RESULTS

Group 2: The hypothyroid children

This consisted of two female cases, aged four and seven years with a juvenile (primary) hypothyroidism, one three year old male with a familial congenital hypothyroidism and a fourth case; a female Turner whose hormonal studies were identical with tertiary (hypothalamic) hypothyroidism, but was diagnosed as an autoimmune thyroiditis. The male case with secondary (pituitary) hypothyroidism was included within the GHD group.

Group 3: The growth delayed children

This formed the largest group. It consisted of ten children, eight were males and only two were females. Seven cases presented around puberty (ie. just before, within or after puberty), the remaining presented at period coinciding with the mid-growth spurt.

The three groups were chosen specifically as they were intended to represent examples of impairments in the major hormones affecting growth, which are: growth hormone (in GHD), thyroid hormones (in the hypothyroid group) and presumable impairments in sex hormones, of pituitary gonadal or adrenal origin (growth delay group). It is hoped that this may bear some importance in our forecoming correlative studies.

Group 4: Miscellaneous cases of short stature

This consisted of two cases with disordered SM activity; a Laron dwarf and a case with an end organ or cell insensitivity to circulating somatomedin. One female case, an insulin dependent diabetic, with growth delay possibly due to Mauriac syndrome. Another male case (HA) with the Silver-Russell syndrome. The case was chosen as he presented with severe stunted stature and was cryptorchoid with a micropenis, a picture suspicious of MPHD (GH + gonadotropin hormone deficiency). The patient was revealed to be a case of growth delay, after his normal hormonal studies and his spontaneous catch-up growth on follow-up. A hypogonadal patient with short stature (case SMH), who probably was stunted in growth because of a simple delayed growth associated with his hypogonadal state and not part of a MPHD.

Also there was a female case (AAO) with short stature of a mixed familial and delay aetiology. Finally a male (IN), 2.2 years of age, whose delay in growth was presumed to be due to an impairment in the secretion and/or action of prolactin ; a hormone whose action in the immediate postnatal period and first two years of life may bear positive implications with respect to growth during that period. This comes up to seven cases with mixed disorders of growth presenting with short stature. It is evident that of these 7 cases, 4 cases also had growth delay, either primarily (cases AAO, SM) or secondary to their primary clinical state (cases EAS, HA). So that there were actually fourteen cases of growth delay out of the total twenty six cases presenting with short stature.

II - Results of the Hormonal Studies

The results of the combined insulin induced hypoglycaemic test (ITT) and thyrotropin releasing hormone (TRH) test for the radioimmunoassayable growth hormone (GH) in ng/ml thyrotropin (TSH) in μU/ml and prolactin (PRL) in ng/ml are displayed according to the time in minutes the blood sample was drawn during the test. The coincident blood glucose levels in mg% at the time the blood sample is drawn is also included within the tables. The results are tabulated according to their clinical diagnosis, with the control group in table (5), the GHD group in table (6), the hypothyroid group in table (7), the growth delay group in table (8) and finally the mixed or miscellaneous group in table (9). The same tables showed the results of thyroxine (T_4) basal levels in μg/dl measured by radioimmunoassay.

The results of bioassayable somatomedin activity (in units/ml) are shown in tables (5) to (9), ranging from no dose response or < 0.1 units/ml to just over 2 units/ml, with the normal range being between 0.5 units/ml to about 1.5 units/ml. The dose response curves are shown in figures (13) to (18). For the thirty four cases in this study we have performed seven different assays each with its own individual set of standards as shown in the figures. The importance of studying the dose response curves is to differentiate the cases

age group (ages 5 - 10 years in females and 5 - 12 years in males) and the pubertal age group (10 - 14 years in females and 12 - 16 years in males). The clinical disorders included in this statistical analytic study were the growth hormone deficient group, the hypothyroid group and the growth delay group with the control children used for comparative studies.

When analysing the age related variations of basal, peak values and degrees of response of each hormone we used the F-test (one way analysis of variance). But when comparing one response with another in either sex or between pubertal and pre-pubertal periods of growth or between one clinical disorder and another, we used the t-test. The correlation coefficient was used extensively for the correlation of the hormones with one another in the age related variations and in the clinical disorders of growth. In one instance the Chi-square was used to define the intensity of an association between two hormones in a clinical disorder. These statistical methods have been facilitated by the use of a micro-computer using a "BASIC" statistical program "INTER-STAT". This was made possible at the Institute of Child Health of London University, courtesy of Dr M.A. Preece. The detailed results will be presented with the discussion in order to surmise and facilitate the understanding of such an extensive study.

TABLE(1) GROWTH ASSESSMENT DATA OF CASES WITH GROWTH HORMONE DEFICIENCY

Case Initials	Sex	Chron. Age (yrs)	Height (cm) &(SD)	Weight (kg) &(SD)	Bone Age ('yrs')	Height Velocity (cm/yr)	Parental Height Mother	Parental Height Father	Pubertal Stage	Peak GH ng/ml	Peak TSH mIU/ml	Peak PRL ng/ml	Basal T4 ng/dl	Basal SM-C units/ml	Final Diagnosis
1. J.F.	M	2.75	76.3 (-4)	9.0 (-3)	1.45	2.4	-1	-1	P1	1.16	18.04	>100	11.05	0.48	MPHD, GHD and GnD
2. M.H.H.	M	4.16	87.0 (-4)	13.5 (-1)	1.0	4.0	-1	-1	P1	2.03	5.05	>100	5.39	<0.1	MPHD, GHD & TSH defi'nt
3. K.G.	M	10.16	107.0 (>-4)	18.0 (>-3)	6.6	2.0	-1	-1	P1	1.6	8.83	>100	8.95	<0.1	IGHD
4. S.I.	M	16.35	128.0 (>-4)	25.0 (>-3)	10.0	4.0	-1	-2	G /PH2	5.65	24.1	>100	10.9	1.137	IGHD
5. N.A.R.	F	10.16	97.0 (>-4)	17.0 (>-3)	6.1	2.0	+1	Mn	P1	1.6	9.38	56.0	9.84	1.011	IGHD

TABLE (2) GROWTH ASSESSMENT DATA OF CASES WITH HYPOTHYROIDISM

Case Initials	Sex	Chron. Age (yrs)	Height (cm) & (SD)	Weight (kg) & (SD)	Bone Age ('yrs')	Height Velocity (cm/yr)	Parental Height Mother SD	Parental Height Father SD	Pubertal Stage	Peak GH ng/ml	Peak TSH mIU/ l	Peak PRL ng/ml	Basal T4 ng/dl	Basal SM-C units/ml	Final Diagnosis
1. G.S.	F	4.55	91.0 (-2)	12.5 (-2)	1.75	2.1	Mn	Mn	P1	12.6	52.6	>100	1.68	1.089	Acquired Hypothyroidism
2. H.A.	F	7	104.0 (-3)	31.5 (+3)	3		Mn	Mn	P1	3.26	51.56	94.7	1.34	0.581	ditto
3. M.K.I.	F	13.15	124.8 (-4)	22 (-3)	10.5	4	-1	-1	B2/P1/A1	>50	>80	>100	10.13	1.369	Turner's Syndrome Autoimmune Thyroiditis
4. M.M.	M	3.6	78.0 (-4)	8.0 (>-3)	0.5		-2	-1	P1	14.10	44.06	>100	3.79	1.129	Congenital Hypothyroidism

TABLE (4) MISCELLANEOUS CASES WITH SHORT STATURE

Case Initials	Sex	Chron. Age (yrs)	Height (cm) & (SD)	Weight (kg) & (SD)	Bone Age ('yrs')	Height Velocity (cm/yr)	Parental Height Mother SD	Parental Height Father SD	Pubertal Stage	Peak GH ng/ml	Peak TSH mU/ml	Peak PRL ng/ml	Basal T4 ng/dl	Basal SM-C units/ml	Final Diagnosis
1. Y.M.F.	F	10	110.0 (>-4)	12.0 (>-4)	5	-			P1	>50	17.66	>100	11.37	0.706	?Laron Dwarfism
2. S.M.H.	M	11.25	132.0 (-2)	30.5 (<-1)	8	4	-1	-2	P1	26.37	15.12	>100	6.29	1.040	Hypogonadism & Gr. Delay
3. I.N.	M	2.24	72.5 (>-4)	9.0 (-4)	0.66	9	Mn	Mn	P1	45.7	39.14	80.27	9.00	0.783	?PRL Disorder
4. E.A.S.	F	7.4	104.3 (-3.5)	12.5 (>-3)	-	6.6	-2	-1	P1	>50	9.20	>100	11.48	0.681	?Mauriac Syndrome +Gr. Delay
5. R.S.A.	F	3.33	78.9 (-4)	8.0 (-4)	2 TW2 1.5 GP	7.6	-1	M	P1	>50	13.44	>100	14.92	2.09	? End organ unresponsiveness
6. A.A.O.	F	3.92	87.5	11.0	2	8.0	-1	-3	P1	40.23	6.25	>100	8.11	0.737	Familial Short Stature +Gr. Delay
7. Y.M.M.	M	6.58	102.0 (-3)	16.0 (-2)	5.5	4.0	-2	Mn	P1	9.6	8.65	>100	11.45	NDR <0.1	Constitutional Short Stature + Gr. Delay
8. H.A.	M	5.33	93.5 (-4)	14.0 (-2)	4.0	3.0	Mn	-	P1	>50	12.03	70.7	11.03	-	Silver-Russel Syndrome+ Gr. Delay.

