requirements of diabetic patients alter with changes in physiological stress without simultaneous alteration in insulin antibody levels. This does not of course prove that insulin antibodies do not influence the insulin requirements from patient to patient. The studies reported here, showing that the majority of beef-insulin-treated diabetic patients can be maintained on a smaller dose of pork insulin, which can be predetermined by preferential insulin antibody-binding studies, indicate that antibodies to insulin account for a fixed aliquot of the daily insulin requirement.

The immediate clinical problem raised by this study is the necessity to exercise caution in changing diabetic patients from a pure beef-insulin preparation to a pure pork-insulin preparation. The theoretical possibility of deliberately inducing bovine-insulin antibodies and subsequently altering to porcine insulin in view of the failure of porcine insulin to produce a primary antibody response under these circumstances (Devlin and Stephenson, 1966) must be considered.

SUMMARY

The majority of a beef-insulin-treated diabetic population preferentially bind beef, pork, and human insulins in the order beef>pork>human. The theoretical implications of this observation are briefly discussed.

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REFERENCES

Berson, S. A., and Yalow, R. S. (1959a). *J. clin. Invest.*, **38**, 1996.
—— —— (1959b). Ibid., **38**, 2017.
—— —— (1963). *Science*, **139**, 844.
Devlin, J. G., and Brien, T. G. (1965). *Metabolism*, **14**, 1034.
—— and Stephenson, N. (1966). British Diabetic Association, May 6.
Feldman, R., Grodsky, G. M., Kohout, F. W., and McWilliams, N. B. (1963). *Amer. J. Med.*, **35**, 411.
Lerman, J. (1944). *Amer. J. med. Sci.*, **207**, 354.
Lockwood, D. H., and Prout, T. E. (1965). *Metabolism*, **14**, 530.
Moinat, P. (1958). *Diabetes*, **7**, 462.
Oakley, W., Field, J. B., Sowton, G. E., Rigby, B., and Cunliffe, A. C. (1959). *Brit. med. J.*, **1**, 1601.
Palumbo, P. J., Molnar, G. D., and Tauxe, W. N. (1964b). *Diabetes*, **13**, 634.
—— —— —— (1964a). *Diabetes*, International Congress Series, No. 74, p. 173. Amsterdam.
Skom, J. H., and Talmage, D. W. (1958). *J. clin. Invest.*, **37**, 787.

Medical Memoranda

Case of Cobalt Poisoning

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The main therapeutic use of cobalt in large doses has been in the treatment of refractory anaemias, particularly associated with renal failure. While it is sometimes effective in raising the haemoglobin level, there have been several reports of toxicity (Gardner, 1953 ; Kriss *et al.*, 1955). The following case is reported because of the unusually widespread nature of the toxic effects of cobalt.

CASE REPORT

A 35-year-old spinster first began to feel unwell in January 1965, complaining of nausea, vomiting, and breathlessness on exertion. In June she was investigated at another hospital, and found to have a haemoglobin level of 9.3 g./100 ml. and a blood urea of 196 mg./100 ml. A diagnosis of chronic nephritis was made. The only history relevant to the genitourinary system was that of cystitis at the age of 18. She was treated with a 20-g. protein diet and calcium lactate. For the anaemia she was given cobalt chloride 25 mg. q.d.s.

She was fairly well until November, when she started complaining of paraesthesiae in her limbs, numbness and occasional cramps in her legs, and unsteadiness on walking. At the same time she developed a slowly progressive swelling of the neck and an increasing difficulty in hearing. She also had frequency of micturition and nocturia, occasional dizzy spells, and bouts of nausea and vomiting, and by January 1966 she had lost 2 stone (12.7 kg.) in weight.

On admission to hospital in January 1966 the cobalt chloride was discontinued after six months' treatment, when she had had a total dose of approximately 18 g. Clinical examination showed a diffuse goitre without signs of hypothyroidism, bilateral nerve deafness, absent ankle jerks, tender calves, and a loss of vibration sense in the legs. The urine contained a little albumin, and a positive Clinitest showed the presence of glucose.

