Cross-infection may be reduced by keeping infants in separate rooms with their mothers (Hutchison and Bowman, 1957). But for "rooming-in" to be effective, contact with nurses must be kept to a minimum. Some contact is unavoidable, especially in the first few days of life, when it is most likely to lead to dangerous colonization. Consequently the provision of separate rooms cannot be the whole answer to the cross-infection problem.

Precautions may also be directed against the sources of the staphylococci. It is impracticable to exclude all adult carriers from a hospital. An attempt might be made to exclude, or to treat, the carriers of exceptionally virulent strains; but such a policy would be difficult to enforce. If even a few staphylococci were allowed to enter the nursery, they might colonize some infants and multiply so as to form a large staphylococcal reservoir from which other infants would be cross-infected. Moreover, an infant who has been colonized by a virulent strain is a danger to himself as well as to other infants, and probably is a danger to his mother also. The prevention of the staphylococci from multiplying on the infants is an effective way of reducing cross-infection and sepsis. Fortunately, the infants' carrier sites, being superficial, are accessible to disinfectants. The use of hexachlorophane powder for more than a year has greatly reduced staphylococcal infection. Pustules and cutaneous abscesses, hitherto common, are now rare, their incidence among the infants having fallen from about 6% to less than 1%. The most pronounced effect of hexachlorophane on cross-infection was its reduction of staphylococcal colonization of the umbilicus and skin. Nasal colonization was reduced by more than half, but, despite this, about 40% of infants still left hospital as nasal carriers. In work now in progress in a nursery where hexachlorophane is used, this rate has fallen to less than 10% following the twice-daily application of a neomycin-chlorhexidine cream to the infants' nostrils, as suggested by Dr. K. G. Green (personal communication).

The reduction in staphylococcal infection among infants has been followed by a corresponding reduction among mothers. Hexachlorophane powder has been in routine use in most maternity hospital nurseries in Bristol for more than a year. During this period there have been remarkable reductions in the numbers of breast abscesses recorded by the hospitals and health department of the city (personal communications from Professor G. G. Lennon, Dr. Sheila Eades, Mr. H. K. Bourne, and Dr. Sarah Walker).

No single precaution can prevent all staphylococcal cross-infection. A high standard of nursing and the avoidance of overcrowding may in practice keep the incidence of sepsis sufficiently low; but this will depend partly on factors outside the control of the nursing staff, such as the virulence of the staphylococci which become prevalent in the nurseries. If appreciable numbers of infants or mothers suffer from sepsis, the additional use of hexachlorophane dusting powder is a worth-while and easy precaution.

Summary

The repeated application of hexachlorophane dusting powder to the umbilicus and the front of the abdomen greatly reduced staphylococcal cross-infection among newborn infants. Still better results were obtained by starting the treatment before the infants entered the

nursery, and by treating the whole trunk, including the groins, perineum, and axillae. The routine use of the powder has been followed by a greatly diminished incidence of staphylococcal sepsis in infants and mothers.

Changes in nursery techniques which reduced contacts between the infants and the nurses' uniforms failed to reduce cross-infection appreciably.

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REFERENCES

- Forfar, J. O., and Maccabe, A. F. (1958). *Brit. med. J.*, **1**, 76.
Gillespie, W. A., Simpson, K., and Tozer, Rosemary C. (1958). *Lancet*, **2**, 1075.
Hutchison, J. G. P., and Bowman, W. D. (1957). *Acta paediat. (Stockh.)*, **46**, 125.