TABLE (5) COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST IN CONTROL CASES

Case Initials	Sex	Age (yrs)	Time (min)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS) Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C units/ml
1. A.S.	M	6.33	0	100	5.00	5.43	22.89	11.05	0.885
			15	55	2.73	24.53	>100		
			30	60	4.37	18.67	>100		
			45	70	21.60	12.31	>100		
			60	38	21.31	14.92	>100		
			90	80	13.28	8.52	>100		
2. M.A.S.	M	6.8	0	110	>50	2.97	>100	10.94	1.070
			15	90	5.63	8.34	>100		
			30	95	3.95	9.59	37.21		
			45	45	32.03	7.54	64.45		
			60	30	>50	6.62	46.29		
			90	40	>50	4.90	24.30		
3. O.A.	M	7	0	115	4.3	3.16	79.49	11.88	0.632
			15	25	3.28	6.61	68		
			30	35	8.40	6.45	30.07		
			45	31	15.45	5.47	93.16		
			60	35	22.31	5.08	>100		
			90	50	16.75	4.33	>100		
4. O.E.S.	F	9	0	132	1.33	4.49	18.73	10.2	0.586
			15	33	1.38	11.13	29.79		
			30	33	6.76	10.01	35.25		
			45	33	33.10	7.77	32.03		
			60	34	>50	7.07	32.81		
			90	35	>50	5.18	36.33		

TABLE (5) (continued)

Case Initials	Sex	Age (yrs)	Time (min)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS) Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C units/ml
5. E.G.	M	10	0	62	1.3	2.6	6.41	7.34	1.411
			15	34	1.45	8.54	35.35		
			30	29	1.8	9.39	50.2		
			45	27	7.97	7.32	>100		
			60	27	>50	6.19	>100		
			90	38	>50	5.59	54.49		
6. A.A.	M	12	0	130	1.33	1.71	>100	11.42	1.692
			15	25	1.56	7.11	25.02		
			30	34	25.34	7.03	>100		
			45	35	15.39	5.2	>100		
			60	38	16.21	3.83	>100		
			90	39	15.42	2.84	97.65		
7. W.G.	F	13	0	72	1.82	2.91	6.99	8.24	no dose response
			20	23	7.05	13.44	40.82		
			40	30	>50	12.05	>100		<0.1
			60	33	>50	9.53	>100		
			90	42	>50	7.13	>100		
8. N.S.	M	14	0	110	1.7	4.1	4.08	10.43	0.726
			15	25	1.4	7.32	86.7		
			30	49	2	4.9	>100		
			45	42	>50	3.83	>100		
			60	54	>50	3.62	95.11		
			90	65	>50	3.36	84.37		
9. F.A.S.	F	14	0	76	15.39	2.24	12.20	8.82	1.621
			20	72	>50	13.44	85.94		
			40	70	>50	10.49	18.20		
			60	75	24.30	12.07	23.83		
			90	75	19.84	7.29	14.10		

TABLE (6) COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST IN CASES OF SHORT STATURE

I. CASES OF GROWTH HORMONE DEFICIENCY

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TESTS (ITT AND TRH STIMULATION TESTS) Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C units/ml
1. J.F.	M	2.75	0	50.0	0.98	11.91	>100	11.05	0.480
			15	28	1.16	18.04	>100		
? MPHD			30	28	0.63	4.63	53.13		
			45	28	1.07	9.39	>100		
			60	31	0.78	7.67	68.75		
			90	57	0.41	6.19	31.54		
2. M.H.H.	M	4.25	0	95	2.03	0.70	>100	5.39	No dose
			15	56	1.47	2.48	>100		response
MPHD			30	31	1.52	5.05	>100		<0.1
			45	32	1.08	2.29	>100		
			60	36	1.21	2.26	>100		
			90	39	1.45	2.29	>100		
3. N.A.R.	F	10.15	0	90	<1.0	3.41	35	9.84	1.011
			15	55	1.6	9.22	56		
? MPHD			30	40	1.2	9.38	56		
			45	60	1.6	7.91	42		
			60	44	-	6.64			
			90	45	1.3	4.05	36		
4. K.G.	M	10.9	0	118	1.49	2.36	18.20	8.95	No dose
			15	39	1.35	8.83	>100		response
IGHD			30	36	1.35	8.67	>100		<0.1
			45	34	1.21	6.43	67.19		
			60	25	1.29	5.15	>100		
			90	43	1.52	3.16	39.06		
5. S.I.	M	16.4	0	115	2.22	3.61	11.8	10.9	1.137
			15	45	5.65	20.94	52.3		
IGHD			30	30	5.2	24.14	51.4		
			45	44	3.2	15.70	>100		
			60	52	2.07	11.66	>100		
			90	43	2.4	8.85	>100		

TABLE (7) COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST IN CASES OF SHORT STATURE

II. CASES OF HYPOTHYROIDISM (ACQUIRED HYPOTHYROIDISM, AUTOIMMUNE THYROIDITIS AND CONGENITAL HYPOTHYROIDISM)

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS)					
				Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C units'/ml
6. G.S.	F	4.58	0	98	2.9	52.58	>100	1.68	1.089
			15	55	7.6	35.70	>100		
			30	67	12.6	39.65	>100		
			45	65	2.6	35.20	>100		
			60	64	1.7	39.34	>100		
			90	47	1.3	37.04	>100		
7. H.A.A.	F	7	0	85	2.03	38.24	23	1.34	0.581
			20	66	1.76	35.70	17.91		
			40	45	2.51	41.09	91.21		
			60	72	3.20	51.56	32.42		
			90	81	3.26	44.3	94.72		
8. M.M.	M	3.5	0	85	2.10	39.73	>100	3.79	1.129
			20	50	11.35	38.91	>100		
			40	50	14.10	42.5	>100		
			60	16	2.55	44.06	>100		
			90	16	1.95	41.29	>100		
9. M.K.I.	F	13.16	0	110	11.2	7.79	3.41	10.13	1.369
			15	50	>50	13.09	>100		
			30	35	>50	9.98	96.87		
			45	40	>50	7.83	>100		
			60	60	>50	8.09	>100		
			90	55	>50	>80	75.39		

TABLE (8) COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST IN CASES OF SHORT STATURE

III. CASES OF GROWTH DELAY

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS) Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C units/ml
10. W.B.	M	6.16	0	92	1.14	8.42	4.48	11.91	0.977
			15	50	2.6	7.72	>100		
			30	45	3.12	5.98	>100		
			45	80	6.3	6.93	>100		
			60	95	2.12	4.79	>100		
			90	95	7.5	3.24	27		
11. A.S.	M	7.33	0	84	2.17	2.85	28.37	11.6	No dose response (marked inhibition)
			15		19.38	22.27	>100		
			30	61	>50	10.7	>100		
			45	42	>50	9.36	>100		
			60	56	>50	9.64	>100		<0.1
			90	77	>50	6.88	80.47		
12. E.S.	F	11.66	0	96	1.8	2.36	25.09	10.03	1.801
			15	35	>50	10.59	>100		
			30	40	>50	7.05	>100		
			45	46	>50	4.95	>100		
			60	42	>50	5.20	>100		
			90	62	>50	3.52	98		
13. A.S.H.	M	10.9	0	103	>50	2.71	7.6	8.85	1.492
			20	44	>50	13.44	>100		
			40	55	>50	11.72	>100		
			60	43	>50	8.87	>100		
			90	53	>50	7.27	>100		

TABLE(8) continued

III. CASES OF GROWTH DELAY (continued)

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS)					
				Glucose mg%	GH ng/ml	TSH [illegible]/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C unit[illegible]/ml
14. T.A.	M	14.5	0	120	1.62	3.95	27	7.98	1.533
			15	100	2.28	10.35	>100		
			30	50	1.6	9.53	>100		
			45	45	1.9	8.42	>100		
			60	92	1.4	6.93	>100		
			90	100	9.2	4.34	96		
15. O.A.	M	15	0	70	12.7	2.21	5.29	10.15	1.031
			20	20	3.7	2.21	91		
			40	33	3.2	5.8	>100		
			60	31	4.8	5.03	87		
			90	30	10.6	4.67	32		
16. M.B.	M	15.5	0	112	1.7	2.37	4.3	8.59	1.413
			15	38	>50	8.71	95.7		
			30	49	>50	6.13	76.17		
			45	60	>50	5.27	22.12		
			60	50	11.17	4.96	24.32		
			90	55	16.0	2.77	5.25		
17. M.A.R.	M	17	0	120	1.02	1.79	3.60	9.61	0.641
			15	52	1.07	7.52	27.30		
			30	31	0.73	7.60	41.02		
			45	55	20.66	7.54	>100		
			60	39	>50	5.80	>100		
			90	37	>50	4.32	>100		
18. H.M.A.	F	10.88	0	120	1.26	2.03	16.86	11.37	0.581
			15	39	3.17	9.90	53.5		
			30	28	20.78	11.25	>100		
			45	28	>50	8.98	49.22		
			60	-	33.20	7.68	84.38		
			90	31	22.42	5.12	24.53		
19 Y.M.	M	6.56	0	110	9.6	2.97	90.03	11.45	No dose response (inhibition) <0.1
			15	43	1.4	8.65	20.6		
			30	66	6.2	6.99	89.45		
			45	36	-	6.87	>100		
			60	42	5.8	5.86	>100		
			90	34	5.6	4.30	>100		

TABLE (9) COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST IN CASES OF SHORT STATURE