Investigations.—Haemoglobin 14.6 g./100 ml. ; blood urea 90 mg./100 ml. ; serum calcium 8.3 mg./100 ml. ; serum proteins—total 6.9 g./100 ml., albumin 2.9 g./100 ml. ; serum cholesterol 242 mg./100 ml.

The glucose-tolerance test was normal, the fasting level being 76 mg./100 ml., with a maximum rise of 160 mg./100 ml. after half an hour. Radioactive iodine uptake carried out three weeks after stopping the cobalt was 77% in 24 hours. On repeating the uptake, 33% of radioactive iodine was discharged after giving 400 mg. of potassium perchlorate, indicating that there was a considerable amount of inorganic iodine in the gland. The urine was examined by chromatography and several amino-acids were identified, showing that these were increased generally. Audiometry demonstrated a general decrease of sound perception in all frequencies and caloric tests were also found to be abnormal. A diagnosis of chronic renal failure complicated by cobalt chloride poisoning was made.

During her stay in hospital the symptoms gradually improved, the goitre regressed in size, and she was walking better. Her dietary protein was increased to 40 g. daily and she was maintained on a high fluid intake.

The glycosuria persisted for a week after admission and then ceased. She was discharged from hospital in February, by which time her walking had greatly improved. In April the goitre had almost gone and she had no difficulty in hearing or walking. At that time the haemoglobin was 13.3 g./100 ml. ; blood urea 90 mg./100 ml. ; and chromatography of the urine showed no amino-acid, though the albuminuria persisted, and there was no discharge of radioactive iodine after administration of potassium perchlorate.

DISCUSSION

Cobalt chloride was first used therapeutically about 15 years ago as a haemopoietic in the anaemia of renal failure and other refractory anaemias. Though cobalt is often effective in raising the haemoglobin, its mode of action is not known, but it may act by causing direct anoxia of the bone-marrow cells by enzyme inhibition (Weissbecker, 1950).

Gardner (1953) and Kriss *et al.* (1955) reported certain side-effects after administration of cobalt even for short periods. These effects included nausea, vomiting, damage to the eighth cranial nerve nuclei, thyroid hyperplasia and myxoedema, and congestive heart failure (Goodman and Gillman, 1965).

The case described above showed some of these toxic effects. The central nervous system was severely affected ; the vestibular and cochlear parts of the eighth nerve were damaged, as was shown by the abnormal caloric tests and audiometric curves. Paraesthesiae in the limbs, absent tendon jerks, and calf tenderness indicated that the patient also had a peripheral neuritis. The difficulty which she experienced in walking was probably due to a combination of vestibular damage and the peripheral neuritis.

In the series published by Kriss *et al.* (1955) cobalt chloride was given to children with sickle-cell anaemia, and it was found that cobalt depressed the uptake of iodine by the thyroid gland and caused thyroid hyperplasia. In the above case the iodine uptake was greatly increased. This test, however, was carried out three weeks after withdrawal of cobalt chloride, during the rebound recovery phase after thyroid suppression. The exact lesion in the thyroid has not been elicited. However, Kriss *et al.* cite evidence that cobalt chloride inhibits the tyrosine iodinase system, which catalyses the iodinization of tyrosine to form monoiodotyrosine. This view is strengthened by the fact that in the case reported here potassium perchlorate caused an immediate discharge of radioactive iodine from the gland, indicating that much of the iodine was still in the inorganic form.

