relation to survival time showed after eight hours a progressive diminution in size (Fig. 8).

In the absence of evidence that the injected starch was transported elsewhere, and because of the diminution in particle size associated with increasing leucocytic infiltration of the omentum, it was concluded that the disappearance of the starch was due to local enzymic action by the surrounding cells.

Fate of Starch Particles Within the Peritoneum of Other Species

No direct observations, comparable with those in mice, have been made or are possible in humans. The relatively speedy disappearance of starch from the peritoneum in mice is paralleled by the observations of Postlethwait *et al.* (1949), who

FIG. 6.—Section of mouse omentum four hours after intraperitoneal injection of maize starch suspension. Haematoxylin and eosin, polarized light, $\times 110$.

FIG. 7.—Section of mouse omentum 24 hours after intraperitoneal injection of maize starch suspension. Haematoxylin and eosin, polarized light, $\times 110$.

found only minimal adhesions and only one granulomatous type lesion containing visible starch particles in a series of four dogs and nine rabbits killed at intervals of from two hours to 37 days after starch had been introduced into the peritoneal cavity. The cellular response, as described by these authors, and that in humans and in mice do not differ essentially, and it seems probable therefore that the mechanism whereby starch disappears from the human peritoneal cavity is essentially the same as that described here for mice. In reviewing the histology of the human lesions, it will be noted that the starch appeared to have been first incarcerated within blood clot, which probably protected the starch from early dissolution.

Route of Entry of Starch into the Human Peritoneal Cavity

In none of the cases recorded here was there any history of previous laparotomy, as has been recorded so frequently in cases of talc granulomata. The mechanism of its introduction must therefore be different, and, in view of the evidence that starch disappears relatively rapidly, it seems

probable that the starch had been introduced only a few days before operation. These observations, coupled with the fact that in cervical smear preparations, used in the investigation of sterility,

FIG. 8.—Diminution in maximum, mean, and minimum particle diameters of maize starch after intraperitoneal injection into mice.

starch particles are a common finding, suggested that the starch had been introduced at vaginal examination made at admission, and had traversed the genital tract to enter the peritoneum. McCartney and Fraser (1922) showed that a similar method of spread operated in primary pneumococcal peritonitis, thus accounting for the very high incidence of the disease in young girls as compared with young males.

The number of cases of starch granulomata was too small to provide any idea of the relative frequency of occurrence of intra-abdominal granulomata developing as a response to the introduction of foreign particles by routes other than that provided by a previous laparotomy. Therefore a series of 50 cases of talc granulomata was reviewed to determine the case incidence, where no previous laparotomy could account for the peritoneal seeding; in six of the series there was no evidence of previous laparotomy, pre-operative attendances as out-patients, when vaginal examinations were made, varying from two to 10 times.

Discussion

Three cases of starch granulomata within the peritoneal cavity of women have been described, and evidence has been adduced to show that the starch was derived from the glove powder in current use in the hospital. In mice, starch disappears from the peritoneal cavity within a few days of its introduction, this being accomplished largely by digestion by polymorphonuclear leucocytes. The absence of previous intraperitoneal operative procedures in the cases described, and the fact that intraperitoneal talc granulomata can occur in cases where there had been no previous operative interference, indicates that the starch

had reached the peritoneal cavity via the genital tract, and if, as seems probable, the rate of disappearance of starch from the human peritoneum is similar to that in mice, the starch was probably introduced during vaginal examinations made a few days before operation.

Starch absorption within the peritoneal cavity may be delayed if the starch is entrapped in blood clot, and, although it is probable that starch lesions are merely transitory phenomena and unlikely to be of such serious import as talc granulomata, it would seem desirable to limit the chances of intraperitoneal adhesions from this cause. Attention is drawn once more to the importance of a careful peritoneal toilet at the end of intra-abdominal procedures, particular attention being paid to the removal of small fragments of blood clot, wherein glove powder might be entrapped. It is desirable also that glove powder should be removed from gloved hands by washing, both before embarking upon all operative procedures and also before making vaginal examinations.

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