IV. MISCELLANEOUS CASES OF SHORT STATURE

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS) Glucose mg%	GH ng/ml	TSH m·IU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C unitm/ml
20. R.S.A.	F	3.33	0	79	10.2	3.81	4.29	14.92	2.090
			15	50	6.5	11.50	>100		
			30	32	>50	13.44	>100		
			45	39	>50	8.48	>100		
			60	-	-	-	-		
			90	-	-	-	-		
21. A.A.O.	F	3.9	0	100	18.79	5.20	25.87	8.11	0.737
			20	35	2.81	6.25	20.13		
			40	48	14.98	5.47	79.68		
			60	40	15.16	4.20	>100		
			90	48	40.23	3.25	>100		
22. Y.M.	F	10	0	93	>50	5.59	20.31	11.37	0.706
			15	-	>50	16.17	>100		
			30	30	>50	17.66	>100		
			45	28	>50	13.87	>100		
			60	32	>50	9.57	>100		
			90	33	>50	6.01	40.82		
23. S.M.	M.	11.33	0	100	1.75	1.87	3.35	6.29	1.040
			15	34	3.07	13.59	41.21		
			30	44	26.37	15.12	>100		
			45	40	8.01	12.05	>100		
			60	31	13.75	8.93	>100		
			90	48	25.10	6.46	48.83		

continued

IV. MISCELLANEOUS CASES OF SHORT STATURE

Case Initials	Sex	Age (yrs)	Time (mins)	COMBINED HYPOTHALAMO-PITUITARY FUNCTION TEST (ITT AND TRH STIMULATION TESTS)					
				Glucose mg%	GH ng/ml	TSH mIU/ml	PRL ng/ml	Basal T4 µg/dl	Basal SM-C unit/ml
24. H.A.	M	5.33	0	95	1.7	6.21	22.65	11.03	-
			15	42	9.1	11.41	70.7		
			30	38	15.4	11.37	35.93		
			45	-	>50	12.03	28.46		
			60	63	>50	9.28	33.10		
			90	65	7.8	6.11	24.23		
25. E.A.S.	F	7.5	0	312	20.66	2.69	5.66	11.48	0.681
			15	278	4.12	8.87	24.88		
			30	202	2.99	9.20	16.68		
			45	176	4.52	7.83	12.7		
			60	134	6.32	6.35	13.28		
			75	77	6.05	5.39	9.3		
			90	67	>50	4.75	20.78		
			105	65	>50	3.83	34.18		
			135	154	6.13	2.79	>100		
26. I.N.	M	2.33	0	100	6.88	3.42	80.27	9.00	0.783
			20	38	7.34	39.14	4.22		
			40	17	45.70	10.82	33.78		
			60	28	3.24	7.66	31.93		
			90	40	12.34	6.93	25.09		
27. E.A.A.	M	15	0	-	2.34	2.51	21.7	9.39	0.446
			20	-	2.92	9.00	30.71		
			40	-	3.17	7.81	29.98		
			60	-	4.00	6.82	-		
			90	-	-	-	-		

TABLE (10) BASAL LEVELS OF SOMATOMEDIN (SM) AND THYROXINE (T4) BASAL, PEAK VALUES DEGREE AND TYPE OF RESPONSE OF GROWTH HORMONE (GH), THYROTROPIN (TSH) AND PROLACTIN (PRL) IN A COMBINED ITT &TRH STIMULATION TEST IN THE AGE GROUP 2-5 YEARS.

Case Initials	Sex	Age (yrs)	Basal SM U/ml	Basal T4 µg/dl	Basal GH ng/ml	Peak GH ng/ml	Degree of response	Type of response	Basal TSH µIU/ml	Peak TSH µIU/ml	Degree of response	Type of response	Basal PRL ng/ml	Peak PRL ng/ml	Type of response
1. I.N.	M	2.2	0.78	9	6.9	45.7 at 40'	38.8	N	3.4	39.14 at 15'	36.1	E	80.3	-	? PAR + ? P
2. J.F.	M	2.75	0.48	11.05	0.98	1.16 at 15'	0.18	P	11.91	18.04 at 15'	6.14	N	>100	-	PAR
3. M.H.H.	M	4.25	<0.1	5.39	2.03	-	-	PAR + P	0.7	5.05 at 30'	4.35	P	>100	-	Pt
4. M.M.	M	3.5	1.13	3.79	2.1	14.1 at 40'	12.0	P	39.7	44.06	5.6	Pt	>100	-	Pt
5. R.S.A.	F	3.33	2.09	14.92	10.2	>50 at 30'	>39.8	N	3.8	13.44 at 30'	9.64	N	4.3	>100	? Pt
6. A.A.O.	F	3.9	0.74	8.11	18.79	40.2 at 90'	21.4	D	5.2	6.25 at 15'	1.05	N	25.9	>100	D
7. G.S.	F	4.58	1.09	1.68	2.9	12.6 at 30'	9.7	P	52.6			Pt	>100		Pt

Types of response: N = Normal, E = Exaggerated, Pt = Persistent, D = Delayed, PAR = Paradoxical, P = Poor

TABLE (11) BASAL LEVELS OF SOMATOMEDIN (SM) AND THYROXINE (T4), BASAL LEVELS, PEAK VALUES, DEGREE AND TYPE OF RESPONSE OF GROWTH HORMONE (GH), THYROPIN (TSH) AND PROLACTIN (PRL) DURING A COMBINED ITT & TRH TEST IN THE AGE GROUP 5-12 YEARS .

Case Initials	Age (yrs)	Basal SM U/ml	Basal T4 µg/dl	Basal GH ng/ml	Peak GH ng/ml	Degree of response	Type of response	Basal TSH µIU/ l	Peak TSH µIU/ml	Degree of response	Type of response	Basal PRL ng/ml	Peak PRL ng/ml	Type of response
1. W.B.	6.15	0.98	11.9	1.14	7.5 at 90'	6.36	P + D	8.42	-	-	PAR	4.48	>100	N
2. Y.M.M.	6.58	<0.1	11.45	9.6	-	-	PAR + P	2.97	8.65 at 15'	5.68	N	90.03	>100	PAR
3. A.S.	7.33	<0.1	11.6	2.17	>50 at 30'	>47.8	N	2.84	22.27 at 15'	19.43	N	28.4	>100	N
4. H.A.	5.33		11.03	1.7	>50 at 45'	>48.3	N	6.2	12.03 at 45'	5.8	N	22.6	70.7	P
5. K.G.	10.89	<0.1	8.95	1.49	1.52 at 90'	0.03	P	2.36	8.8 at 15'	6.44	N	18.2	>100 at 15'	N
6 S.M.H.	11.33	1.04	6.29	1.75	26.37 at 30'	24.6	N	1.87	15.12 at 30'	13.25	N	3.35	>100 at 30'	N
7. A.S.H.	6.33	0.885	11.05	5	21.6 at 45'	16.6	N	5.4	24.5 at 15'	19.1	N	22.9	>100	E
8. O.A.	7	0.63	11.88	4.3	22.3 at 60'	18	D	31.6	6.6 at 15'	3.44	N	79.5	>100 at 60'	D
9. E.G.	10	1.4	7.3	1.3	>50 at 60'	>48.7	D	2.6	9.4 at 30'	6.8	N	6.4	>100 at 45'	N
10. M.A.S.	6.5	1.07	10.94	>50	>50 at 60'	>46.05	PAR	2.97	9.6 at 30'	6.63	N	>100		PAR

Abbreviations as before

TABLE (12) BASAL LEVELS OF SOMATOMEDIN (SM) AND THYROXINE (T4), BASAL LEVELS, PEAK VALUES, DEGREE AND TYPE OF RESPONSE OF GROWTH HORMONE (GH), THYROTROPIN (TSH) AND PROLACTIN (PRL) DURING A COMBINED ITT & TRH TEST IN MALES AGED 12-16 YEARS.

Case Initials	Age (yrs)	Basal SM U/ml	Basal T4 µg/dl	Basal GH ng/ml	Peak GH ng/ml	Degree of response	Type of response	Basal TSH µIU/ml	Peak TSH µIU/ml	Degree of response	Type of response	Basal PRL ng/ml	Peak PRL ng/ml	Type of response
1. A.A.	12.0	1.69	11.42	1.33	25.3 at 30'	23.97	N	1.7	7.1 at 15'	5.4	N	>100	-	PAR
2. N.S.	14.0	0.73	10.43	1.7	>50 at 45'	>48.3	N	4.1	7.3 at 15'	3.2	N	4.08	>100 at 30'	N
3. T.A.	14.5	1.5	7.98	1.62	9.2 at 90'	7.58	P + D	3.95	10.35 at 15'	6.4	N	27	>100 at 15'	N
4. E.A.	15.0	0.45	9.39	2.34	4.0 at 60'	1.66	P + D	2.5	9.0 at 20'	6.5	N	21	-	-
5. O.A.	15.0	1.03	10.15	12.7	-	-	PAR	2.2	5.8 at 40'	3.6	N	5.3	>100 at 40'	N
6. M.B.	15.5	1.4	8.6	1.1	>50 at 15'	>48.3	N	2.4	8.7 at 15'	6.3	N	4.3	95.7 at 15'	N
7. M.A.R.	17.0	0.64	9.6	1.02	>50 at 60'	>49.08	D	1.8	7.6 at 30'	5.8	N	3.6	>100 at 45'	N
8. S.I.	16.4	1.14	10.9	2.2	5.65 at 15'	3.43	P	3.6	24.14 at 30'	20.5	N	11.8	>100 at 45'	N
9. A.S.H.	12.9	1.5	8.85	>50	-	-	PAR	2.7	13.44	10.7	N	7.6	>100 at 15'	E

Abbreviations as before

TABLE (13) BASAL LEVELS OF SOMATOMEDIN (SM) AND THYROXINE (T4), BASAL LEVELS, PEAK BALUES, DEGREE AND TYPE OF RESPONSE OF GROWTH HORMONE (GH), THYROTROPIN (TSH) AND PROLACTIN (PRL) DURING A COMBINED ITT & TRH STIMULATION TEST IN FEMALES AGED 5-10 AND 10-14 YEARS.