CHRONIC MILK-ALKALI SYNDROME WITH GENERALIZED OSTEOSCLEROSIS AFTER PROLONGED EXCESSIVE INTAKE OF "RENNIE'S" TABLETS

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It has long been appreciated that the treatment of peptic ulcer with alkalis given in excess may lead to complications, and three distinct clinical states have been recognized. Acute alkalosis and temporary renal insufficiency from such a regime has often been described (Hardt and Rivers, 1923; Cooke, 1932; Kirsner and Palmer, 1942). Secondly, Cope (1936) reported four cases with hypercalcaemia as well as alkalosis and a raised blood urea that quickly responded to antacid withdrawal, though their renal abnormalities took several weeks to disappear. The existence of this syndrome has also been confirmed on many occasions (Scholz and Keating, 1955; Wenger *et al.*, 1957). Finally, Burnett *et al.* (1949) described the occurrence of the following syndrome in six patients each with a chronic duodenal ulcer which was being treated with large quantities of milk and absorbable alkalis: hypercalcaemia without hypercalciuria or hypophosphataemia, a normal serum alkaline phosphatase, marked chronic renal insufficiency with azotaemia, mild alkalosis, and calcinosis especially manifested by ocular lesions resembling a band keratitis. Some improvement in the clinical state was noted when the intake of milk and alkalis was reduced. Cases broadly corresponding to these have been reported since by McQueen (1952), Miller *et al.* (1952), Wermer *et al.* (1953), Dworetzky (1954), Dufault and Tobias (1954), Foltz (1954), Kyle (1954), Rodnan and Johnson (1954), and Snapper *et al.* (1954).

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The following case is reported as it is believed to be another example of this third, rare group and to show some features of special interest.

Case Report

The patient, a housewife aged 48, was admitted to hospital on August 19, 1958. She gave a history of loss of energy and general ill-health over the previous two years, with an intensification of these symptoms during the three weeks prior to admission. She had also been troubled recently with severe pruritus, mainly affecting her back, and complained of frequent occipital headaches, nocturia, and some breathlessness on exertion.

She had suffered for about 12 years from dyspepsia and had experienced a haematemesis on two occasions. Investigations on account of this had been carried out elsewhere,

cubic microns; M.C.H.C., 33%; white-cell count, 5,300/c.mm., with normal appearances and distribution; E.S.R., 38 mm. in the 1st hour (Westergren). Blood urea, 180 mg./100 ml.; serum calcium, 9.3 mg./100 ml.; serum inorganic phosphorus, 6.1 mg./100 ml.; alkali reserve, 20 mEq/l.; potassium, 5.0 mEq/l.; chloride, 100 mEq/l.; alkaline phosphatase, 9 King-Armstrong units; total protein, 6.9 g./100 ml. (albumin 3.3 g., globulin 3.6 g.). Liver-function tests were normal. Urine: pH 5.4, specific gravity, 1008-1004 on concentration and dilution testing. Slight proteinuria and a moderate microscopic pyuria were noted on occasion, but urinary culture was repeatedly sterile. Mantoux was negative using 1/10,000 old tuberculin, as were the blood Wassermann and Kahn reactions. The 24-hour urinary calcium excretion was 78 mg. There was histamine-fast achlorhydria.

E.C.G. and chest x-ray films were normal. A barium-meal examination showed no abnormality in the oesophagus, stomach, or duodenum. Intravenous pyelography revealed small renal outlines and bilateral nephrocalcinosis. Glandular calcification was present in the lower abdomen and there was calcification of the abdominal aorta. Radiology of the skeleton showed a marked increase in the density of the ribs, femora, lumbar spine, and metacarpals. A skeletal survey of a femur, lumbar spine, and hands (Fig. 1) was carried out by Drs. Barnett and Nordin and scored according to their technique (Barnett and Nordin, 1960). The total score of 223 was the highest which they had encountered in their experience of 125 normal patients and 150 with suspected bone disease, indicating an increase in cortical thickness. An iliac crest biopsy (Fig. 2) was also carried out by Dr. Nordin, who during the procedure commented on the extreme hardness of the bone. It was reported on as follows by Dr. Swanson Beck: "The biopsy consists of dense trabecular bone, the trabeculae being numerous and of more than average thickness, and are formed of mature normal bone. There is no increase in osteoblastic or osteoclastic activity and there are no osteoid borders."

and barium-meal examinations in 1956 and 1957 revealed several small gastric ulcers, which subsequently appeared to heal. Her haemoglobin in February, 1956, was 11.3 g./100 ml. and M.C.H.C. 32.5%. Slight proteinuria was then noted and a chest x-ray film was reported as negative. On account of her ulcer symptoms she had treated herself with "Rennie's" tablets. She developed a liking for these, taking them even when free from symptoms, and for 10 years had consumed about 30 tablets daily. This represents an intake of 20.148 g. of calcium carbonate and a relatively insignificant amount of calcium phosphate each day. She did not take more than 1 pint (570 ml.) of milk daily, nor was there any evidence of an excessive intake of vitamin D. There was no history suggestive of previous renal disease.

