dosage, and included insomnia, headache, giddiness, and palpitation. It may well be, in view of our results, that such untoward effects are evidence of some vitamin deficiency induced by the large excess of the single vitamin.

Little is known as yet regarding human requirements of pyridoxine, but some results recorded by Spies, Bean, and Ashe (1939) are of interest. They found that 4 patients who had been treated successfully for pellagra and beriberi, but who remained on their deficient diets, complained of such symptoms as extreme nervousness, insomnia, irritability, abdominal pain, weakness, and difficulty in walking. All the symptoms disappeared within 24 hours of an injection of 50 mg. of pyridoxine. Later, Spies, Ladisch, and Bean (1940), studying the urinary excretion of B₆ in human subjects, found indications of B₆ deficiency in patients suffering from other clinical deficiency diseases. It is thus evident that pyridoxine deficiency can arise in man under certain circumstances.

It is becoming increasingly recognized that in the treatment of pellagrins with nicotinic acid it is essential to provide other members of the B complex and to prescribe a liberal and well-balanced diet. Our experiments would suggest the necessity for adopting a similar procedure for other B factors, and in particular, when B₁ therapy is indicated, for supplying the whole B complex instead of the single vitamin. It was suggested in the previous paper (Richards, 1943) that the improvements effected in a poor human diet by means of such simple supplements as inorganic calcium, milk, and dried yeast provided a useful pointer for the post-war feeding of the starved populations in Europe. The present results emphasize the need for caution in any attempt to improve the diet of these populations by indiscriminate addition of large supplements of single synthetic B vitamins.

REFERENCES

- Bichel, J., and Meulengracht, E. (1941). *Klin. Wschr.*, **20**, 913.
 Brøndstrup, P. (1940). *Ugeskr. Laeg.*, **102**, 95.
 Chick, H., Copping, A. M., and Edgar, C. E. (1935). *Biochem. J.*, **29**, 722.
 — El Sadr, M. M., and Worden, A. N. (1940). *Ibid.*, **34**, 595.
 Daniel, E. P., Kline, O. L., and Tolle, C. D. (1942). *J. Nutrit.*, **23**, 205.
 György, P. (1934). *Nature*, **133**, 498.
 Klopp, C. T., Abels, J. C., and Rhoads, C. P. (1943). *Amer. J. med. Sci.*, **205**, 852.
 Lehmann, J., and Nielsen, H. E. (1939). *Nord. Med.*, **1**, 289.
 Leitner, Z. A. (1943). *Lancet*, **2**, 474.
 Patton, R. A., Karn, H. W., and Longenecker, H. E. (1944). *J. biol. Chem.*, **152**, 181.
 Richards, M. B. (1943). *British Medical Journal*, **2**, 418.
 Salvesen, O. (1940). *Nord. Med.*, **5**, 279.
 Sebrell, W. H., and Butler, R. E. (1938). *Publ. Hlth. Rep. Wash.*, **53**, 2282.
 — (1939). *Ibid.*, **54**, 2121.
 Spies, T. D., Bean, W. B., and Ashe, W. F. (1939). *J. Amer. med. Ass.*, **112**, 2414.
 — Ladisch, R. K., and Bean, W. B. (1940). *Ibid.*, **115**, 839.
 — Vilter, R. W., and Ashe, W. F. (1939). *Ibid.*, **113**, 931.
 Steinberg, C. L. (1938). *Amer. J. digest. Dis.*, **5**, 680.
 Sydenstricker, V. P., Sebrell, W. H., Cleckley, H. M., and Krus, H. D. (1940). *J. Amer. med. Ass.*, **114**, 2437.
 Unna, K., and Clark, J. D. (1942). *Amer. J. med. Sci.*, **204**, 364.

DUCT PAPILOMATA OF THE BREAST A PLEA FOR CONSERVATIVE TREATMENT

BY

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There is too great a tendency to-day to regard duct papillomata of the breast as malignant or potentially malignant, and therefore requiring amputation of the breast. To my mind it shows a lack of thought, of experience, and of a thorough examination of every breast removed, when such opinions are held. Local amputation of the breast is an easy operation, and it is wishful thinking to say that because a young woman has a blood-stained discharge from the nipple the breast should be removed owing to the possibility of cancer supervening. It is quite true that a blood-stained discharge from the nipple may be caused by carcinoma, chronic cystic mastitis, or papilloma: it is the responsibility of the surgeon to make a differential diagnosis of these three conditions.