Case Initials	Age (yrs)	Basal SM U/ml	Basal T4 µg/dl	Basal GH ng/ml	Peak GH ng/ml	Degree of response	Type of response	Basal TSH µU/ml	Peak TSH µU/ml	Degree of response	Type of response	Basal PRL ng/ml	Peak PRL ng/ml	Type of response
1. H.A.A.	7	0.58	1.34	2.03	3.26 at 90'	1.23	P	38.24	51.56 at 60'	13.32	Pt	23	94.7 at 90'	D
2. E.A.S.	7.5	0.68	11.48	20.7	>50 at 90'		PAR + D	2.69	9.2 at 30'	6.5	N	5.7	24.9^{1} $>100^{2}$	N^{1} D^{2} (TRH) (ITT)
3. O.E.S.	9	0.59	10.2	1.33	>50 at 60'	>48.7	D	4.5	11.13 at 15'	6.63	N	18.7	36.3	P
4 Y.M.F.	10	<0.1	11.4	>50	-	-	Pt	5.59	17.66 at 30'	12.07	N	20.3	>100 at 15'	N
1. W.G.	13	<0.1	8.24	1.8	>50 at 40'	>48.2	N	2.9	13.44 at 20'	10.5	N	6.99	>100 at 40'	N
2. F.A.S.	14	1.6	8.8	15.4	>50 at 15'	>34.6	N	2.24	13.44 at 20'	11.2	N	12.2	85.9 at 15'	N
3 N.A.R.	10.15	1.01	9.84	<1.0	1.6 at 15'	>0.6	P	3.4	9.4 at 30'	6	N	35	56	P
4. H.M.R.	10.83	0.58	11.37	1.26	>50 at 45'	>48.7	N	2.03	11.25 at 30'	9.22	N	16.86	>100 at 30'	N
5 E.S.	11.66	1.8	10.03	1.8	>50 at 15'	>48.2	E	2.36	10.6 at 15'	8.24	N	25.09	>100 at 15'	N
6 M.K.I.	13.16	1.4	10.13	11.2	>50 at 15'	>38.8	E	7.79	>80 at 90'	>72.2	E	3.41	>100 at 15'	N

Abbreviations in Tables (1) to (13):

C/A = chronological age
Ht/A = height age
B/A = bone age
Ht = height
wt = weight
GV = growth velocity
Part. ht = parental heights Mn = mean
Pubert = pubertal stage of development
Pk GH = peak growth hormone
Pk TSH = peak thyroid stimulating hormone
Pk PRL = peak prolactin
Basal T_4 = basal thyroxine
Basal SM-C = basal somatomedin-C
Pk FSH = peak follicular stimulating hormone
Pk LH = peak leutinizing hormone

Tr. ski. f. th = triceps skinfold thickness
Subs. ski. f. th. = subscapular skinfold thickness
perc. = percentile
M = male sex, F. = female sex

IGHD = isolated growth hormone deficiency
MPHD = multiple pituitary hormone deficiency
Gndr. defc. = gonadotropin deficiency
Acq. hypothyr. = acquired hypothyroidism

Figure 8 Heights and weights in the short male cases of the study and the follow-up data after investigation in some cases (OA, TA, ASH) and after treatment in others (HA, YMM, JF).

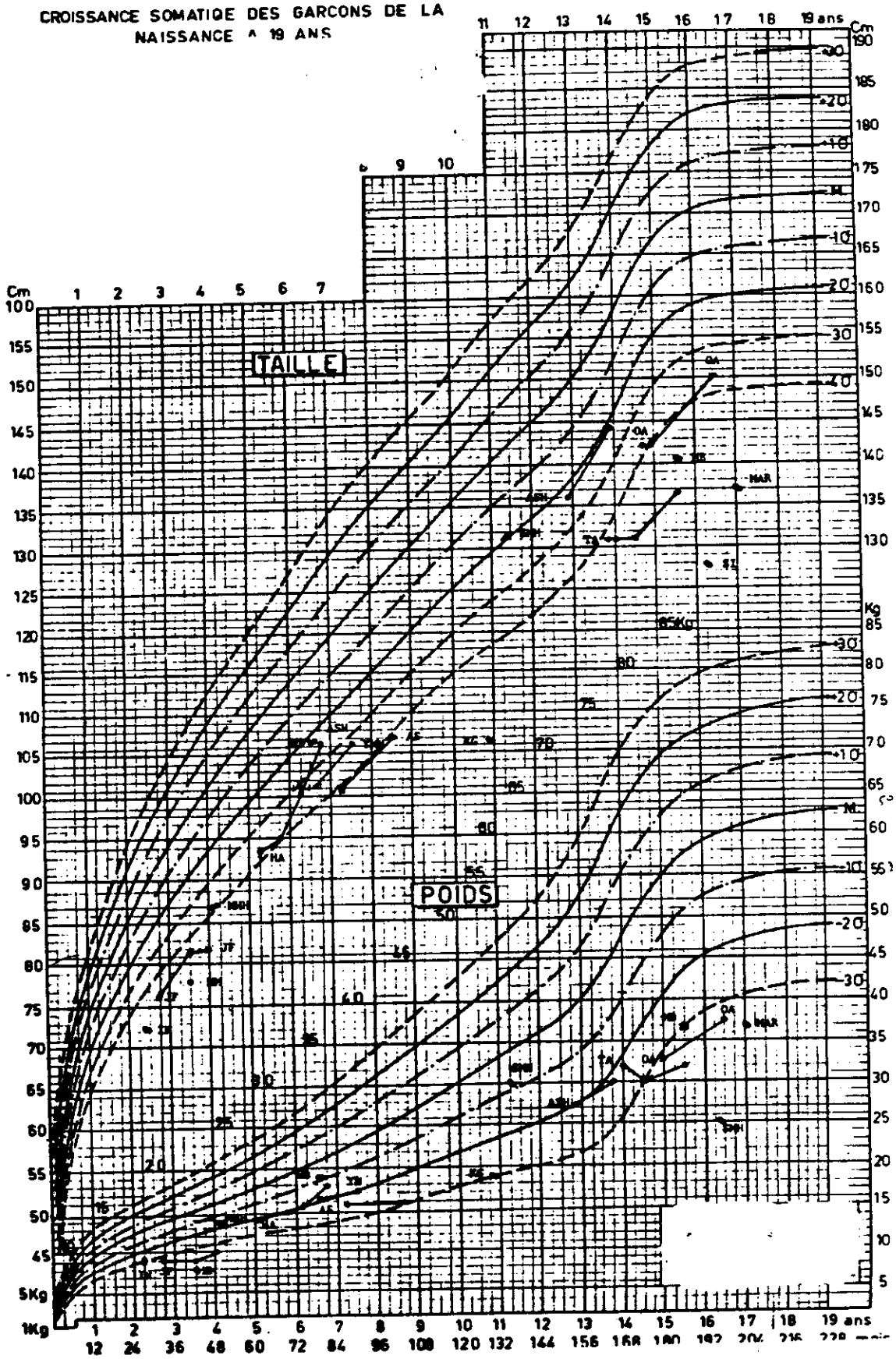


Figure 9 Heights and weights of short females in the study with follow-up data after investigation in some (AAO, RSA, ES) and after treatment in others (GS and HAA).

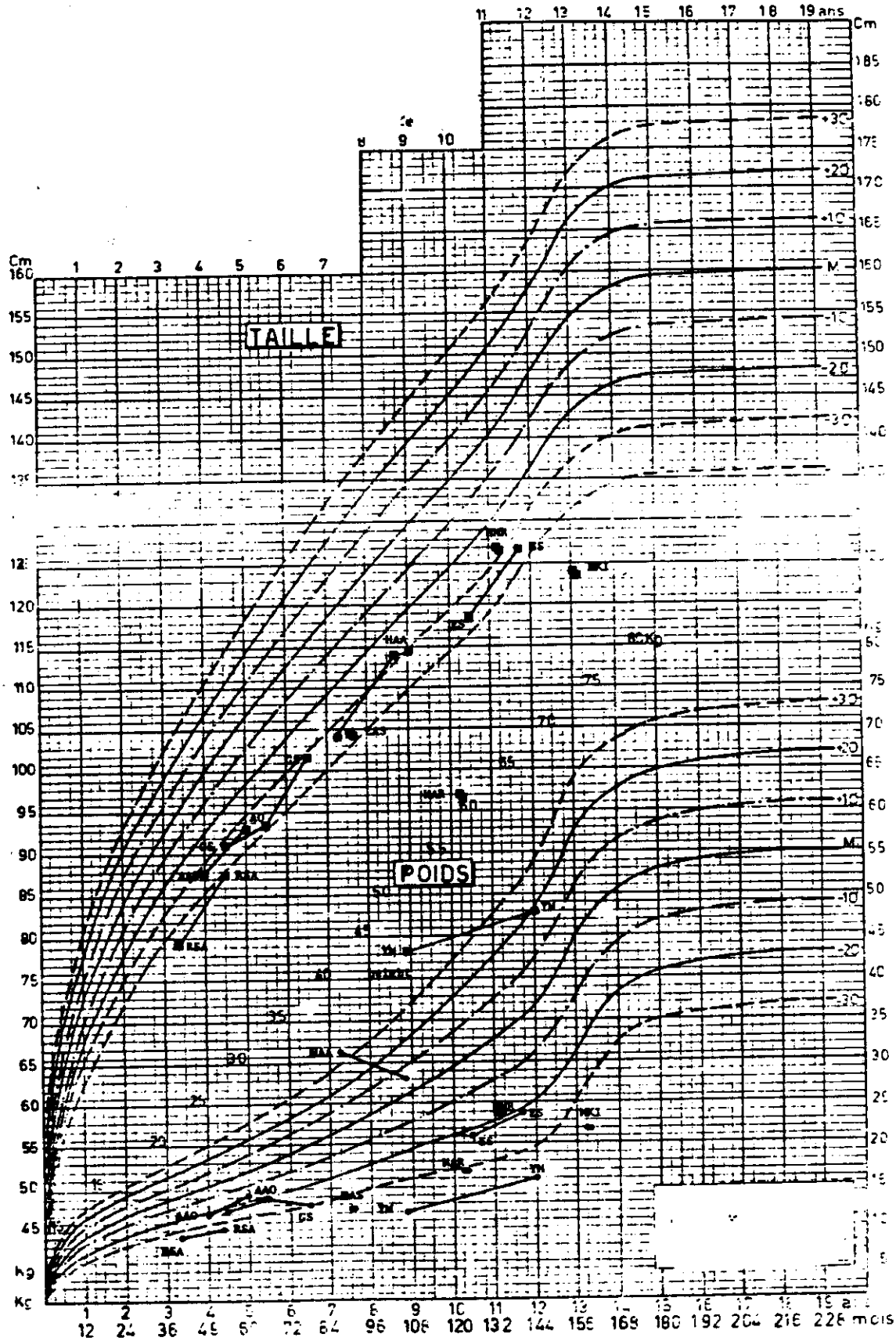
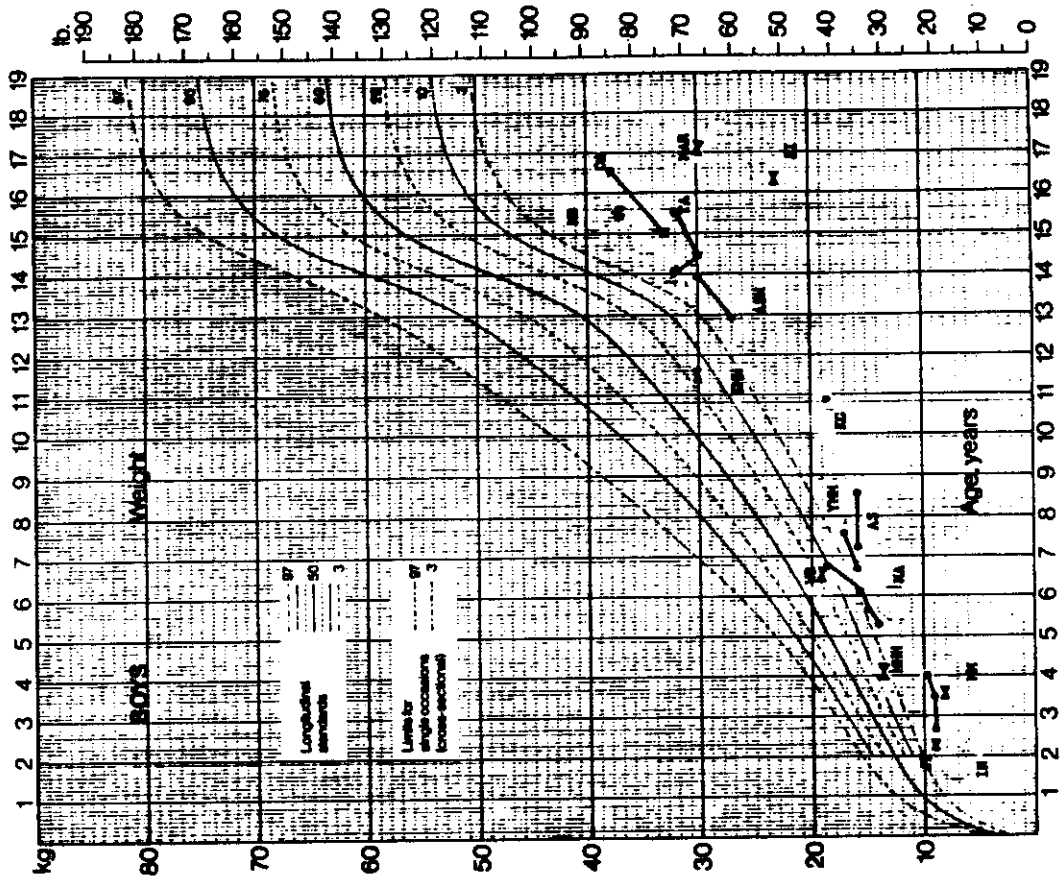


