that venous compression by arm tourniquet for five minutes may increase protein-bound iodine by 22.4%.³

The present study was designed to test the effects of postural change and venous compression on the serum concentrations of thyroxine (T4) and triiodothyronine (T3).

Patients, methods, and results

Three studies were performed on 19 nonfasted normal subjects. No subject was oedematous or had any abnormality of hepatic, renal, or thyroid function. Blood was taken without hand squeezing. In the first study, to test the effect of posture, blood was taken without a tourniquet from 8 subjects who had been lying supine for 15 minutes and again after sitting for 5 minutes. In the second study, to test the effect of venous compression, blood was taken from 11 subjects who were seated with a tourniquet applied for 5 minutes and then immediately again from the other arm without a tourniquet. In the third study, to test the combined effect of both factors, 15 subjects had blood taken without a tourniquet while supine for 15 minutes and then after being seated for 5 minutes with a tourniquet applied. Serum T3 and T4 were measured by specific radioimmunoassays⁴ on all samples in the same assay. Intrassay variation for both T3 and T4 was less than 5%. Free thyroxine index (FTI) was calculated as the product of T4 and T3 resin uptake (T3 RU) measured by a kit method (NML). Results were analysed with the paired Wilcoxon test for matched samples.

The effect of the procedures are illustrated in the figure.

Effect of haemoconcentration of serum levels of triiodothyronine and thyroxine.

(1) Postural change caused a mean ($\pm$ SEM) increase in serum T3 from 113 ± 4.3 to 124 ± 4.7 ng/100ml, and in serum T4 from 7.4 ± 0.2 to 8.1 ± 0.3 μg/100ml. This represents a mean percentage rise in T3 of 9.7% (range 0-29%) and in T4 of 8% (0-37%). There was a significant decrease in mean T3 RU from $101 \pm 2.9\%$ to $95 \pm 2.4\%$ ($P < 0.05$). The change in FTI from 7.5 to 7.8 was not significant ($P > 0.10$).

(2) Tourniquet compression increased the mean serum T3 from 130 ± 5.0 to 150 ± 7.4 ng/100ml and serum T4 from 8.3 ± 0.4 to 8.9 ± 0.3 μg/100ml. This represents a mean percentage change of 15% (range 0-31%) in serum T3 and 7% (range 0-16%) in serum T4. There was a significant decrease in T3 RU from a mean of $97 \pm 2.3\%$ to $91 \pm 3.0\%$ ($P < 0.01$) but FTI was unchanged.

(3) The combined effect of venous compression and postural change increased the mean serum T3 from 126 ± 7.6 to 153 ± 8.4 ng/100ml and mean serum T4 from 7.4 ± 0.2 to 8.7 ± 0.3 μg/100ml. This represents a mean percentage increase of 21% (range 0-60%) in serum T3 and 18% (range 0-44%) in serum T4. There was a significant decrease in T3 RU from a mean of $100 \pm 1.9\%$ to $91 \pm 2.2\%$ ($P < 0.01$). The increase in FTI from 7.5 to 7.9 was not significant ($P > 0.01$).

Discussion

This study has shown that alterations in posture and venous compression significantly increase the serum concentrations of T3 and T4. The significant decrease in T3 RU but insignificant change in FTI indicates that the increase in total T3 and T4 is due to an increase in thyroid hormone-binding protein proportional to the increases in T3 and T4. This emphasises the need for a careful and standardised technique of drawing blood for thyroid hormone estimations, particularly when serial changes are being interpreted. These effects are also important when establishing normal laboratory ranges for T3 and T4 and when comparing outpatient and inpatient populations. The effects described of posture and venous compression may similarly influence the plasma concentrations of other protein-bound hormones.

This work is supported by grants from the National Health and Medical Research Council of Australia. Requests for reprints should be addressed to Dr S J Judd Garvan Institute of Medical Research, St Vincent's Hospital, Sydney, N S W, Australia. We gratefully acknowledge the help of Professor L Lazarus for his encouragement and advice; Ms C Batley for thyroid hormone estimations; and Ms J Chalmers for typing the manuscript. Dr E Kraegen helped us with the statistical analysis.

¹ Fawcett, J K, and Wynn, V, *Journal of Clinical Pathology*, 1960, 13, 304.

² Gerbrandy J, van Leeuwen A M, Hellendoorn, H B A, and de Vries, L A, *Clinical Science*, 1960, 19, 181.

³ Lewitus, Z, and Steinitz, K, *Clinica Chimica Acta*, 1963, 8, 629.

⁴ Burke, C W, and Eastman, C J, *British Medical Bulletin*, 1974, 30, 93.

