

form. But the recently formed Medical Administrators' Group of the B.M.A. will carry on and extend the principles instituted by the early pioneers and defended so faithfully by a long succession of devoted followers. It is to be hoped that the society's ideals will continue to influence the conduct of medical affairs and will find expression in the wider field of medical management.

<sup>1</sup> *British Medical Journal*, 1967, 4, 187.

## Paget's Disease of the Skin

It is nearly a century since Sir James Paget first described the eczematoid lesion of the skin that bears his name.<sup>1</sup> This is found most often on the nipple and areola of the breast, but has also been described on the penis,<sup>1</sup> anus,<sup>2</sup> vulva,<sup>3</sup> axilla,<sup>4</sup> and eyelid,<sup>5</sup> and in the mucosa of the oesophagus and larynx.<sup>6</sup>

Histologically there is an infiltration of large, round Paget cells, singly or in groups, throughout the lower part of the epidermis. These have a pale, clear cytoplasm and a large vesicular nucleus, in which there may be a prominent nucleolus. Histochemical stains sometimes show much mucopolysaccharide in the cytoplasm, especially in lesions of the anus<sup>2</sup> and vulva, but this is not the rule with mammary Paget's disease.<sup>7</sup> In most cases affecting the breast there is an underlying carcinoma, usually affecting the superficial ducts and contiguous with the skin lesion—though sometimes it is deep-seated and quite separate. Most cases of perianal Paget's disease are also associated with an underlying adenocarcinoma, probably arising from neighbouring apocrine glands.<sup>2</sup> But in Paget's disease of the skin in other sites no underlying malignancy can usually be found.

M. E. Fenn and her colleagues have recently reported seven cases of Paget's disease of the vulva.<sup>8</sup> In all of them the Paget cells, which were rich in mucopolysaccharide, were found in neighbouring pilosebaceous structures as well as in the epidermis, and in two cases the sweat ducts were also involved. In no instance was there an underlying invasive carcinoma, but three patients had a primary cancer elsewhere in the body, either at the time of treatment or previously. One patient had had four primary malignant tumours in addition to Paget's disease over the previous 24 years.

The pathogenesis of Paget's disease has occasioned much controversy. The original view was that it represented an intraepithelial invasion of cancer cells from an underlying carcinoma of a breast duct or an axillary apocrine gland. Nevertheless, the distance of this tumour from the skin in some cases and its absence in others make this hypothesis frequently unacceptable. There is now a growing consensus of opinion that Paget cells arise in the actual epithelium, and that Paget's disease itself is a type of intraepithelial cancer. In some instances a transition to Bowen's disease (intraepidermal carcinoma) is evident,<sup>9</sup> as in two of the patients described by Fenn and her colleagues.<sup>8</sup> Thus while intraepithelial spread might account for a few of those cases of Paget's disease with an underlying carcinoma, more probably these lesions represent a multifocal primary cancer arising in an extensive field of neoplasia. In all cases of Paget's disease it is important to exclude invasive cancer,

not only in the vicinity of the lesion but also elsewhere in the body.

<sup>1</sup> Paget, J., *St. Bartholomew's Hospital Reports*, 1874, 10, 87.

<sup>2</sup> Gunn, A., and Fox, H., *British Journal of Dermatology*, 1971, 85, 476.

<sup>3</sup> Koss, L. G., Ladinsky, S., and Brockunier, A., *Obstetrics and Gynecology*, 1968, 31, 513.

<sup>4</sup> Weiner, H. A., *American Journal of Cancer*, 1937, 31, 373.

<sup>5</sup> Knauer, W. J., and Whorton, C. M., *Transactions of the American Academy of Ophthalmology and Otolaryngology*, 1963, 67, 829.

<sup>6</sup> Yates, R. D., and Koss, L. G., *Archives of Pathology*, 1968, 86, 447.

<sup>7</sup> Lennox, B., and Pearse, A. G. E., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1954, 61, 758.

<sup>8</sup> Fenn, M. E., Morley, G. W., and Abell, M. R., *Obstetrics and Gynecology*, 1971, 38, 660.

<sup>9</sup> Willis, R. A., in *Pathology of Tumours*, 4th ed., p. 284. London, Butterworths, 1967.

