cured even when the antigen is given after the graft. Various bacterial antigens have been tried in the immunotherapeutic treatment of animal malignancies, both solid tumours and leukaemia, among them B.C.G. (Biozzi *et al.*, 1959; Old *et al.*, 1959; Amiel, 1967), *Corynebacterium parvum* (Woodruff and Boak, 1966), *B. pertussis* (Wissler *et al.*, 1968), and *Mycobacterium chelonae* (Mathé *et al.*, 1969). Only B.C.G. has been used in a trial in human leukaemia previous to this series, though *C. parvum* has been used in isolated cases. Since the series reported here has been completed it has been claimed that under certain circumstances *B. pertussis* may accelerate tumour growth (Floersheim, 1967).

It is apparent that the timing of both antigenic stimulation and challenge with tumour is of the utmost importance. Recent work by Parr (personal communication) suggests that immunization with *B. pertussis* vaccine combined with autologous irradiated tumour cells in the mouse L5178Y lymphoma system given 24 hours after the challenge dose may have a beneficial effect.

In whatever way immune assistance is evoked in treatment the initial chemotherapy is critical. Unless adequate cell destruction has been achieved no form of immunotherapy is likely to be effective. In our series the number of patients with remissions in excess of 250 days suggests that cytoreductive chemotherapy was adequate and that the residuum of cells at the end of chemotherapy was small and possibly zero in the one case with an unmaintained remission in excess of 800 days. The role of immunotherapy is more difficult to place, but it may have delayed the onset of relapse in this series. The observation of this partial response without the occurrence of a number of long-term remissions—for example, two to three years—suggests that this form of immunotherapy is not as effective as that described by Mathé *et al.* (1969) using B.C.G. Further experimental and clinical evidence is needed to estab-

lish the role of immunotherapy in general in the management of leukaemia, and in particular to examine whether *B. pertussis* vaccine has a part to play.

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Preliminary Communications

Nasal Mucosal Absorption of Tetracosactrin as Indicated by Rise in Plasma Fluorogenic Corticosteroids

British Medical Journal, 1969, **4**, 407–408

Summary: Tetracosactrin has been administered to six healthy dexamethasone-suppressed subjects by nasal insufflation. The pronounced increase of the plasma fluorogenic corticosteroids suggests that the peptide is well absorbed by this route.

INTRODUCTION

Tetracosactrin (Synacthen) is a synthetic peptide with the primary structure of the corticotrophic fraction of human adrenocorticotrophic hormone. It contains the first 24 amino-acids of all known corticotrophins. Previous reports show that some peptides are absorbed across mucosal surfaces—such as the octapeptides, vasopressin (Mimica *et al.*, 1968) and oxytocin (Ritchie and Brundell, 1967), and also pentagastrin (Wormsley, 1968). It was therefore decided to study the mucosal absorption of tetracosactrin.

METHODS

Six healthy subjects, all of whom were medical or paramedical staff and fully understood the nature of the experi-

ments, were given 4 mg. of dexamethasone by mouth at 22.00 hours to suppress the hypothalamo-pituitary-adrenal axis, thus eliminating diurnal and individual variation in the resting levels of the plasma fluorogenic corticosteroids. Tests were started between 09.30 and 10.30 hours on each occasion on the day after the administration of the dexamethasone. Baseline specimens of heparinized venous blood were collected from indwelling needles. These were kept patent by injecting small amounts of heparin (1,000 units/ml.).

At a time designated zero, tetracosactrin powder was administered by nasal insufflation. Specimens of heparinized venous blood were collected at timed intervals thereafter. The specimens were centrifuged and the supernatant plasma was stored at about -20° C. until analysis.

The tetracosactrin powder was administered by simple insufflation into the nose by means of a Marvic inhaler. Each subject was given, on separate occasions, doses of 0.25 and 1.5 mg. The period of each insufflation was about five minutes. The low dose was administered in one insufflation and the high dose by three insufflations of 0.5 mg. each.

The plasma levels of fluorogenic corticosteroids were measured by the fluorimetric method of Spencer-Peet *et al.* (1965). Replicate analyses were performed.

RESULTS

The plasma fluorogenic corticosteroids showed an unequivocal rise within 60 minutes after the insufflation of tetra-

cosactrin (see Table). During this period there was no significant difference between the response to doses of 0.25 and 1.5 mg. The high dose, however, gave significantly higher responses at 90, 120, and 180 minutes ($P < 0.01$). The peak of the response was seen at 60 minutes and persisted to 90 minutes with the higher dose. At five hours after zero time the plasma fluorogenic corticosteroids were still significantly higher than the baseline specimens after both 0.25 and 1.5 mg. ($P < 0.05$ and $P < 0.01$ respectively).

