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Southampton General Hospital, Southampton SO9 4XY

G HOLDSTOCK, DM, MRCP, senior registrar in medicine
S COLLEY, MB, BS, registrar in medicine

Correspondence to: Dr G Holdstock, Professorial Medical Unit, Level D, South Laboratory and Pathology Block, Southampton General Hospital, Southampton SO9 4XY.

Serum free thyroxine and free triiodothyronine concentrations in pregnancy

Measurements of circulating free thyroid hormone concentrations are generally considered to be an accurate index of thyroid state. It has been reported, however, that the serum concentration of free thyroxine falls during pregnancy,¹ which is at variance with the

a method taking into account the known binding characteristics of the thyroid hormone binding proteins.²

Serum thyroxine binding globulin and total thyroxine concentrations rose during pregnancy, whereas concentrations of free thyroxine and free triiodothyronine were progressively lower in each trimester (table). The changes in measured free thyroxine and free triiodothyronine were paralleled by a reduction in predicted free hormone concentrations.

Comment

Both measured and predicted free triiodothyronine and free thyroxine concentrations were low in the pregnant women. These changes were most pronounced in the third trimester but were already evident in the first, as were changes in thyroxine binding globulin and total thyroxine concentrations. The low free hormone concentrations were not, however, an artefact of the technique in the presence of high concentrations of thyroxine binding globulin since free triiodothyronine and free thyroxine concentrations are normal in subjects in whom concentrations of thyroxine binding globulin are even higher than during pregnancy.⁴

The pregnant women showed none of the clinical features of hypothyroidism despite low circulating free hormone concentrations. The maintenance of a clinically euthyroid state in the face of low free hormone concentrations suggests that pregnancy induced a change in the cellular response to thyroid hormones. We propose that in pregnancy there may be an oestrogen induced alteration in cellular uptake or nuclear receptor binding of thyroid hormones that is countered by a fall in circulating free hormone concentrations.

Mean (SD) concentrations of free thyroxine and triiodothyronine in pregnant women and euthyroid controls

Subjects	Thyroxine binding globulin (mg/l)	Total thyroxine (nmol/l)	Free thyroxine (pmol/l)		Free triiodothyronine (pmol/l)	
			Predicted	Measured	Predicted	Measured
Controls (n = 20)	9.9 (1.9)	80.5 (19.0)	22.1 (6.6)	17.0 (2.7)	5.8 (1.3)	6.6 (1.1)
Pregnant women:						
1st trimester (n = 16)	17.2* (2.6)	113.0* (18.1)	19.8 (4.0)	13.8* (2.0)	4.2† (0.8)	5.4 (0.8)
2nd trimester (n = 18)	24.3* (3.8)	119.0* (29.6)	14.2* (3.1)	11.3* (1.7)	2.9* (0.7)	4.4* (1.2)
3rd trimester (n = 19)	27.4* (3.4)	126.0* (29.3)	14.1* (4.7)	10.9* (1.8)	3.2* (1.0)	4.2* (0.7)

Significance of difference from control group (Student's *t* test for unpaired data): *p < 0.0005; †*p* < 0.0025.

Conversion: SI to traditional units—Thyroxine: 1 nmol/l ≈ 77.7 ng/100 ml. Free thyroxine: 1 pmol/l ≈ 77.7 pg/100 ml. Free triiodothyronine: 1 pmol/l ≈ 65 pg/100 ml.

euthyroid clinical state of pregnant women. A new method for direct radioimmunoassay of serum free triiodothyronine concentrations has been developed.² In this study we measured serum free triiodothyronine as well as free thyroxine concentrations throughout pregnancy and compared the values obtained with predicted values derived from total hormone and binding protein concentrations.

Patients, methods, and results

Blood was taken from women in each trimester of pregnancy at routine antenatal visits. Further samples were collected from an age matched control group of euthyroid women taking no medication.

Free triiodothyronine and free thyroxine concentrations were measured by direct radioimmunoassay (Amerlex Kit methods, Amersham International, Amersham, Buckinghamshire).² These free hormone assays use thyroxine and triiodothyronine derivatives labelled with iodine-125 that have been chemically modified to inhibit severely their binding to serum thyroid hormone binding proteins but that bind normally to thyroxine or triiodothyronine antibodies. In the assays free thyroid hormones and the modified labelled derivatives compete for binding to high affinity thyroxine or triiodothyronine antibodies, and the proportion of labelled derivative bound to the antibody is inversely related to the serum free thyroxine or free triiodothyronine concentration. Total serum triiodothyronine and thyroxine concentrations were measured by in house radioimmunoassay, thyroxine binding globulin concentration by immunoelectrophoresis, and thyroxine binding prealbumin and albumin concentrations by immunodiffusion. Predicted free triiodothyronine and free thyroxine concentrations were derived from total hormone and binding protein concentrations, using

With the increasing use of measurements of free thyroid hormone concentrations as routine thyroid function tests it should be remembered that a lower reference range is appropriate in pregnancy.

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Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Birmingham B15 2TH

JAYNE A FRANKLYN, MB, MRCP, research fellow
M C SHEPPARD, PHD, MRCP, Wellcome Trust senior lecturer
D B RAMSDEN, PHD, FRSC, senior lecturer

Correspondence to: Dr J A Franklyn.