Figure 10 b Weights of males in the study with the follow-up of some of these cases after investigation in some and with treatment in others (British Standards).



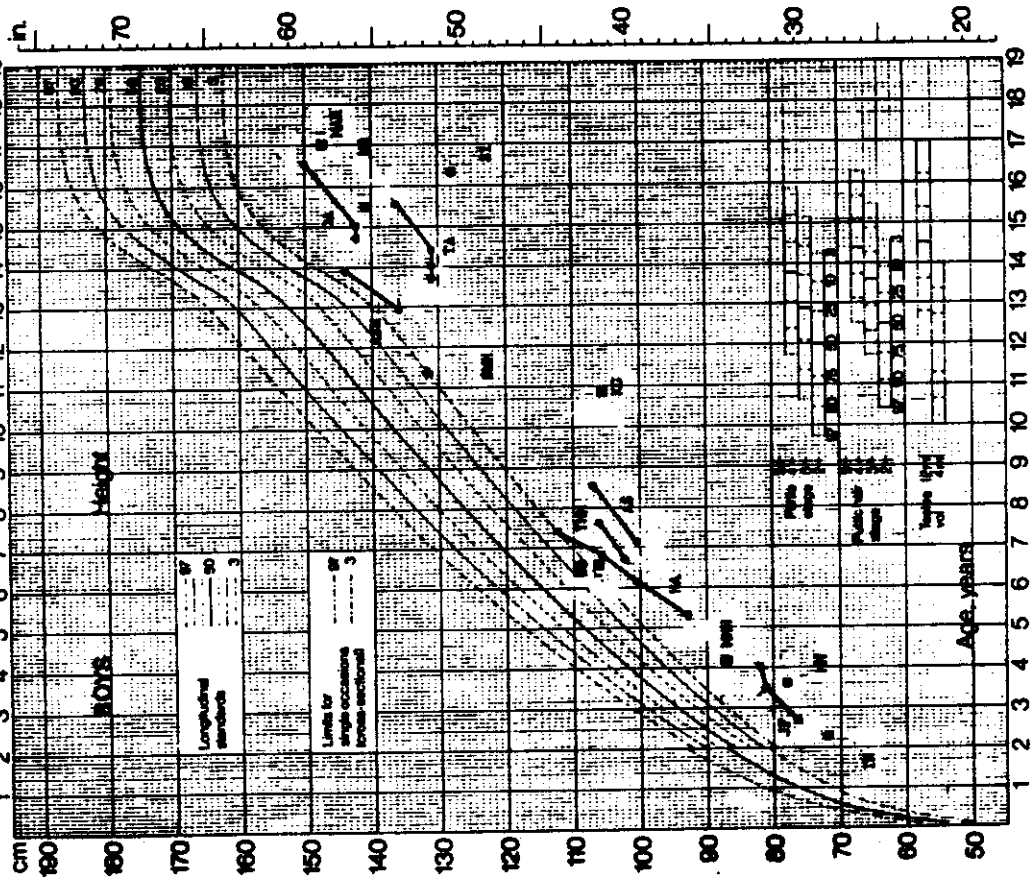


Figure 10a Heights of the males in the study with the follow-up of some of these cases after investigation in some and with treatment in others (British Standards).

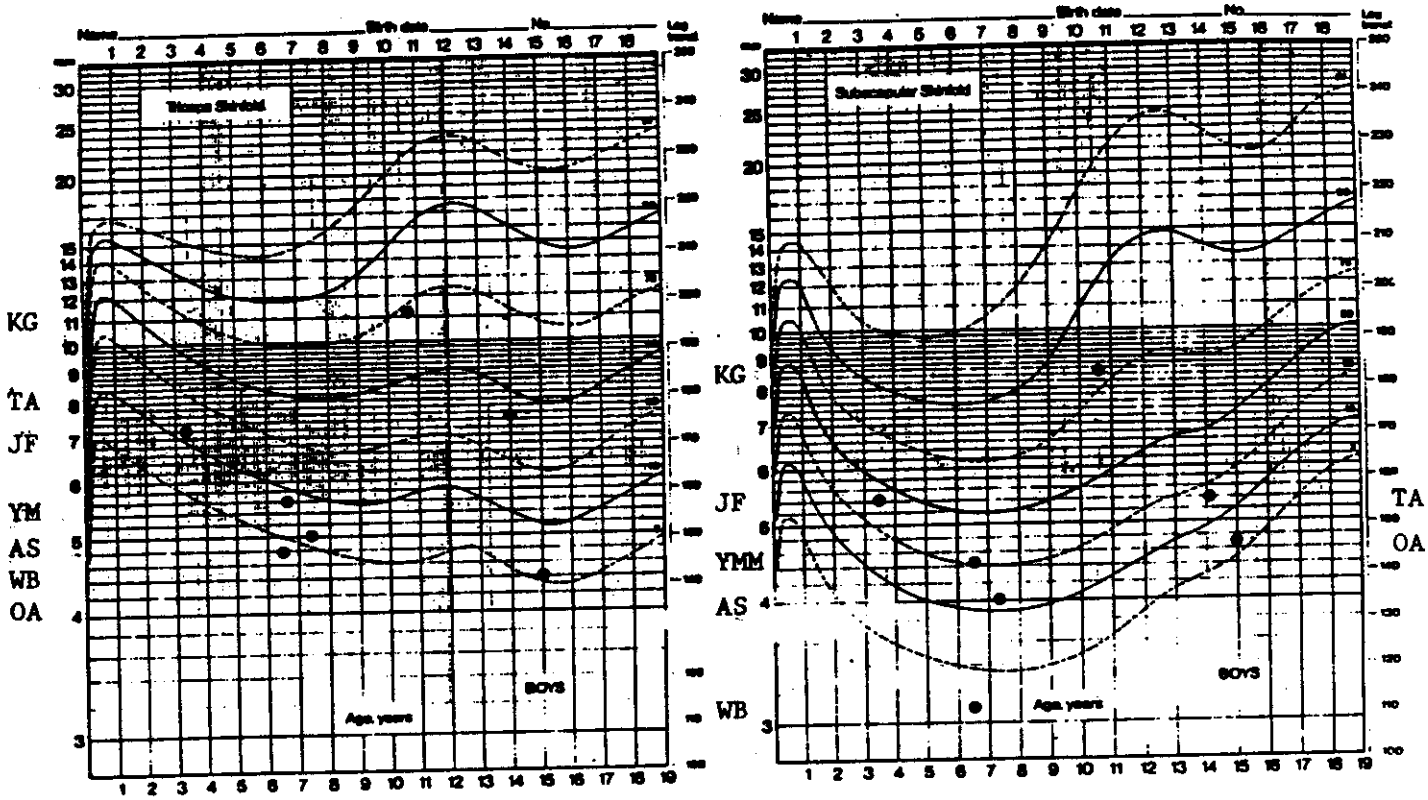


Figure 12a Skinfold thicknesses of some of the male cases of this study: a typical GHD (KG), a GHD resistant to GH therapy (JF), the muscular boys of growth delay (TA, WB) and the lean boys with growth delay (AS, OA, YMM) (British Standards, 1970).

