It is worth noting that the duration of stay necessary after revision operations is consistently longer than that after a primary joint replacement (hips 28 v 20 days; knees 40 v 31 days). The cost of revision arthroplasty in our study was also higher than that of the primary operation in terms of both materials and time consumed.

Comment

The cost of the prostheses themselves made up 6·5% of the orthopaedic unit's annual expenditure for major joint replacement. A further 4·1% was spent on other items used in the operation, the prime aim of which is to reduce the possibility of both early complications and later failure of the operation. The greatest part of the annual cost (£727 100=89·4% of the total) was attributed to keeping the patient in a hospital bed.

The cost of treating each patient could most readily be reduced by shortening the period of inpatient treatment by, for example, improving rehabilitation and social support. Conversely, an increase in the amount spent on prostheses and other items could be justified if it could be established that the items reduced complications and increased the lifespan of the implant: the added cost of performing revision surgery should not be forgotten.

There is increasing demand for major joint replacement because of factors beyond our control. This may mean, in the absence of more finance to permit a further increase in workload, a reassessment of the criteria used to select patients for surgical treatment and rejection of patients who are currently considered to need surgery.

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Severe hyperglucagonaemia during treatment with oxymetholone

Unexplained severe hyperglucagonaemia was found in a boy with aplastic anaemia treated with the anabolic androgen oxymetholone. We have reported hyperglucagonaemia during treatment with danazol, which is structurally similar to oxymetholone.[1] Hyperglucagonaemia was therefore sought in patients receiving oxymetholone.

Subjects, methods, and results

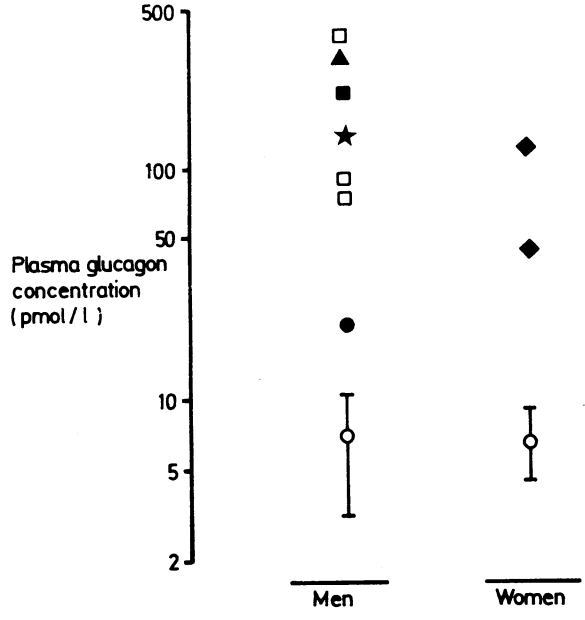
The 16 year old boy initially studied had received oxymetholone (50-200 mg/day) for aplastic anaemia diagnosed five years previously. During investigation of intermittent diarrhoea screening of gut peptide hormones showed grossly raised plasma glucagon concentrations (70-380 pmol/l (24·4-132·4 ng/100 ml); values exceeding 50 pmol/l (17·4 ng/100 ml) are suggestive of glucagonoma). Hepatic and renal function, fasting blood glucose concentration, and serum amylase activity were all normal. Computerised tomographic and ultrasonographic examination showed no evidence of an intra-abdominal tumour.

Five other patients treated with oxymetholone (four men and one woman, aged 26-61 years, mean 39·9 years) were also studied. The duration of aplastic anaemia ranged from 11 months to 34 years (mean 8·8 years), and duration of treatment with oxymetholone ranged from seven months to seven years (mean 3·2 years); current dosages were 100-150 mg/day. Three patients were also taking prednisolone (10-20 mg/day), of whom two were diabetic, treated with diet alone and insulin, respectively. Results of biochemical screening were otherwise normal except for increased serum aspartate transaminase activity (41-163 IU/l; normal range 20-40 IU/l) in three patients, consistent with oxymetholone treatment.[2] None of the patients had the necrolytic rash, stomatitis, or cachexia of the glucagonoma syndrome.[3]

Fasting glucagon concentrations were also measured in healthy, non-obese control subjects (10 men aged 25-43 years, mean 31·2 years, and 11 women aged 20-53 years, mean 31·1 years), none of whom were taking any drugs.

Samples of 10 ml venous blood were taken after an overnight fast into a lithium and heparin tube containing 200 µl aprotinin (20 000 Kallikrein inactivator units/ml) and were centrifuged immediately. Plasma was stored at −30 C. Plasma glucagon and insulin concentrations were measured by radioimmunoassay and plasma glucose concentration by an autoanalyser (glucose oxidase method).

All six subjects treated with oxymetholone had significant hyperglucagonaemia (>3 SD above the mean control value for the appropriate sex), and in five cases this exceeded 50 pmol/l (17·4 mg/100 ml) (figure).



Fasting plasma glucagon concentrations in six patients with aplastic anaemia treated with oxymetholone, compared with mean (SD) values in 10 normal men (left) and 11 normal women (right). Each symbol represents a single patient; measurements were repeated in one man (□=3 estimations) and one woman (◆=two estimations).
Conversion: SI to traditional units—Plasma glucagon: 1 pmol/l≈348 pg/100 ml.

Plasma insulin concentrations in the group treated with oxymetholone (excluding the diabetic patient who was treated with insulin) were 45·3 (SD 36·3) mU/l, significantly greater than in the 21 control subjects (7·1 (3·8) mU/l, $p<0·01$; Wilcoxon test). Fasting plasma glucose concentration was 7-10 mmol/l (126-180 mg/100 ml) in the two diabetic patients and normal (5-5·2 mmol/l (90-94 mg/100ml)) in the four other patients and the normal subjects (4·9 (0·5) mmol/l (88 (9) mg/100 ml)).

