SUMMARY AND CONCLUSION

SUMMARY & CONCLUSION

This study consisted of 26 cases of children presenting with short stature and nine control cases from the D.E.M.P.O. Clinic in the Cairo University Children's Hospital. The following is a summary of its most prominent findings :-

1. Growth delay was the commonest cause of understature forming about 35% of the overall cases, 66.7% of whom were males and 33.3% were females. Fifty percent of the males in the study were growth delayed and only 20% of the females were so diagnosed.

2. Growth hormone deficiency (GHD) formed 19% of Egyptian children presenting with short stature in our clinic of whom 80% were males and 20% were females. Whereas 25% of the males in the study were GHD and only 10% of the females were GHD.

3. Juvenile primary hypothyroids formed about 12% of the cases and were all females.

4. The remainder of the cases comprising the miscellaneous group consisted of a Laron dwarf, an end organ unresponsiveness to somatomedin, a Mauriac syndrome, a Russell-Silver syndrome a query case of prolactin insufficiency, a hypogonadal short prepubertal boy and two cases with familial short stature with superimposed growth delay.

5. Stature was most severely affected in the Laron dwarf, being far below -4 SD from the mean (of French standards). Patients with GHD were 4 SD below the mean, patients with thyroid failure were 3 SD below the mean and those with growth delay ranged from -2 SD to -4 SD below the mean. So that the extent of height deficit correlated with the extent to which the hormone affected was involved in skeletal growth. This indicates that skeletal (linear) growth is primarily controlled by SM followed by GH and last but not least thyroid hormones. Growth delay, being due to the interaction of a multiplicity of factors including some transient hormonal disturbance and consisting of a heterogenous group of delayed children, showed this wide range in height deficit among the group.

6. Underweight was common in all the cases, mainly below the mean (mostly -3 SD). Skinfold thickness was normal in the GHD group, but markedly affected in the growth delayed one, reflecting probably the degree of malnutrition, and hence the role played by the latter in the

pathogenesis of growth delayed children.

7. The combination of estimation of SM activity together with a combined hypothalamo-pituitary function test (ITT + TRH) proved to be very successful in the diagnosis of our cases. The ITT test was simple and rapid to perform, required minimal personnel and minimal handling of the patients, and has minimal side-effects, was considerably cheap compared to other tests, and hence very convenient to use in developing countries such as Egypt.

8. Aetiologically; GHD was due to perinatal insult, idiopathic and/or hereditary. Hypothyroidism was due to late decompensation in a congenital disorder and autoimmune thyroiditis. Growth delay was due to a combination of hereditary, environmental and social factors. Malnutrition and parasitism played a major role in pathogenesis.

9. The growth delayed group fell into two well defined categories; a muscular variety in which hereditary factors predominated and a lean variety in which nutritional and parasitic factors played a major role. Growth delay was difficult to differentiate from conditions such as familial short stature, hypogonadism and cases with transient GHD.

10. We have described three peculiar cases of short stature:- The first was a GHD male Russell-Silver who did not respond to GH therapy, had a lean body appearance, was dysmorphic and cryptorchoid. The second was a male with slow growth in the first two years of life, no organic disorder and hypothalamo-pituitary function tests suggestive of diminished prolactin reserve. The third case was a female with dysmorphic features, infantile body proportions, stunted growth and high bioassayable SM activity and very much resembling a case described by Lanes et al (1980). The defect being probably due to a cellular insensitivity to somatomedin.

11. We have also detected two cases with an enlarged sella turcica. The first case was a juvenile hypothyroid and the second was a Loron dwarf. The enlarged sella was due to hyperplasia of the cells secreting thyrotropin - in the first case - and to GH - in the second case - secondary to thyroxine and somatomedin deficiency respectively.