On physical examination she was noted to have a dry, sallown skin with pale mucous membranes. There was no swelling in the neck. A few small glands were found in the axillae and inguinal regions. Her blood-pressure was 115/75 mm. Hg, and there was no evidence of cardiac enlargement. Examination of the lenses of both eyes with the slit-lamp and microscope did not show any opacities, but in the palpebral regions there were interstitial deposits of small thin white plaques at the limbus, extending for about 0.5 mm. into the cornea, with similar deposits in the adjacent sclera. In the lower part of the limbus of each eye white lines running radially towards the centre of the cornea about 1 mm. from the limbus were seen. These deposits were presumably composed of calcium. Physical examination was otherwise negative.

Laboratory Investigations.—Haemoglobin, 9.9 g./100 ml.; red-cell count, 3,300,000/c.mm.; P.C.V., 30%; M.C.V., 91

FIG. 1.—Femur, metacarpals, and lumbar spine, showing generalized osteosclerosis. Glandular calcification is also apparent.

FIG. 2.—Iliac crest bone biopsy, showing the dense, numerous, and thickened trabeculae. ($\times 15$)

Rennie's tablets were discontinued on admission, and shortly afterwards she was put on a high fluid intake with a low phosphate diet. The latter was soon stopped, as it was unpalatable. On this regime she improved symptomatically and a fall in the blood urea occurred. The serum calcium, however, gradually rose above the normal range, and a low calcium diet (290 mg./day) was therefore introduced. She also received sodium bicarbonate for a period to see the effect of counteracting the acidosis. The time relationships of the various treatment regimes and the progress of the serum calcium, inorganic phosphorus, urea, and alkali reserve are shown in Fig. 3. The serum calcium

FIG. 3.—Changes in blood urea, alkali reserve, serum calcium, and inorganic phosphorus, and associated treatment.

ultimately returned to normal. The haemoglobin rose to 11.9 g./100 ml. and her nocturia disappeared. X-ray films taken six months after admission suggested that the renal calcinosis was less marked than previously.

Discussion

The name "milk-alkali syndrome" has been applied to two distinct clinical states: the short-lived alkalotic episodes with hypercalcaemia, first described by Cope (1936), and the more chronic upsets characterized by soft-tissue calcinosis and advanced renal damage which Burnett *et al.* (1949) later separated, albeit rather tentatively, from primary hyperparathyroidism. As Wenger *et al.* (1957) point out, there is often a failure in the literature to differentiate between these two syndromes, and though it is reasonable to suspect that they merely represent varying stages of the same disease, it is of interest that in few, if any, of the chronic cases so far described has there been a history of such acute incidents, and, conversely, Wenger *et al.* (1958), in their series of acute cases, did not find evidence of permanent renal damage. Thus we feel that the term "milk-alkali syndrome" should be qualified by "acute" or "chronic" as suits the case. We also deplore the current tendency to label all acute or chronic cases as "the Burnett syndrome," as Cope was the first to recognize the hypercalcaemia, which is the leading feature common to both groups. Even the name "milk-alkali syndrome" is open to some criticism, as one of the cases of Snapper *et al.* (1954) had no history of an excessive intake of milk, nor did Rodnan and Johnson's

(1954) case or our own. However, we feel that, generally, the term is a useful one as an indication of the circumstances with which the condition is usually associated.

Burnett *et al.* (1949) suggested several features which they thought favoured the diagnosis of their syndrome rather than primary hyperparathyroidism, though this, they admitted, could not be completely excluded. These were: a history of prolonged intake of milk and alkali, no hypercalciuria or hypophosphataemia, absence of skeletal changes and a raised serum alkaline phosphatase, the presence of renal insufficiency with mild alkalosis, calcinosis, and finally improvement on a low calcium and alkali intake. They state that, taken individually, none of these points excludes primary hyperparathyroidism, but taken as a group they constitute strong evidence against that disease, and in one of their patients who died the parathyroids were not located at necropsy. Kyle (1954) has discussed the above points, and throws some doubt on their validity even when considered together. He cites a case which conformed with the criteria of Burnett *et al.* but in which a parathyroid adenoma was subsequently demonstrated. It is evident that the differentiation of the chronic milk-alkali syndrome from primary hyperparathyroidism may be very difficult, an added complication being the fact that peptic ulcer is not infrequently a feature of the latter disease.