Garvan Institute of Medical Research, St. Vincent's Hospital, Sydney, N S W 2010.

S J JUDD, MB, FRACP, clinical fellow in endocrinology

J N CARTER, MB, FRACP, clinical fellow in endocrinology

J M CORCORAN, BSC, scientific officer

Five separate malignancies in one patient all apparently successfully treated

The finding of more than one malignancy of different origin in a patient is not uncommon at necropsy, though usually only one malignancy has contributed to death, the others being incidental findings. A patient who develops and is treated for five separate malignancies is likely to be unique.

Case History

A 51-year-old woman was admitted for the investigation of painless haematuria and found to have a 6 cm tumour at the right bladder base causing fixation to the pelvic side wall. Biopsy showed a poorly differentiated transitional cell carcinoma with muscular invasion. Thirteen years previously she had had a bilateral ovarian cystectomy for treatment of a torsion of a left ovarian cyst, shown histologically to be a moderately differentiated papillary adenocarcinoma. The capsule was intact and the right ovary normal. One year later she developed intermenstrual bleeding and curettage suggested the presence of a uterine tumour. The hysterectomy specimen showed a localised adenocarcinoma with deep invasion of the myometrium at the fundus; moreover, the cervix also showed areas of carcinoma in situ. After her operation she underwent a radical course of pelvic irradiation. Seven years later a hemicolectomy was performed for the removal of an adenocarcinoma of her caecum. The neoplasm had invaded all layers of the intestinal wall but no lymph nodes in the specimen were affected, nor was there evidence of abdominal or pelvic metastases.

The patient had remained well for five years before presenting with haematuria. Three months later, after a palliative course of radiation, cystoscopy showed no evidence of residual growth and she has remained symptom free for a further eighteen months.

Discussion

A search of published work has shown one other patient with five separate malignancies,¹ affecting the breast, colon, skin, ureter, and body of the uterus. My patient was fortunate that her tumours presented at an early stage and were readily curable. After surgical removal of early localised ovarian, uterine, cervical, and colonic carcinomas the prognosis is known to be good.

Unsuspected preinvasive cervical carcinoma is found in 4% of hysterectomy specimens, while a review of all cases of ovarian malignancy registered in the Cambridge area during 1960-74 showed six cases of concurrent cervical neoplasm, of which four were in situ. Cook² found that women who have a primary ovarian carcinoma have a significantly increased risk of developing endometrial cancer ($P > 0.05$), though his data provide no evidence of any relation between ovarian or uterine malignancy with colonic, bladder, or cervical carcinoma. Nevertheless, 3% of Polk's³ cases of colonic carcinoma had a history of cancer elsewhere in the body and according to him a

second malignancy of colonic or extracolonic origin may be expected to develop later in about one-third of patients who survive their colonic cancer. The bladder cancer that this patient developed may have been induced by irradiation, since the bladder would have been within the field of treatment thirteen years previously. McIntyre and Pointon⁴ have shown a causal relationship between the development of bladder tumours and previous external pelvic irradiation. In their series of 950 cases they found 16 patients who had developed bladder neoplasm up to 28 years after irradiation, when they would only have expected nine. Castro *et al*⁵ reported 26 patients with colonic carcinoma who had had pelvic irradiation for gynaecological malignancy 5 to 30 years previously. Hence possibly the colonic carcinoma in my patient may also have been irradiation-induced.

This case illustrates two important points: firstly, that radical treatment is not contraindicated for second primary neoplasms; secondly, that routine follow-up after radical treatment and the investigation of new symptoms are worthwhile because of the increased risk of second primary neoplasms. Moertel¹ has shown that the incidence of developing new malignancies increases with each successive new cancer even though the patient's chance of surviving to acquire another lesion decreases progressively with each episode.

¹ Moertel, C G, *Recent Results in Cancer Research*, vol 7. Springer Verlag, 1966.

² Cook, G B, *Cancer*, 1966, 19: 2, 959.

³ Polk, H C, *American Journal of Surgery*, 1965, 109, 71.

⁴ McIntyre, D, and Pointon, R C S, *Journal of the Royal College of Surgeons of Edinburgh*, 1971, 16, 141.

⁵ Castro, E B, Rosen, P P, and Quan, S H Q, *Cancer*, 1973, 31, 45.

Department of Radiotherapeutics, Addenbrooke's Hospital, Cambridge

M J OSTROWSKI, FRCS, DMRT, senior registrar

Incidence of protein-losing enteropathy in primary lymphoedema using chromium-51 chloride technique

Several cases of protein-losing enteropathy (PLE) in primary lymphoedema have been reported¹ but no one has yet attempted to discover the true incidence of PLE in this condition.