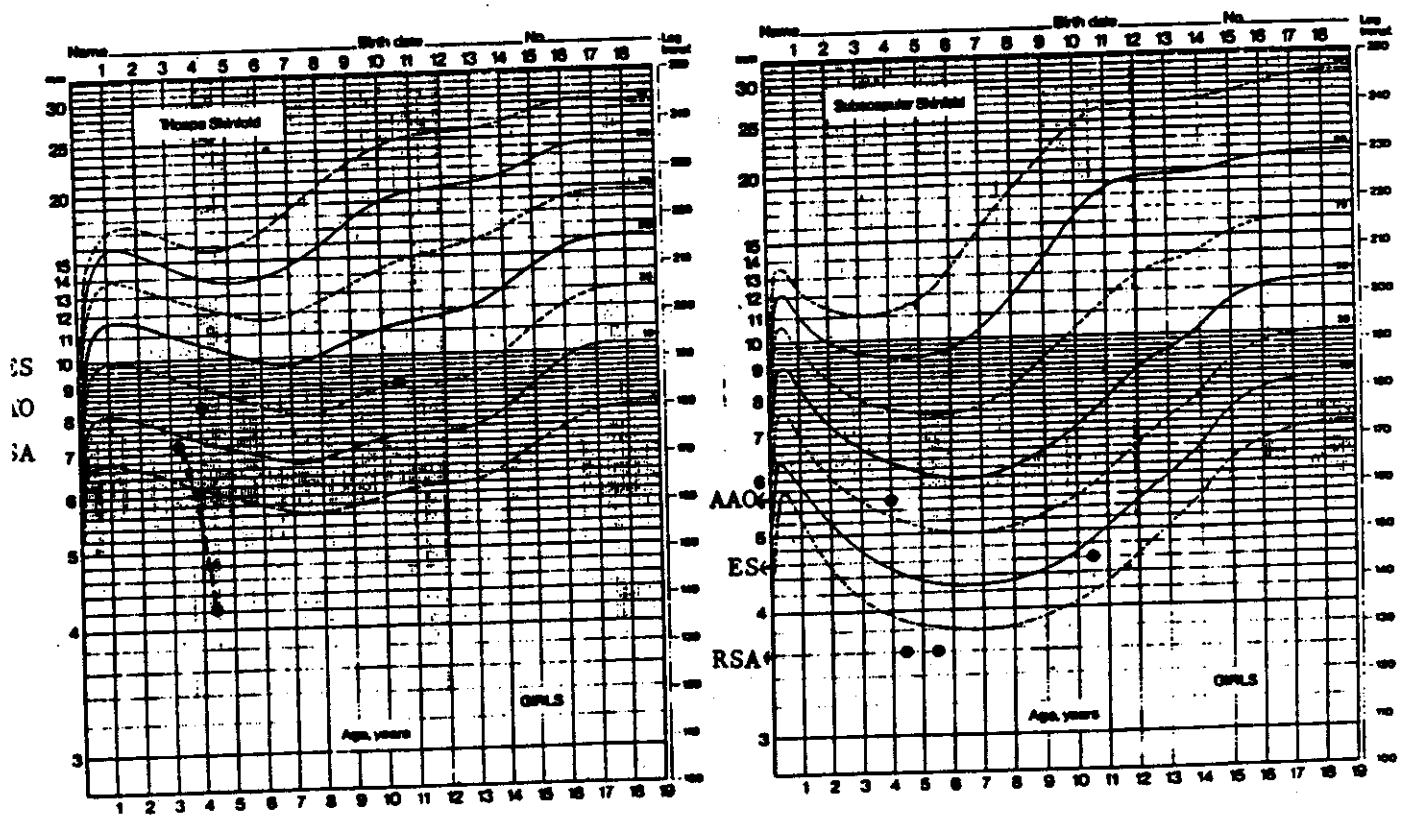


Figure 12b Skinfold thicknesses of some of the female cases of this study: a growth delayed girl (ES), familial shortness and growth delay (AAO) and a girl with raised SM activity (RSA) (British Standards, 1970).

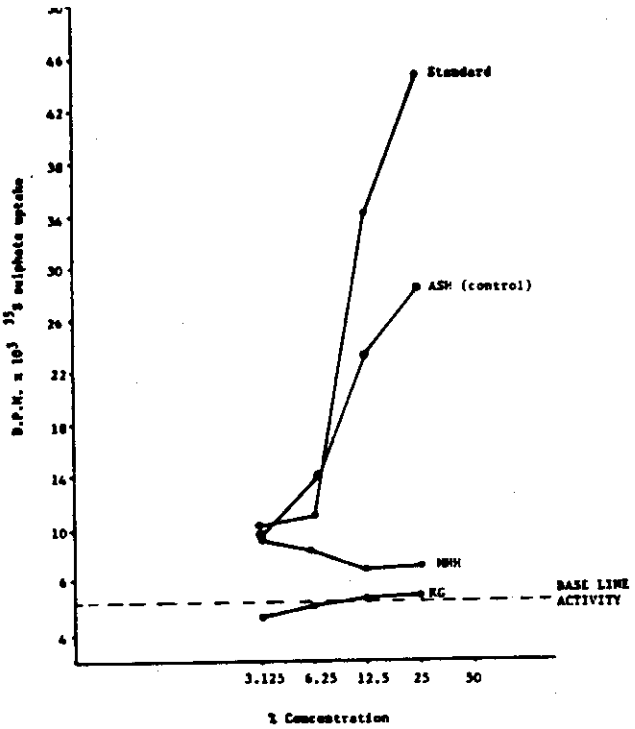


Figure 13 Dose response curves of patients with GHD (MHH, KG) as compared with a control case (ASH)

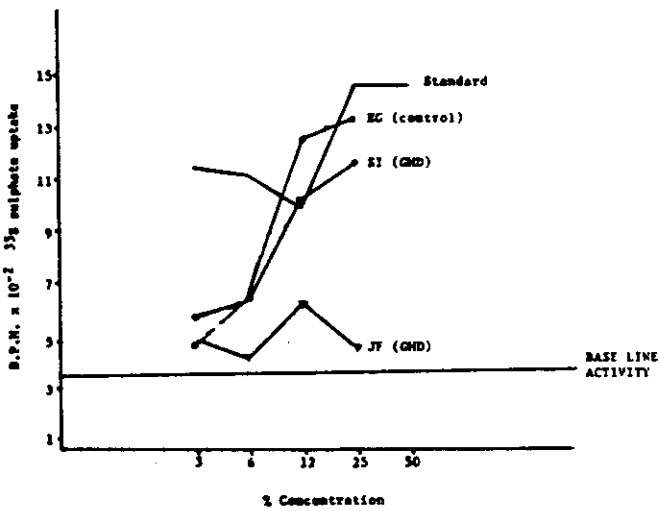


Figure 14 Dose response curves of a normal SM activity in a pubertal GHD patient (SI) and low and inhibited SM activity in a GHD patient resistant to GH therapy (JF), as compared to a normal control (EG)

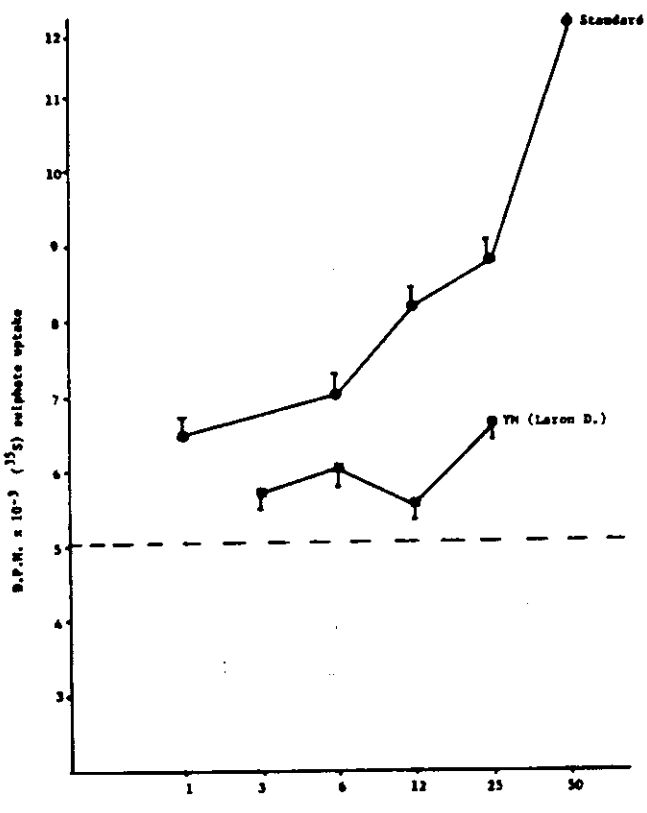


Figure 15 Dose response curve in the female Laron dwarf (YM)

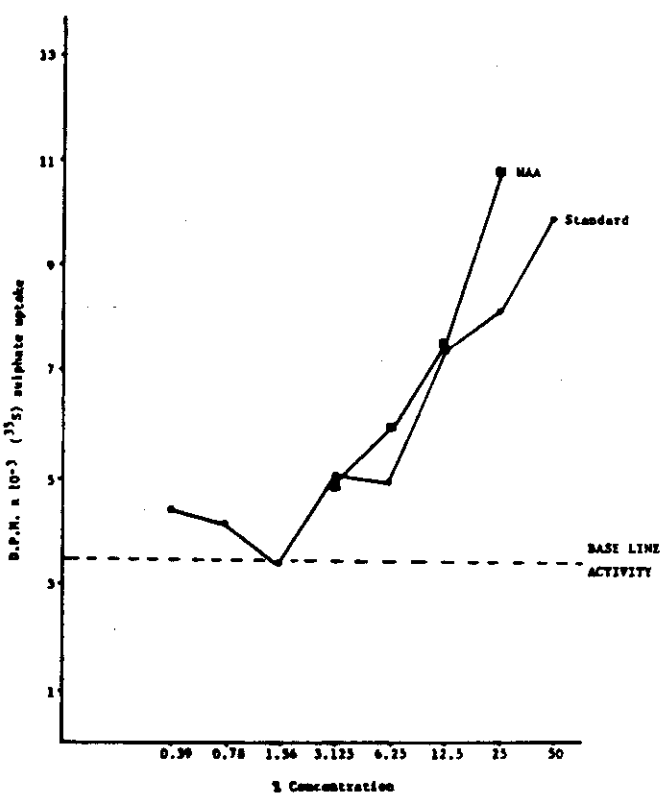


Figure 16 Dose response curve of a case of juvenile hypothyroidism with marginally low serum SM activity.