The second part of the study consisted of analysing hormonal interrelationships. Positive conclusive data included briefly the following:

1. Peak responses of growth hormone (GH) were higher in girls than boys in the pubertal age period.
2. The peak response and the degree of response of GH to insulin induced hypoglycaemia was the same in the late childhood and pubertal age periods and double that seen in early childhood.
3. Very high peak GH responses were observed in some patients of the lean variety of growth delay indicating some type of peripheral resistance to GH. Partial GH responses were present in patients of the muscular variety of growth delay indicating a transient type of GHD in these children.
4. Somatomedin (SM) activity was observed to increase with age in the male control group of this study.
5. Bioassayable SM activity measurement in the growth delayed group gave a wide range of values varying from marked inhibition (<0.1 units/ml) to values of 1.8 units/ml, giving a fair idea of the state of the growth conditions in the child at that particular time. SM activity gave a flat response in the prepubertal GHD patients and a marginally low SM activity in one of the hypothyroid patients.
6. There was a significant correlation between the basal SM activity and the degree of response of GH during an ITT that increased with age in the cases of the study as a whole.
7. Patients with GHD and hypothyroidism showed a significant correlation between the degree of GH response in an ITT and the basal SM activity. Patients with hypothyroidism also showed a significant correlation between their basal SM activity and peak GH response during an ITT. The correlation coefficient was high in patients with hypothyroidism indicating that SM deficiency in these patients is related mainly to the secretory status of GH in this disease While in patients with GHD, SM activity is under the net control of other hormones, especially that thyroid hormones are secreted normally in these patients.
8. In the growth delay group the disruption of the normally present correlation between basal SM activity and the degree of response of GH to ITT indicates a disturbance in growth in these patients and may be a diagnostic feature for this condition.
9. Basal and peak TSH levels decreased with age in the cases of the study as a whole. On analysing the sex differences during puberty,

males showed the progressive decline in the basal and peak levels, while in females the degree of response of TSH to TRH was significantly higher in girls in puberty than in boys of the same age group. Also there was a highly significant correlation between the basal and peak TSH values that increased with age. Furthermore it was the female sex that evidenced this correlation, males showed a weaker correlation only at puberty. Basal and peak responses of TSH were negatively correlated with the basal levels of thyroxine only in females prepubertally. From the study of basal, peak and degree of responses of TSH to TRH and basal T_4 in hypothyroid patients, it was deduced that the most useful diagnostic tool in detecting hypothyroid patients is the basal TSH levels.

10. Under physiological states there is no evident correlation between basal GH, TSH and T_4 in relation to age and sex. In hypothyroidism GH peak levels were reduced. On the other hand thyroid function in patients with GHD is not entirely normal.
11. The type of prolactin secretory response during the combined ITT and TRH test was analysed and correlated with other hormones, the following was observed:-

The PRL responses to the TRH+ ITT test observed fell into six distinct patterns, namely, the normal, the persistently elevated, the exaggerated, the delayed and the poor responses. On analysing the responses in relation to age, sex and in relation to other hormones the following was observed:-

1. There were no sex differences in the PRL responses which tended to be increasingly 'normal" with age.
2. Lowered, absent or inhibited SM activity was associated with raised or normal PRL responses, indicative of some positive interrelation, whether direct or indirect, between both hormones.
3. High PRL responses were a common finding in cases with poor GH response but not vice versa. While a poor PRL response was not affected or associated with the abnormal GH response and was found to be an independent finding. It was also common to find delayed responses of PRL when the GH response was delayed but not vice versa.

It was concluded that the high PRL response in the cases with poor GH response may enable us to differentiate between isolated GHD of pituitary origin and that of hypothalamic origin, as PRL responses will be raised in the former not in the latter. Also that isolated PRL deficiency is a primary condition independent of other pituitary hormones and should be taken into account when diagnosing multiple pituitary hormone deficiency. Finally that the delayed responses of PRL in a TRH + ITT test are due to the response of PRL to hypoglycaemia and is usually higher because of the priming effect the TRH has on the PRL secreting cells.

4. Persistently elevated PRL responses were characteristic to hypothyroidism whether primary, secondary or tertiary, probably related to the modality in which TRH is secreted. Hence PRL and TSH are regulated independently from one another.

Last but not least, by analysing our control group and comparing it with our delay group we were able to identify a new entity of delay, namely, the marginal growth delay, which have some endocrine features in common with the delay group but are clinically normal.