## Contaminated Drip Fluid

Sterilizing bulk supplies is recognized to be an inherently difficult process. Because of the scale of operations only steam sterilization can be used; one container may be adequately sterilized while its neighbour is not; and there is still no certain indicator that the entire contents of an autoclave have been sterilized. To avoid the presence of pyrogens in the final product particular emphasis has been placed on aseptic conditions, and special sterilizing cycles and designs for infusion bottles have also been developed. As a final check the usual practice after the autoclaving process is to test a random sample of the bottles bacteriologically. Nevertheless, clearly the bottles which are used for actual infusions cannot be sampled in this way.

With all these precautions only one previous episode involving fatality from contaminated drip fluid has apparently been reported in Britain in recent years,<sup>1</sup> and doctors have been able to set up a drip confident that the infusion solution is as sterile as that in any drug ampoule. Yet if contamination has escaped detection by routine checks it may unfortunately be revealed only by the occurrence of rigors, severe illness, or even death in the patients receiving the fluid. Thus any inquiry into the recently reported contamination of dextrose solution should ask several questions. Where did the contamination arise—in the distilled water used for preparing the solution, or in the cooling process used after autoclaving? Were these episodes caused by live organisms—and if so why were they so uniformly serious—or by endotoxin? If the solution was initially contaminated by bacteria why were these not killed by autoclaving? Do the tests for sterility and pyrogens suggested in the *British Pharmacopoeia* give adequate protection? Are they carried out at a stage in the process likely to reveal contamination? And, if not, is there a case for sampling after the bottles have been set aside for some time? All these questions must be answered satisfactorily, for, though contamination of intravenous fluid seems very rare, its effects are so disastrous that this episode must not be repeated.

<sup>1</sup> *British Medical Journal*, 1966, 2, 597.

## Birth Control Campaign

Public opinion seems to be moving in favour of wider provision of contraceptive advice and appliances, and there is increasing pressure to include these services within the

N.H.S. A comprehensive *Birth Control Plan for Britain*, published<sup>1</sup> this week by the Birth Control Campaign,<sup>2</sup> deserves doctors' support, since its reasonable suggestions for a national family planning service are backed up by clear and unemotional argument.

The plan urges that advantage should be taken of the reorganization of the N.H.S., planned for 1974, to include full birth control services in the new structure. Senior staff at the Department of Health and on regional health authorities should have birth control among their named responsibilities, says the plan, and birth control clinics should be set up by every area authority. The key figures would be 90 or so area health authority birth control officers, who would co-ordinate the activities of general practitioners, hospitals, health visitors, and social workers. The realistic tone of the proposals is shown by the suggestion that general practitioners should be compensated for their loss of income from prescriptions for the pill by a regular payment from the Department to those prepared to give contraceptive advice and to keep up to date by attending periodic refresher courses.

Whatever the merits of the mathematical arguments about population trends, no one would dispute that unwanted children are often unhappy and underprivileged. The plan stresses as its primary aim reduction in the 300,000 unwanted pregnancies in Britain each year, most of which end either in abortion or in the birth of an unwanted child. The Birth Control Campaign estimates the cost of provision of free contraception to all who want it at about £20 million a year. Compared with the cost to society of coping with the medical and social problems created by unintentional conception this would be an excellent bargain.

<sup>1</sup> *A Birth Control Plan for Britain*. Sussex, The Birth Control Campaign, 1972.

<sup>2</sup> *British Medical Journal*, 1971, 2, 231.

## Second Cancer of Colon

It is not unusual for cancers of the large bowel to be multiple. They may coexist (synchronous), or a second cancer may grow after resection of the first (metachronous). E. S. R. Hughes<sup>1</sup> found that 25 out of 1,015 patients operated on for cancer of the large bowel had a second tumour and nine others developed a second cancer 2-20 years after their first resection. J. C. Goligher and colleagues<sup>2</sup> noticed 98 examples of multiple tumours in 3,220 specimens of cancer of the rectum and colon examined at St. Mark's Hospital, an incidence of 3%. Multiple synchronous tumours are more common in patients with ulcerative colitis, benign adenomas, and polyposis coli.