Duct papillomata are nearly always found in the larger ducts, and are therefore situated beneath the nipple or the areola. The majority of these tumours are single, but in some cases

multiple papillary growths are to be found in the ducts. The common single papilloma often has a stalk, and some pathologists have termed them "single-stalk" papillomata. They always occur beneath the nipple, and frequently cause bleeding from it.

It is difficult to be dogmatic about the common age when symptoms develop, but it can be said that duct papillomata are uncommon before the age of 25, although I have removed one from the breast of a girl aged 20. A small proportion of patients have papillomatous growths elsewhere, the commonest site being the skin.

The clinical course of these cases is interesting, as the papillomata grow very slowly and may continue for many years. The haemorrhagic discharge from the nipple is intermittent, and may be serous with no sign of blood. At times a small tumour may be felt in the region of the nipple. This swelling may be tense or soft, and may entirely disappear after a discharge of blood-stained fluid from the nipple.

In many cases the thickened duct can be felt by careful palpation; quite often it is situated under the areola, and pressure on it will cause a haemorrhagic discharge from the nipple. There is no sign of any hardness or infiltration, such as would be felt if a carcinomatous condition had supervened on the papilloma.

Treatment

Every case must be examined carefully and at definite intervals until it is certain that a dilated duct can be felt. When this is established a local excision of the dilated duct, with the papilloma, can be undertaken (see Fig.). An incision is

Diagrammatic drawing of an intracystic duct papilloma. The outer side of the breast is dissected to show the lactiferous ducts during the period of lactation. Inset: the skin incision united by sutures.

made radiating from the nipple over the dilated duct. The skin edges are held apart, the cystic dilatation is opened, and the intracystic papilla is completely excised. The operation is simple, and no damage is done to the ducts on either side. The skin incision is closed with a few interrupted sutures, and when healed is hardly noticeable. Every papilloma excised should be examined microscopically for any evidence of malignant disease. The patient should be examined at three-monthly intervals during the first year; after this time a yearly examination will suffice.

Having performed this operation on 52 cases during the last 30 years I have no doubt that it is the very best form of treatment. What are the alternatives? They are radiotherapy and amputation of the breast. Radiotherapy is usually of little use in curing the condition. The papillomata are not radio-sensitive, and at the best fibrosis of the rest of the breast occurs; this is often painful, and produces a functionless breast.

Local amputation of the breast in young women produces a very unsatisfactory state of affairs. The patients become introspective, worry a lot, and tend to become chronic invalids. Many drift to the out-patient departments of the neurological hospitals. I have case reports of 20 unmarried women under 30 years of age who have been subjected to local removal of one or both breasts because of a history of a blood-stained discharge from the nipple. These women are afraid to marry because they consider that they are not normal. This state of affairs must not be allowed to continue, as it means a life of constant misery.

The following up of operation cases is most important if we are to get a clear idea of the real value of conservative surgery. Of my 52 cases of duct papilloma of the breast I have "follow-up" records of 35; six patients are abroad and I cannot trace them. However, the clinical history of three cases will show the real advantage of conservative surgery for duct papilloma.

Case Histories

Case 1.—A nurse, aged 24, who had just finished her training in a London hospital, was seen in July, 1915, with a history of a blood-stained discharge from the left breast for some nine months. Nothing could be felt on examination and no discharge was visible from the nipple. The patient was told to come and see me when there was any further discharge from the nipple. In Sept., 1915, she came again, and a small cystic lump could be felt just lateral to the nipple in the lower and inner quadrant of the breast. A slight blood-stained discharge could be expressed from the nipple. Operation was undertaken, and a small intracystic papilloma was excised. The papilloma had a definite stalk, and microscopically was quite innocent. The patient left hospital a week later. She was seen in 1919 before her marriage, as she was concerned about the effect of pregnancy on the breast. The breast was quite normal, and there had been no discharge from the nipple since the operation. The patient was reassured that no ill effects would supervene if pregnancy took place. She was seen again in 1936 because of cholecystitis due to gall-stones. She had five children—three boys and two girls—and had breast-fed all of them without any difficulty whatever. Cholecystectomy was carried out in July, 1936, and recovery was uneventful.

Case 2.—A married woman aged 32 was seen in Jan., 1920; she was sent to me to have her right breast removed because of an intermittent blood-stained discharge. She was a big woman with large firm breasts. A small lump the size of a pea could be felt in the lower and outer quadrant of the breast. She was prepared to have the breast removed, but was advised to undergo excision of the lump instead. Local excision of the papilloma was carried out and the growth was found to be innocent. The patient was last seen in 1939, when she was in good health; the breast was quite normal, although somewhat atrophic. Her periods had stopped some three years previously.