Accepting that the chronic milk-alkali syndrome does, in fact, represent an entity, we feel that our own case corresponds sufficiently to include it as a further example of the condition. Particularly strong evidence for its being so is the general improvement in well-being after withdrawal of Rennie's tablets, with the fall of urea, the rise of the haemoglobin, and the presence of osteosclerosis rather than any evidence of bone destruction. The changes in the calcium levels are difficult to interpret, but we suggest the following course of events. The chronic renal failure had depressed the serum calcium into the normal range when the patient was first seen by us. Presumably, if the calcium had been estimated prior to the onset of severe renal damage it would have been found to be elevated. With the initial improvement in renal function the calcium rose and persisted at hypercalcaemic levels for some months. Persistent hypercalcaemia was also described in some of the original chronic cases and is unexplained. Gradually, on account of the low calcium diet and high fluid intake, the calcium fell back into the normal range. The rise in the urea which latterly occurred may also have contributed to this. The occasional presence of pus cells in the urine suggests a chronic pyelonephritis which may have existed prior to the onset of the present condition or merely represents a complication of it. The ocular calcification also seems to be strong evidence in support of the diagnosis, since of 19 cases of chronic milk-alkali syndrome described in the literature 16 had such calcification in the form of conjunctival crystals or a band keratitis best revealed by slit-lamp examination. Pruritus was present in 10 cases, though it is probably a reflection of renal failure and therefore non-specific. It was a leading symptom in our patient. Alkalosis occurred in 10 cases, in four the alkali reserve was normal, and in the remaining five (including four fatal cases) acidosis was present, as in our case. Acidosis probably represents a later stage in the syndrome, and is indicative of severe renal damage.

The widespread osteosclerosis, which is greatly against a diagnosis of primary hyperparathyroidism, is of interest. Burnett *et al.* (1949) noted periosteal new bone formation in one of their cases and demonstrated dense cortical bone in another by bone biopsy. Reifstein (1958), in a general discussion on bone metabolism, states that increased matrix calcification does not occur. Unfortunately, we did not measure the proportion of mineral phase of the bone in our patient. The radiological findings coupled with those of the bone biopsy indicate that increased trabeculation and new bone formation had occurred, and it is reasonable to link this up in some way with the gross increase in calcium intake. Another explanation is that the osteosclerosis may be secondary to the renal failure (Crawford *et al.*, 1954).

All but one of the cases of the chronic milk-alkali syndrome so far reported have occurred in the U.S.A., this perhaps being related to the generous milk-drinking habits and pronounced self-medication in that country. We believe the present case to be the first to have been described in Britain and to be the second time that this syndrome has occurred in a woman.

The exact aetiology of these cases is obscure. Becker *et al.* (1952) noted at necropsy on 99 patients, each with a chronic duodenal ulcer, the presence of renal parenchymal calcification in 36% of them, compared with an incidence of 13% in a non-ulcer control group. In 68% of these cases with renal calcification there was a history of a high intake of alkali, well above the rate in the ulcer cases without such changes. They postulated the occurrence of transient, asymptomatic, hypercalcaemic incidents in these patients taking a high calcium diet. Burnett *et al.* suggest that there is an interference with the renal handling of calcium in such cases, and Kyle offers the following sequence of events: an initial alkalosis causing renal impairment, with a resulting decrease in the renal excretion of calcium, and this, in conjunction with the increased intake, producing the hypercalcaemia. In some of the reported cases the presence of antecedent renal damage has been noted. Carpenter and Pautler (1954) suggest that the chronic milk-alkali syndrome is probably primary hyperparathyroidism with atypical changes due to excess alkali therapy, but, as Kyle points out, it is doubtful if their own case conformed to the syndrome, as no history of excess milk and alkali intake was present.