Levels of Plasma Fluorogenic Corticosteroids After Nasal Insufflation of Tetracosactrin (Results Expressed in $\mu\text{g./100 ml. of Plasma}$)

Time	Dose of Tetracosactrin			
	0.25 mg.		1.5 mg.	
	Mean	S.E.	Mean	S.E.
Baseline	1.5	0.5	2.0	0.4
15 min.	15.9	2.8	17.3	1.5
30 "	24.2	0.8	27.0	1.4
60 "	29.1	2.0	33.6	1.3
90 "	21.3	2.3	32.9	1.4
120 "	13.9	1.3	31.3	1.4
180 "	8.7	1.0	16.4	1.2
300 "	4.6	1.0	6.4	1.2

No side-effects were experienced by any of the subjects, apart from a slight tendency to sneeze.

COMMENT

These results provide evidence of the efficient nasal absorption of tetracosactrin even at low doses. The duration of the

response is equal to that occurring after doses of 0.25 mg. injected intramuscularly (Greig *et al.*, 1966). It is suggested that administration of the peptide by this route could be used for diagnostic purposes and indeed for therapy if the duration of the rise of the fluorogenic corticosteroids can be prolonged. Work on this and other adrenocorticotrophic peptides is in progress.

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Medical Memoranda

Transient Hypertension Caused by Segmental Renal Artery Occlusion

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It has been well established, both clinically and experimentally, that systemic hypertension can be caused by renal ischaemia resulting from constriction of a renal artery. On the other hand, systemic hypertension caused by local ischaemia resulting from a segmental renal infarct is scarcely mentioned in the literature. It was, however, experimentally evoked in rabbits, where it decreased spontaneously within a few weeks (Alexander *et al.*, 1961).

The details of the mechanism relating systemic hypertension to the changes in the kidney are as yet not fully understood, but there are strong indications that the initial phase of renovascular hypertension is closely connected with increased activity of the renin-angiotensin system, both in arterial constriction and in infarction caused by occlusion of a branch of the renal artery.

In the few publications on segmental infarction as an unequivocal cause of systemic hypertension (Brown *et al.*, 1960; Stamey, 1963) the patients are reported to have been treated by nephrectomy. To our knowledge there are no reports on patients with acute severe hypertension caused by segmental infarction who were satisfactorily treated by gradually diminishing doses of antihypertensive drugs.

CASE REPORT

The patient, a 35-year-old task analyst, had repeatedly visited his family doctor for minor complaints. At these consultations his blood pressure had always been normal, as it was over a period of four years when measured by the physician at his place of employ-

ment. In November 1965 his blood pressure suddenly rose to 250/150 mm. Hg. He was examined by one of us (H. B. B.) and admitted to our clinic on 13 November. He had no history of acute pain in the loins, nor any symptoms suggesting pre-existent renal disease. His urine had always looked normal. There was no family history of hypertension. On physical examination the only abnormal findings were a blood pressure of 250/150 mm. Hg and a red face. There were no abdominal bruits; the ocular fundi were normal.

INVESTIGATIONS

Blood: haemoglobin 16.0 g./100 ml.; plasma urea 30 and creatinine 1.2 mg./100 ml.; plasma sodium 140, potassium 4.2, chloride 99.0, and bicarbonate 22.5 mEq/l. Urine: highest specific gravity of spontaneously voided urine 1028; no albuminuria; microscopy normal; vanillyl-mandelic acid 4.4 mg./24 hours (normal). Electrocardiogram showed only left ventricular strain. X-ray examination showed the heart to be of normal size and configuration. Intravenous pyelograms taken 1, 3, 5, and 10 minutes after injection of iopanoic acid (Telepaque) showed normal anatomy and normal arrival and clearance times of the contrast medium. Arteriography of the kidneys by Seldinger's method showed normal main renal arteries and their branches, except in the upper pole of the left kidney, where selective angiography showed occlusion of a branch of a renal artery (Figs. 1A and 2A).

Renal Biopsy.—The greater part of the left kidney was inspected directly at operation (Mr. A. Lammers, urologist). In one area the surface of the upper pole showed a bluish-red elevation, measuring 3 cm. in diameter, evidently a fresh infarct. About 2 cm. below this there was a greyish depression 1.5 cm. in diameter, in all likelihood an old infarct. Biopsy specimens were taken from both these areas and from the normal tissue.

HISTOLOGY

Fresh Infarct.—Haematin-phloxine stain: the glomeruli were normal; the most striking feature was tubular atrophy (Fig. 3);