Case 3.—An unmarried woman, aged 26, a well-known golfer, was seen in 1922 because of a blood-stained discharge from the left nipple. There was little to make out on clinical examination, and the patient was told not to worry and to forget about her breast. She was seen in 1923 and again in 1924, and on neither occasion could anything be felt in the breast, although there was a slight intermittent discharge of blood-stained fluid from the nipple. When seen in May, 1925, a small lump could be felt in the lower part of the breast just below the nipple. This was excised, and proved to be a simple papilloma. Six months later the patient married and was not seen again till 1932, when her child, aged 6, was operated upon for appendicitis. Her breasts were then quite normal and there had been no discharge from the nipple since the operation. She had not breast-fed her child, as her doctor thought it might cause trouble in the breast. This idea, which still prevails in some quarters, is quite erroneous.

Conclusion

These three cases clearly demonstrate the value of conservative surgery in the treatment of duct papilloma of the breast. Every hospital of any size has specimens of small innocent papillomata because of which the breast had been removed. Conservative surgery will not provide such nice museum specimens, but it will produce contented and very thankful patients.

B. Levant (*J. Urol.*, 1944, 52, 63) records a fatal case of sarcoma of the penis in a negro aged 29. Deep x-ray therapy was beneficial. Biopsy from an inguinal gland, though confirmatory of metastases, hastened the spread of the tumour, with general systemic failure.

"NEUTRAL PROFLAVINE SULPHATE" (MONOSULPHATE OF 2:8-DIAMINO- ACRIDINE)

ITS LOCAL ACTION IN INFECTED WOUNDS INVOLVING BONE

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It has been realized for a considerable time that the high acidity of proflavine sulphate *B.P.* is a serious drawback, and various methods have been suggested for countering this, such as a preliminary neutralization with sodium bicarbonate or the addition of a buffering salt. There is now available, however, "neutral proflavine sulphate," which possesses all the activity of the *B.P.* salt and yet gives a neutral solution. The relationship of neutral proflavine sulphate to proflavine sulphate *B.P.* may be compared with that of quinine sulphate to quinine bisulphate—i.e., the neutral sulphate has one equivalent of acid, while the *B.P.* salt contains two equivalents. In a 0.1% solution neutral proflavine sulphate is stated to have a pH of 6.5, as contrasted with pH 2.5 of proflavine sulphate *B.P.* Our brief experience with a sample of neutral proflavine sulphate indicates, however, that its action towards the tissues is the same as that of proflavine sulphate *B.P.*, and consequently, like it, should be used (1) in small doses of from 0.2 to 0.5 g. in discharging wounds, and (2) diluted to 0.5% in sulphathiazole powder for local application to wounds subjected to fresh debridement. We would also suggest that the optimum concentration of proflavine sulphate *B.P.* in sulphathiazole-proflavine powder is 0.2%, rather than the strength of 1% at present employed prophylactically in "debrided" wounds.

The cases treated were with us for only a short time. They comprised gunshot and similar wounds with compound fractures (often comminuted) which had been infected and relatively untreated for from six months to two years. The majority had had repeated sequestrectomies, with, in some instances, sulphonamides locally and/or orally in support. By the time of our observations general nutrition was restored; none of the patients were more than slightly anaemic (less than 80% Hb). Neutral proflavine sulphate powder, sterilized as are the sulphonamides, was applied to the wound area at the time of the last sequestrectomy and the wound lightly packed. In a few cases it was applied 2 to 14 days after sequestrectomy, and in others it was inserted into sinuses from the depths of which sequestra had been removed earlier. Thus the powder was applied to surfaces with granulations forming and established and with exudate in varying amount, as well as to wounds "debrided" afresh, with curetted and guttered bone, curetted sinuses, etc., in which no granulation tissue and little exudate or pus was present.

Technique of Treatment

At first, having regard to the relatively neutral character of neutral proflavine sulphate, doses of from 1 to 5 g. were applied, the former to small and the latter to large wounds. Many patients complained of some burning pain, which during the first 24 to 48 hours was accompanied by moderate pyrexia (101–102° F.), partly attributable to surgical measures. Locally, the soft tissues around the wound were inflamed, and brawny oedema extended for a short distance. The immediate wound margin was of firm, rubber-like consistence. On removing the excess neutral proflavine sulphate on the 4th, 6th, or 10th day the wounds were dry and the appearance of the walls everywhere up to but not involving the skin margins was that of "tanning"—superficial coagulative necrosis—to a depth of 2 to 4 mm. This was most pronounced in freshly "debrided" wounds, which were relatively dry, and less pronounced where