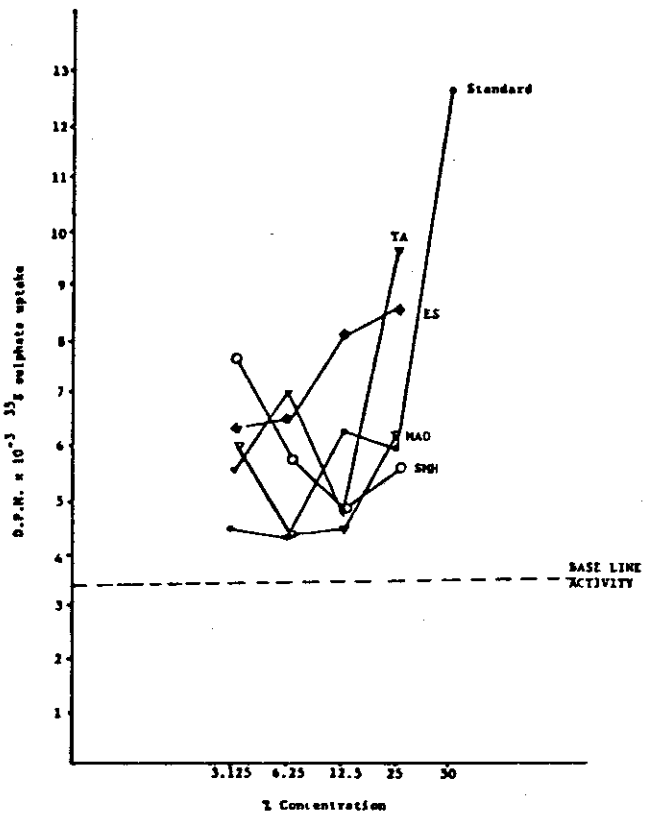


Figure 17 Dose response curves in cases with growth delay: case TA, a male case of the muscular variety of growth delay (normal SM activity), case MAD, a male of the lean variety (inhibitory activity) and case E^S, a female with growth delay. A male, SMH, with hypogonadism and receiving sex steroids (inhibitory SM activity).

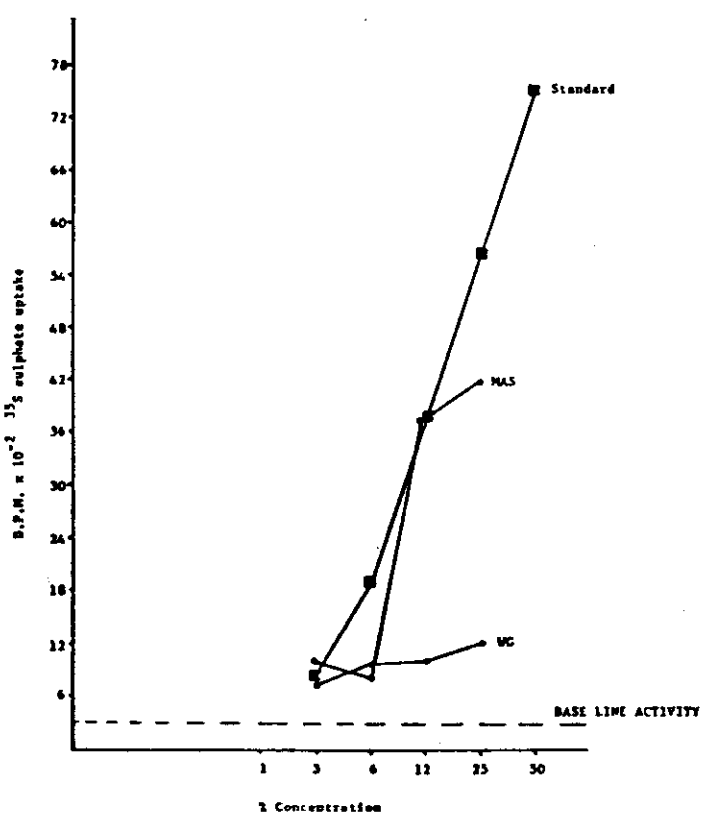


Figure 18 Showing the control cases that had normal SM activity (MAS) and those that had an inhibited SM activity (MG)

Figure 19 Characterization of the different patterns of response of GH during a combined ITT and TRH test

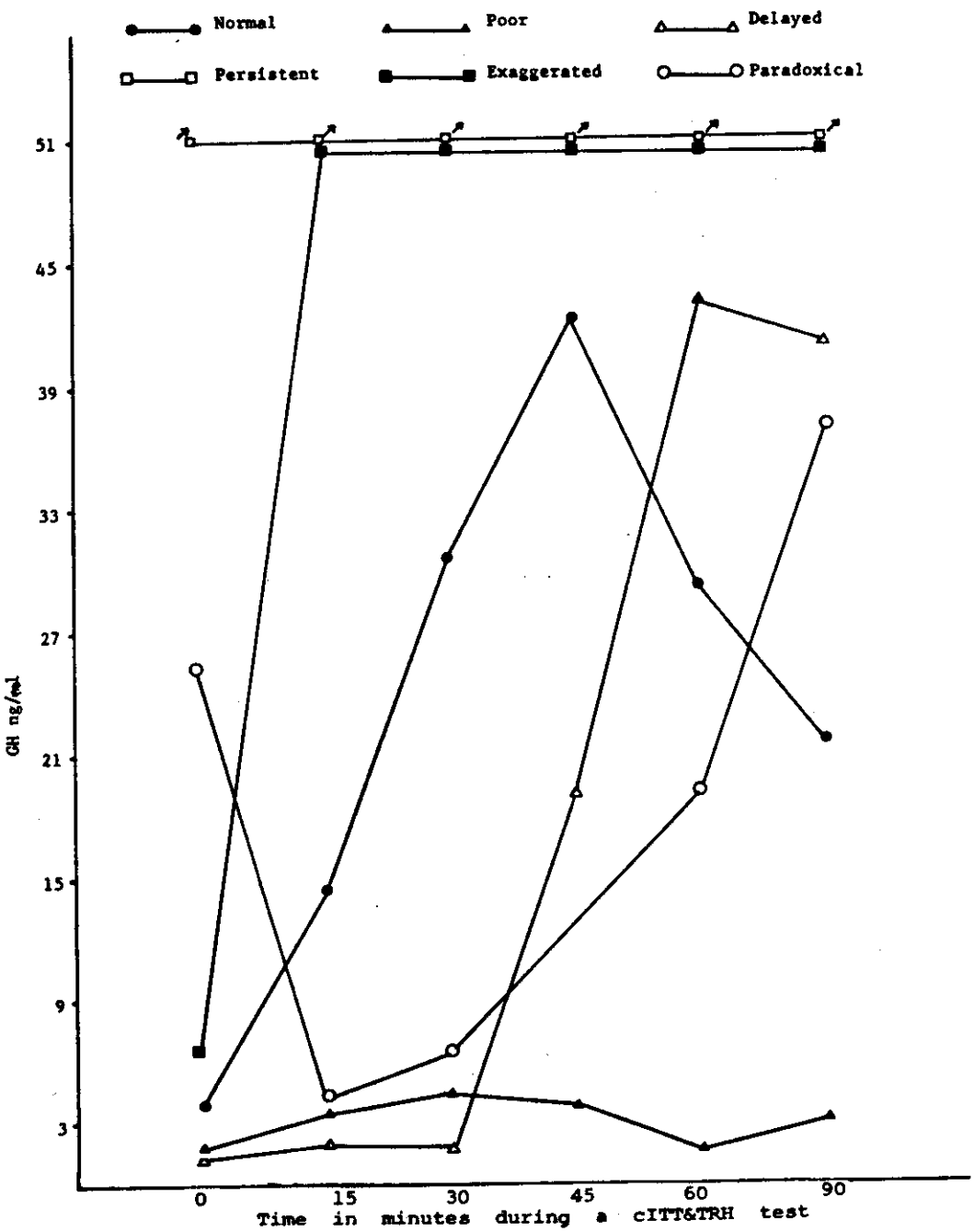


Figure 20 Patterns of response of TSH to TRH illiceted during a combined ITT and TRH stimulation test.