Holly (1955) stated that cobalt is excreted primarily by the kidney, and he showed that rats receiving high doses of intraperitoneal cobalt developed renal tubular necrosis, though no glomerular damage was noted. There appear to be no previous reports of renal toxicity in man. The above patient had evidence of tubular damage, as was shown by the temporary glycosuria and the amino-aciduria. The chromatographic pattern of the amino-acids was very similar to that produced by other heavy metals—for example, copper in Kinnier Wilson's disease. There is no specific pattern of amino-aciduria caused by the different metals, and the basic lesion is again probably due to enzyme inhibition, perhaps the phosphorylation mechanism which is important in the active reabsorption of amino-acids. It was proved, by the disappearance of the tubular lesion three months after stopping the drug, that this damage was not due to the underlying kidney disease but to the cobalt administered.

In the above case it appears that the effect of cobalt on the body is of a temporary nature. Indeed it was gratifying to find that the effects on the thyroid gland, central nervous system, and renal tubules were completely reversible after the drug was stopped. The underlying condition of her renal failure, however, did not improve. The reason that this patient suffered so severely from the toxic effects of cobalt may be the combination of prolonged time of administration of the drug and the poor underlying renal clearance.

From this case and from previous reports it appears that cobalt chloride is very effective in raising the level of haemoglobin in refractory anaemias, especially that of renal failure. This asset of the drug, however, seems to be outweighed by the widespread side-effects which it can produce. Therefore, therapeutically, cobalt chloride seems to have no place in modern medicine.

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REFERENCES

Gardner, F. H. (1953). *J. Lab. clin. Med.*, **41**, 56.
Goodman, L. S., and Gillman, A. (1965). *The Pharmacological Basis of Therapeutics*, 3rd ed., p. 1406. New York.
Holly, R. G. (1955). *J. Amer. med. Ass.*, **158**, 1349.
Kriss, J. P., Carnes, W. H., and Gross, R. T. (1955). *J. Amer. med. Ass.*, **157**, 117.
Weissbecker, L. (1950). *Med. Mschr.*, Suppl. No. 9.

Prevention of Regurgitation During Induction of Anaesthesia with a Cuffed Oesophageal Catheter

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The importance of preventing regurgitation of stomach contents during induction of anaesthesia, particularly in operative obstetrics and emergency general surgery, is appreciated by anaesthetists. Endotracheal intubation with a cuffed tube is still the safest method for protecting the pulmonary system from the hazards of aspiration.

Sellick[1] summarized four approaches to the problem of cuffed endotracheal intubation in emergency surgery, when an empty stomach is but a wishful thought. These techniques are as follows: (1) Intubation under local anaesthesia if intubation is expected to be difficult ; Sellick suggested preliminary tracheostomy if severe maxillo-facial injuries are present. (2) Postural drainage of the pharynx in the lateral or Trendelenburg position during inhalation induction, where gravity and good suction assist in getting rid of any regurgitated contents in the pharynx, until the cuffed endotracheal tube has been passed. (3) Postural retention of gastric contents by inducing anaesthesia in the sitting position or 30 degrees head-up posture. Such technique requires rapid induction with barbiturate and muscle relaxant to achieve passage of the endotracheal tube without much delay. (4) Temporary oesophageal occlusion by means of cricoid pressure during the induction–intubation period.[2] Control of active vomiting by cricoid pressure is contraindicated, since obstruction to forcible vomiting might damage the oesophagus.

A further method, based on oesophageal occlusion by a balloon catheter to control regurgitation of gastrointestinal contents during the critical induction–intubation period, is described below. This method also prevents inflation of the stomach (a potent cause of regurgitation) during the positive-pressure ventilation preceding intubation with the aid of muscle relaxant. The wide-bore catheter acts as a safety-valve against any build-up of high pressure in the oesophagus behind the balloon, should active vomiting occur.

METHOD

Foley's haemostatic catheter is used—the type which acts as a self-retaining urethral catheter after prostatic operation. This has a strong balloon of 30–100 ml. capacity. The catheter, in variable sizes, has two terminal bores. A No. 26 F.G.S. is suitable for an adult patient. Analgesia of the mouth and pharynx facilitates insertion of the catheter into the oesophagus in the conscious patient without difficulty. In most cases this is not needed. The catheter is passed down the oesophagus as