Comment

All six patients treated with oxymetholone showed pronounced hyperglucagonaemia, in most cases in excess of 50 pmol/l (17·4 ng/100 ml). Oxymetholone, like danazol,[1] is therefore a cause of "pseudoglucagonoma." The association between oxymetholone and hyperglucagonaemia is not described in the drug's data sheet or in the standard text on glucagon,[4] although a study of carbohydrate tolerance during oxymetholone treatment briefly mentions that plasma glucagon concentrations were raised in two out of seven patients.[2] We believe that this observation is important because hyperglucagonaemia induced by oxymetholone may be both frequent and severe. With the increasing use of screening for gut endocrine hormones causes of gut peptide hypersecretion not related to tumours must be recognised in order to avoid unneccessary and often highly invasive attempts to identify intra-abdominal tumours; patients with hyperglucagonaemia induced by danazol have been mistakenly subjected to both angiography and laparotomy.[1]

Danazol, a substituted ethisterone derivative, is mildly androgenic. Hyperglucagonaemia has not been reported during treatment with other androgenic steroids, although high dose glucocorticoids may cause mild hyperglucagonaemia; glucagon secretion may be indirectly stimulated by increased plasma amino acid levels.[5] As with danazol, hyperglucagonaemia induced by oxymetholone was not associated with the clinical features of glucagonoma, although impaired carbohydrate tolerance and hyperinsulinaemia (possibly secondary to high glucagon levels) occurred with both drugs.

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Where do lean diabetics inject their insulin? A study using computed tomography

The aim of injecting insulin is to deposit the hormone in subcutaneous fat. The lateral aspect of the thigh has been recommended as an injection site since the introduction of insulin treatment. For many years long needles were used, angled at about 45°, but recently shorter needles (12-13 mm) and a new injection technique were introduced. Most diabetics are recommended to use the perpendicular technique, inserting almost the whole length of the needle to ensure the same depth of injection every time. Very lean diabetics are instructed to angle the needle at about 45°. The risk of penetrating the muscle has been considered small. In this study we used computed tomography to investigate the subcutaneous fat layer in diabetics of normal weight.

Patients, method, and results

We studied 14 patients, three of whom were women. We assumed that the fat layer would be sufficient in most women and therefore concentrated on men. Two patients (one man and one woman) had type II diabetes and the rest had type I diabetes; all were being treated with insulin. Three of the patients had insulin pumps. All patients were in a state of good metabolic control, and none had a history of recent weight loss. Ages ranged from 22 to 60 (mean 39). Non-enhanced computed tomography was performed with a GE 9800 scanner with a 512×512 matrix and a display field of view of 40 cm, making the pixel size 0·78 mm. Measurements were taken from skin surface to muscle, which we refer to as fat. Computed tomograms 1 cm thick were obtained immediately below the umbilicus and one third and two thirds of the distance from the inguinal ligament to the patella. Three measurements were made from each scan: lateral, intermediate, and medial.

The table shows the results. The lower part of the thigh had less subcutaneous fat, as expected, and data for that section are not included. The mean thickness of abdominal fat at the thickest point was 14 mm (range 4-26 mm). Mean values for fat around the thigh were: lateral 6 mm (range 2-19 mm), upper 8 mm (range 3-15 mm), and medial 14 mm (range 4-25 mm).

Comment

The striking finding in most patients was the thinness of the subcutaneous fat layer in the lateral aspect of the thigh. All patients except those with insulin pumps used the thigh as their injection site, and some of them were asked to insert their usual needle in their usual way. The result was intramuscular injection in many cases. These patients experienced no pain and had evidently been injecting intramuscularly for years, as, probably, have many lean diabetics. Another striking finding was the uneven distribution of fat: one woman (case 1) had 26 mm of abdominal fat, 25 mm of fat medially in the thigh, but only a meagre 5 mm laterally in the thigh. She was reasonably well endowed with fat except where she was supposed to inject her insulin. One man (case 14), who had had diabetes for 30 years and was very thin, had under 9 mm of subcutaneous fat in the abdominal area; in the lateral aspect of the thigh, however, he had 19 mm of fat. The fat was evenly distributed around the thigh and could not have been the result of localised lipohypertrophy.

These findings show that many diabetics of normal weight have a very thin layer of subcutaneous fat in the lateral aspect of the thigh, and many probably regularly inject intramuscularly, at least when using the modern technique—that is, a perpendicular injection with a 12-13 mm needle.

This study was aided by Becton Dickinson, Sweden.

Measurements of fat in the abdomen and thigh in 14 diabetics

Case No	Sex	Height (cm)	Weight (kg)	Abdominal fat (mm)			Thigh fat (mm)		
				Lateral	Intermediate	Medial	Upper lateral quadrant	Upper middle line	Medial
1	F	174	63	15		26	5	7	25
2	M	176	69	4	9	14	5	10	15
3	F	166	55	5	15	11	7	9	17
4	M	176	74	3	7	9	3	5	16
5	M	177	76	9	18	20	12	7	18
6	M	181	65	2	14	18	4	8	18
7	M	178	67	3	10	12	3	15	13
8	M	180	63	3	15		2	5	10
9	M	193	76	2	9	8	2	7	10
10	M	173	65	5	23	9	7	9	13
11	M	178	66	8	5	5	2	8	14
12	M	179	66	4	3	3	2	3	4
13	F	167	55	12	8	5	8	9	11
14	M	183	61	5	9	8	19	13	15

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