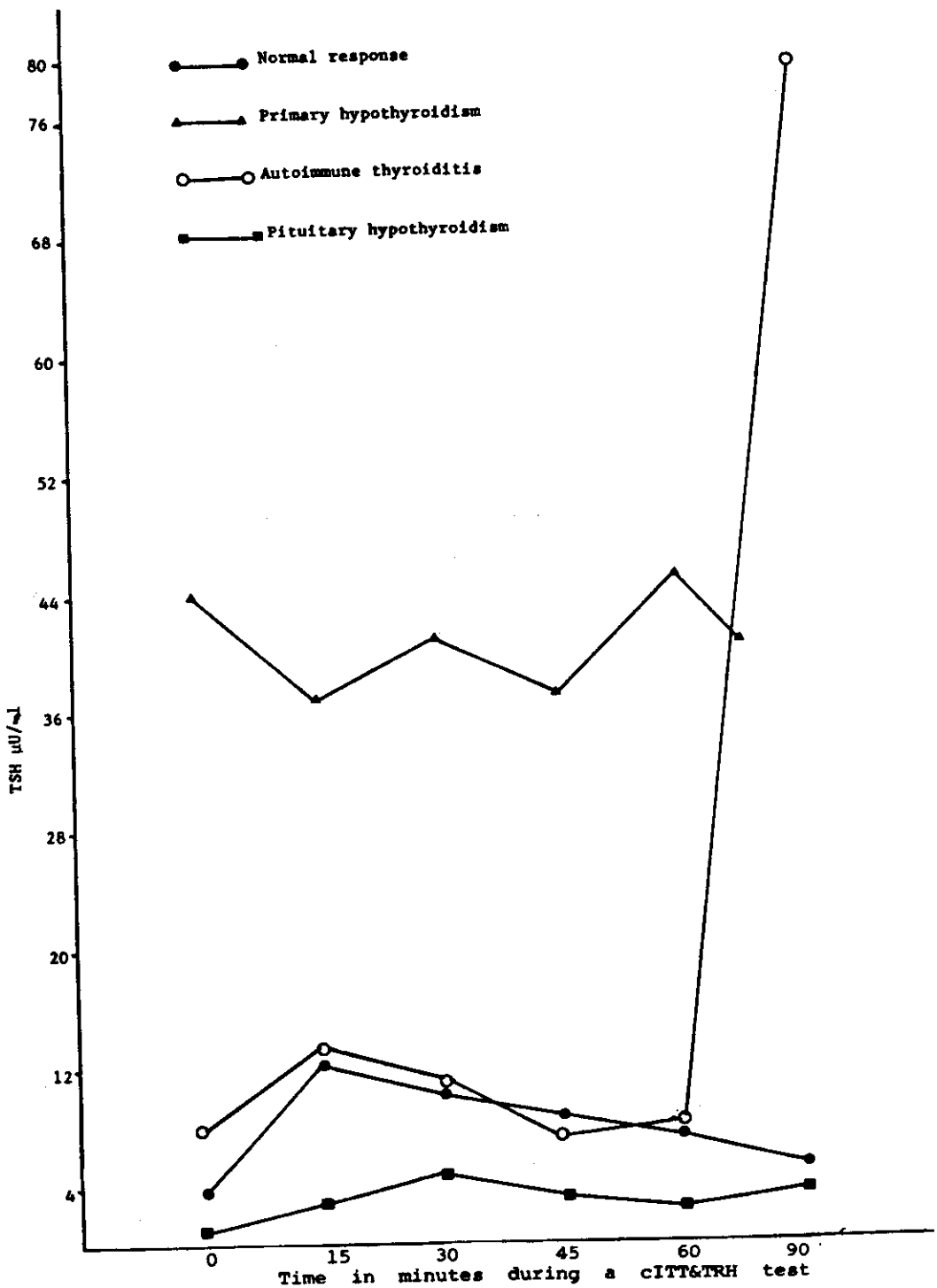
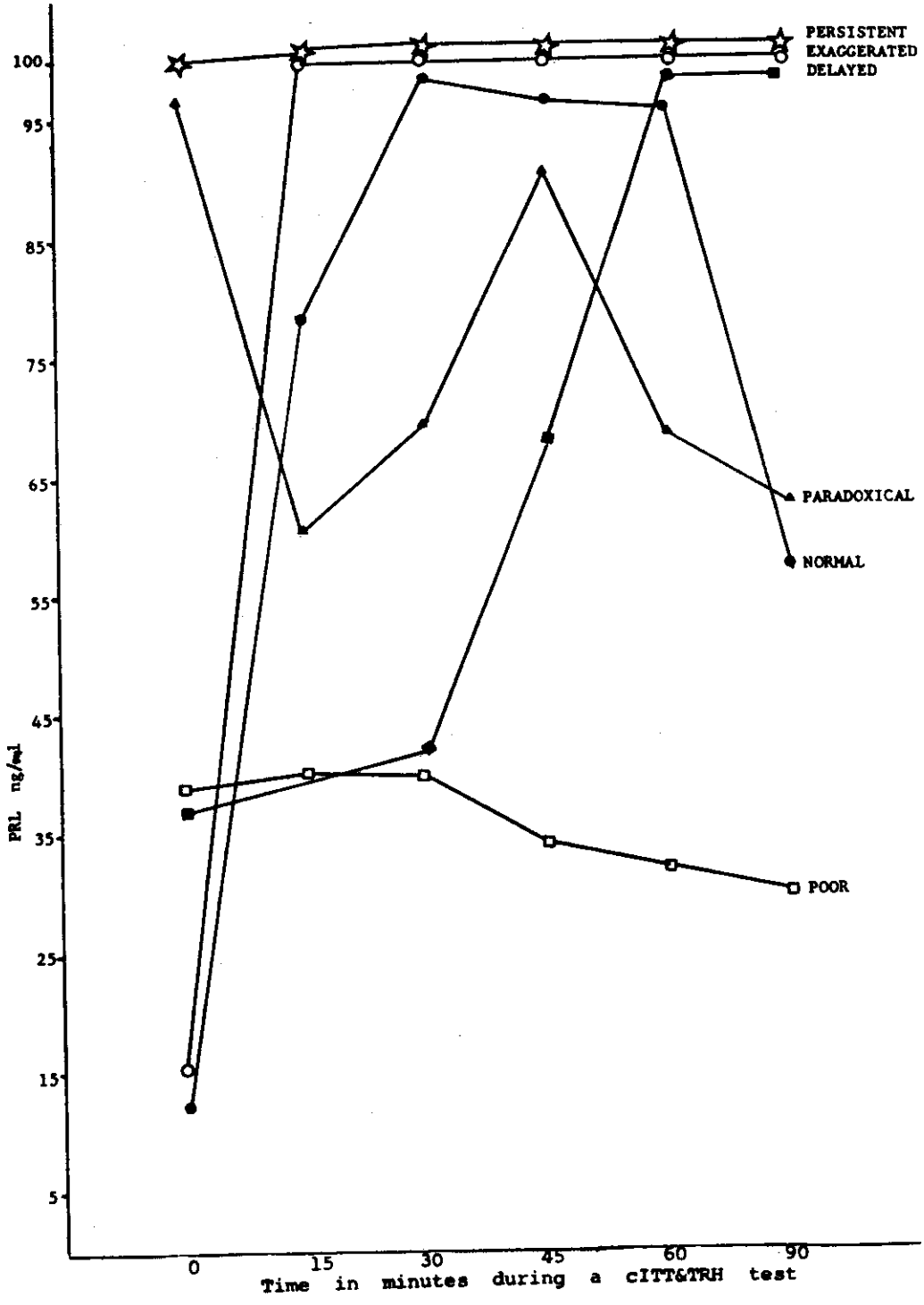


Figure 21 The different types of the patterns of response of PRL in a combined ITT and TRH stimulation test



ANALYSIS AND DISCUSSION OF RESULTS

The purpose of this work was to identify common endocrine causes of short stature which present with short stature as a sole clinical feature. This was done by investigating the hormonal secretory pattern in some apparently normal children and comparing them with the symptomatic cases. The hormones studied were the growth hormone (GH), thyroxine (T_4), thyroid stimulating hormone (TSH), prolactin (PRL) and somatomedin-C (SM-C). The GH and SM-C are known to have a direct effect on growth especially linear growth. The T_4 has pronounced effects on the maturational processes in the epiphysis. The study of the TSH and PRL was done to complete the investigation of the hypothalamo-pituitary thyroid axis and the pituitary function test respectively. Such a study enabled us to correlate clinical data and hormones with one another and with the final diagnosis of the clinical condition.

The introduction of the somatomedin concept, as a prominent growth factor affecting linear growth and being affected by growth hormone, and nutritional factors, almost equally, has attracted the attention of many workers. In this study the problem was an intriguing one to look into; knowing how much nutritional deficiencies and parasitic infestations affect our Egyptian children. The diagnosis of cases with marginal malnutrition is not easy and it is usually the long term effects of such states that cause us to face the problem cases such as growth delay and learning disorders as impairment of concentration, fatigue, general weakness and psycho-social problems. The combination of inadequate intake and gastrointestinal disorders play equally important roles in determining the degree of marginal malnutrition that interferes with the comsumption of the vital nutrient elements necessary for growth. The gastrointestinal disorders may not fall into well defined diagnostic categories such as coeliac disease and/or Crohn's disease but may be due to the more common parasitic infestations which are endemic in Egypt. Parasitic infestations include gardiasis, ascariasis, ancylostomiasis, Bilharziasis amaebiasis and others. They produce their effects by not only consuming part of the nutritional

intake of the child, but also by interfering with the absorption, hence creating a malabsorptive state in addition to causing the child to be anorexic, depressed and antisocial. It is not our aim in this study to detect, diagnose or discuss these cases but we hope to point out the importance of the early detection of these cases before presenting as problem cases of growth delay.

Our scheme for this discussion includes:-

I (1) The discussion of the various cases of short stature according to their clinical diagnosis including (a) the growth hormone deficiency (GHD) whether isolated (IGHD) or as a part of a multiple pituitary hormone deficiency (MPHD), (b) primary hypothyroidism whether acquired, congenital or autoimmune thyroiditis, (c) growth delay whether constitutional (or genetic or simple), or acquired and finally (d) short stature of miscellaneous causes.

(2) The analysis of the various auxological data from growth assessment of the patient and the hormonal studies of each group.

(3) The discussion and analysis of the cases from the aetiological point of view.

II The correlation of the hormones with one another by analysing the response of the hormones in the combined hypothalamo-pituitary function test in relation to the stimulus used in the test.

The discussion will be supported by statistical methods of analysis of data using tests of significance, analysis of variance, F-test and correlation coefficients.

Figure 22 Distribution of the cases of short stature under study according to their clinical diagnosis and sex (shaded areas = females, unshaded areas = males).