Waldmann² has summarised the various radioactive excretory tests used in the diagnosis of PLE.² Our test was based on that described by Walker-Smith *et al*,³ in which ⁵¹CrCl₃ is injected intravenously and faecal loss estimated. The test was modified in that one-third of the dose was used.

Patients, methods, and results

Fifty-five patients, ranging in age from 2 to 72 years, were studied over two years. Their usual mode of presentation was with either unilateral or bilateral lower limb oedema, and some patients also had arm, facial, or genital oedema. Four patients had diarrhoea. ⁵¹CrCl₃ 30 µCi was injected intravenously, and 1 ml of the solution was analysed for a baseline radioactivity count. Stools were collected over the next five days, taking care to prevent urinary contamination, and the radioactivity of the whole stool sample was measured in a large plastic scintillation counter specially constructed at St Thomas's Hospital.⁴ Excretion of more than 2% of the administered dose indicated significant PLE.

We discovered significant PLE in 12 of the 55 patients studied (22%). The percentage ⁵¹CrCl₃ excreted in these patients ranged from 2.5% to 18.4%. Total serum protein was normal in two patients and serum albumin in four patients (see table). Three patients, described elsewhere,⁵ had a segment of small bowel excised and were followed for over a year. They maintained clinical and biochemical improvement, the percentage ⁵¹CrCl₃ loss falling.

Discussion

PLE in primary lymphoedema is due to lymphangiectasia resulting from blockage of the small bowel lymphatics. It must be emphasised

Gut protein loss and serum proteins in patients with PLE in primary lymphoedema

Case No	Age and sex	⁵¹ CrCl ₃ Loss (% of administered dose excreted in 5 days)		Protein (normal 63-79 g/l)	Albumin (normal 38-56 g/l)
		Before operation	After operation		
1	15 F	18.4	9.0*	39	28
2	72 M	16.0		42	24
3	24 F	12.0		47	34
4	52 M	10.8	3.4*	38	29
5	12 M	9.3		55	36
6	2 M	7.2		62	43†
7	2 M	6.6			
8	4 F	6.1		63†	40†
9	15 F	5.9		69†	39†
10	56 M	4.6		51	26
11	11 F	4.0		51	34
12	59 M	2.5	1.5*	60	38†

*Gut resected. †Within normal range.

that serum protein and albumin levels may be normal. In our patients with primary lymphoedema ⁵¹CrCl₃ screening revealed an incidence of PLE of 22%.

The ⁵¹CrCl₃ isotope test is a simple and convenient clinical method of screening patients for PLE in primary lymphoedema. It is also reliable as the isotope has a long bench storage life, and less than 1% of the excreted isotope is reabsorbed in the bowel. The test can be performed on outpatients. An adequate stool output is essential and care must be taken to prevent urinary contamination of the stool (especially in children) as up to 30% of the isotope is excreted in the urine.³

We thank Professor J B Kinmonth, under whose care these patients were admitted.

¹ Jarnum, S, and Petersen, V P, *Lancet*, 1961, 1, 417.

² Waldmann, T A, *Seminars in Nuclear Medicine*, 1972, 2, 251.

³ Walker-Smith, J A, Skyring, A P, and Mistilis, S P, *Gut*, 1967, 8, 166.

⁴ Clapham, W F, and Hayter, C J, *Physics in Medical Biology*, 1962, 7, 313.

⁵ Kinmonth, J B, and Cox, S J, *British Journal of Surgery*, 1974, 61, 589.

St Thomas's Hospital, London SE1 7EH

P W EUSTACE, MB, FRCS, lecturer in surgery (present address: Surgical Unit, Regional Hospital and University College, Galway)

J I GAUNT, BSC, senior physicist

D N CROFT, DM, FRCP, consultant physician

Residual biliary calculi: dispersal by irrigation of common bile duct

When residual gall stones are shown in the bile duct after exploration further surgery is usually advised, but this is fraught with technical difficulties and a high mortality rate. A reliable non-operative method for removing such stones would obviously be welcome and recently success has been reported using a simple washout technique. This paper reports two further successful cases using this procedure.¹

Technique

Before starting the washout procedure bile is cultured and, if infected, the patient is started on the appropriate antibiotic. Bile is further cultured if indicated clinically. The washout is performed by connecting the T-tube to a litre of sterile 0.9% saline, to which 40 ml of 1% lignocaine has been added. Probanthine 15 mg is given intramuscularly 30 minutes before the start of the irrigation. The saline is initially dripped in slowly, but once discomfort has settled the saline is allowed to flow rapidly through the T-tube. At the end of the procedure the T-tube is clamped. The criterion for success is a post-washout cholecystogram showing the disappearance of the stone(s).