Metachronous cancers may represent tumours that were overlooked at the first operation, a recurrence of inadequately excised growths, an implantation of tumour cells at an anastomosis suture line, or a second primary tumour. Recurrence at a suture line results from the implantation of free malignant cells during operation. Since C. Naunton Morgan and O. V. Lloyd-Davies introduced the practice of excluding and irrigating the distal rectal stump with a 1:500 solution of mercury perchloride these recurrences have occurred in only about 2% of cases.<sup>3</sup> Other agents, such as a 1% solution of cetrimide, seem equally effective. J. Hale<sup>4</sup> has shown in animals that these cytotoxic agents prevent seeding from taking place but that simple irrigation with saline does not.

J. R. Heald and H. E. Lockhart-Mummery,<sup>5</sup> in a recent survey of 83 patients with metachronous cancer of the large intestine, found a high incidence of second growths in the first two years, but thought that many must have been synchronous tumours missed at the first operation. Corrected for that, the average interval between the first and second operations was just over 11 years. Almost two-thirds of the patients had associated benign tumours. This study illustrates the importance of careful follow-up after resection of large-bowel cancer. Growths in 41 patients among those attending the follow-up clinic were diagnosed much earlier than in most series, whereas no fewer than 8 of 17 patients not attending the clinic had inoperable growths. Prognosis was particularly favourable in patients whose second tumour was diagnosed by sigmoidoscopy or barium enema before signs or symptoms had developed.

A study of the patients in the series whose second tumour was diagnosed within two years of the first (21 cases) suggested that in 18 the growth had existed at the time of the first operation but it was not detected. This emphasizes the danger of resecting the colon without a preliminary sigmoidoscopy, of excising a cancer of the rectum without a preliminary barium enema, or of not palpating the whole colon at the time of laparotomy. With adequate preparation of the bowel and a double-contrast enema a full study of the colon, even when there is early obstruction, is nearly always possible.

A slight constriction normally occurring at the site of an anastomosis may present a difficulty in the diagnosis of recurrent colonic carcinoma. The normal anastomosis should be smooth, symmetrical, and have a regular mucosal pattern.<sup>6</sup> An irregular, asymmetrical filling defect suggests a recurrence. To provide a diagnostic base line the anastomosis should be investigated with a limited double-contrast enema examination six weeks after operation, by which time the configuration of the anastomosis should have become permanent. Subsequent barium enema studies would then show any change.<sup>6</sup> Heald and Lockhart-Mummery suggest sigmoidoscopy at six-monthly intervals and a double-contrast enema every two years. It is encouraging therefore to learn from Heald and Lockhart-Mummery's study that provided the diagnosis is made early the prognosis in cases of metachronous tumour is good. H. Ellis<sup>7</sup> has reviewed 27 patients diagnosed as having a presumed recurrence after previous resections for large-bowel cancer. At laparotomy three were found to have non-malignant conditions with no evidence of recurrence of the original disease. Four had metachronous tumours, ten had recurrence at the anastomosis, five had isolated recurrences elsewhere, two had developed new tumours (a carcinoma of the body of the uterus and a carcinoma of the kidney), and three were found to have disseminated disease. There was a good long-term result in nine of the patients, and two were well within a year of their second operation.

Undoubtedly patients who have had a cancer of the large bowel resected should be followed up carefully and indefinitely. The rewards of early diagnosis of a recurrence or of a metachronous cancer are well worthwhile.

<sup>1</sup> Hughes, E. S. R., *British Medical Journal*, 1963, 2, 9.

<sup>2</sup> Goligher, J. C., Dukes, C. E., and Bussey, H. J. R., *British Journal of Surgery*, 1951-1952, 39, 199.

<sup>3</sup> Keynes, W. M., *Annals of Surgery*, 1961, 153, 357.

<sup>4</sup> Hale, J., *Proceedings of the Royal Society of Medicine*, 1969, 62, 713.

<sup>5</sup> Heald, J. R., and Lockhart-Mummery, H. E., *British Journal of Surgery*, 1972, 59, 16.

<sup>6</sup> Bartram, C., and Hale, J. E., *Gut*, 1970, 11, 778.

<sup>7</sup> Ellis, H., *British Medical Journal*, 1971, 3, 291.