The prognosis is variable and probably depends in general on the degree of renal damage present by the time the condition is first recognized. Improvement has varied greatly in the reported cases and its extent seemed unpredictable. In some, disappearance of calcinosis was dramatic, particularly from subcutaneous deposits and in those in the region of joints, while in others little change was evident.

Summary

A case of the chronic milk-alkali syndrome following prolonged excess intake of alkali but not of milk is described. A favourable response was obtained after withdrawal of alkalis and the prescription of a low calcium, high fluid intake. An interesting feature was the generalized osteosclerosis.

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REFERENCES

- Barnett, E., and Nordin, B. E. C. (1960). *J. Fac. Radiol.* In press.
 Becker, D. L., Baggenstoss, A. H., and Weir, J. F. (1952). *Amer. J. clin. Path.*, **22**, 843.
 Burnett, C. H., Commons, R. R., Albright, F., and Howard, J. E. (1949). *New Engl. J. Med.*, **240**, 787.
 Carpenter, H. M., and Pautler, E. E. (1954). *Ibid.*, **250**, 453.
 Cooke, A. M. (1932). *Quart. J. Med.*, **1**, 527.
 Cope, C. L. (1936). *Clin. Sci.*, **2**, 287.
 Crawford, T., Dent, C. E., Lucas, P., Martin, N. H., and Nassim, J. R. (1954). *Lancet*, **2**, 981.
 Dufault, F. X., and Tobias, G. J. (1954). *Amer. J. Med.*, **16**, 231.
 Dworetzky, M. (1954). *J. Amer. med. Ass.*, **155**, 830.
 Foltz, E. E. (1954). *Gastroenterology*, **27**, 50.
 Hardt, L. L., and Rivers, A. B. (1923). *Arch. intern. Med.*, **31**, 171.
 Kirsner, J. B., and Palmer, W. L. (1942). *Ibid.*, **69**, 789.
 Kyle, L. H. (1954). *New Engl. J. Med.*, **251**, 1035.
 McQueen, E. G. (1952). *Lancet*, **2**, 67.
 Miller, J. M., Freeman, I., and Heath, W. H. (1952). *J. Amer. med. Ass.*, **148**, 198.
 Reifstein, E. C. (1958). In *Principles of Internal Medicine*, edited by T. R. Harrison *et al.*, 3rd ed., p. 663. McGraw-Hill, New York.
 Rodnan, G., and Johnson, H. (1954). *Gastroenterology*, **27**, 584.
 Scholz, D. A., and Keating, F. R. (1955). *A.M.A. Arch. intern. Med.*, **95**, 460.
 Snapper, I., Bradley, W. G., and Wilson, V. E. (1954). *Ibid.*, **93**, 807.
 Wenger, J., Kirsner, J. B., and Palmer, W. L. (1957). *Gastroenterology*, **33**, 745.
 ——— (1958). *Amer. J. Med.*, **24**, 161.
 Wermer, P., Kuschner, M., and Riley, E. A. (1953). *Ibid.*, **14**, 108.

LATE RESULTS AND PROTEIN STUDIES AFTER PARTIAL GASTRECTOMY

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In a recent investigation into the incidence of coronary ischaemia after partial gastrectomy (Walker *et al.*, 1958), a study was made of 40 male gastrectomy patients in whom a Polya type of operation had been performed approximately 10 years before. This provided the opportunity for a simultaneous study of the long-term incidence of post-gastrectomy symptoms, and as each patient had previously been interviewed by one of us in 1952-3 (Anderson *et al.*, 1955) it was possible to make an assessment of their clinical progress.

The incidence of nausea, bilious vomiting, and dumping is initially high after operation (Muir, 1949), but in most cases improvement is rapid and symptoms lessen or disappear in the first few months. Clinical experience suggests that there is a tendency towards improvement after the first post-operative year, but information about the late results is scanty.

Loss of weight is a common sequel of the operation (Anderson *et al.*, 1955), and the labelled-fat studies of Everson (1954) suggest that fat absorption may be impaired in some cases. Evidence of increased nitrogen