HEALTH SCIENCES DIVISION

GROWTH HORMONE ADMINISTRATION IN CHILDREN WITH GROWTH HORMONE DEFICIENCY: A COMPARISON OF VARIOUS TREATMENT REGIMES*

CARMELITA FAGELA-DOMINGO, LORNA RAMOS-ABAD SIOKSOAN CHAN-CUA, and SYLVIA CAPISTRANO - ESTRADA

Department of Pediatrics, College of Medicine
University of the Philippines Manila – Philippine General Hospital
Ermita, 1000 Manila

Advances in research have made possible the production of biosynthetic human growth hormone in sufficient quantities. However, optimal treatment regimens for growth hormone deficiency have not yet been standardized. Differences in dosage, routes and timing of administration, and duration of treatment are of paramount importance. This study was undertaken primarily to determine whether growth hormone given alone continuously or intermittently over short periods of time will result in height increases and whether doses smaller than those recommended will result in comparable increases in height.

Twenty seven prepubertal patients with significant growth hormone deficiency as established by two consecutive stimulation tests using Clonidine, L-Dopa, and insulin induced-hypoglycemia were included in the study. Subjects were randomly assigned to four treatment regimens using biosynthetic human growth hormone daily six times a week via subcutaneous route. Group A received 0.07 IU/kg daily for 3 months, then discontinued for the next three months, after which treatment was resumed for another 3 months to complete 6 months of treatment. Group B received 0.07 IU/kg daily for 6 months. Group C received 0.035 IU/kg daily for 12 months. Group D received 0.07 IU/kg daily for 12 months.

At the end of the study, nineteen boys and six girls were evaluable. Mean chronologic age range from 9.86-12.74 years while mean bone age range from 5.79-7.43 years. Using analysis of covariance, there were no differences in the treatment effects between Groups A and B and between Groups C and D. Four patients

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developed hypothyroidism and one had transient edema. Eleven patients had elevated alkaline phosphatase after several months of treatment which subsequently reverted to normal.

This study demonstrates that all growth hormone deficient children respond positively to biosynthetic human growth hormone. There is no advantage in administering it intermittently. Small doses of growth hormone may result in growth increments which do not produce significant side effects.

MICROCULTURE TETRAZOLIUM ASSAY FOR IN VITRO CYTOTOXICITY TESTING OF RING STAGES OF *Plasmodium falciparum*

J. ENRICO H. LAZARO
Marine Natural Products Group, Marine Biochemistry and Toxinology Laboratory
Marine Science Institute, College of Science
University of the Philippines Diliman
1101 Quezon City

The microculture tetrazolium assay using MTT (3-(4,5-dimethylthiazol-2-yl)2,5-diphenyltetrazolium bromide) was optimized and applied to determine the IC_{50} (50% inhibitory concentration) of chloroquine, quinine, artemisinin, hydroxynapthoquinone, and sixteen sponge extracts compared to the tritiated hypoxanthine assay using a *Plasmodium falciparum* in vitro culture system. The MTT assay was also compared to a previously optimized method, the NBT (2, 2'-di-*p*-nitrophenyl-5,5'-diphenyl-3,3' (3,3'-dimethoxy-4,4'diphenylene)-ditetrazolium chloride) assay proposed by Makler et al. (1993). In general, the results show that the three assays generate comparative results.

Two other vital stains which have not yet been applied to *P. falciparum* were tried. These were Alamar Blue and XTT (2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-5[(phenylamino) carbonyl]-2H-tetrazolium hydroxide). Neither was able to differentiate parasitised and non-parasitised erythrocytes.

The results of this study suggest that the MTT method may be used as a screening alternate to the tritiated hypoxanthine assay. Used in parallel to screen for in vitro activity in 16 sponge extracts, both assays identified the same sponge as a source of a potential antimalarial drug.

THE CLITORAL INDEX: A DETERMINATION OF CLITORAL SIZE IN FULL TERM INFANTS

JOSEPH C. PUA, SIOKSOAN CHAN-CUA, CAROL TEODORO, and VIRGINIA CRISOSTOMO
Department of Pediatrics, College of Medicine
University of the Philippines Manila - Philippine General Hospital
Ermita, 1000 Manila

Although examination of genitalia is an important part of newborn evaluation, few data are available regarding normal newborn clitoral length and width. Therefore, clitoral measurements were taken in three hundred sixty four full term female infants with a mean maternal age of 26.025±0.3 (±SEM), mean birthweight 2952 grams ±16.42 (range 2500-3600), and mean birthlength 48.036 cm ±0.11 (range 45-50 cm). Two hundred eighty five infants (78.30%) were born by vertex vaginal delivery and 79 (21.70%) by caesarian section. No pregnancies were complicated by drug use or maternal illness. Using a plastic ruler calibrated in millimeters, the clitoral length and width were measured twice by a single examiner and a third measurement by the use of calipers, to produce intraobserver reliability and reproductibility. Twenty percent of the total population were again measured by a second examiner for interobserver reliability. The lower limit of measurement was 3 mm. The mean clitoral length measured 5.049 ±0.046 mm (±SEM) and width measured 3.077 ±SEM). The clitoral index among full term infants is 15.84 ±0.457 mm. Therefore, clitoral index measurement is a simple, easy, and economical method and must be part of a general physical examination.

ANOGENITAL RATIO: A CLINICAL ASSESSMENT TOOL FOR THE DIAGNOSIS OF VIRILIZATION IN FULL TERM INFANTS

JOSEPH C. PUA, CARMELITA FAGELA-DOMINGO, CAROL TEODORO, and VIRGINIA CRISOSTOMO
Department of Pediatrics, College of Medicine
University of the Philippines Manila – Philippine General Hospital
Ermita, 1000 Manila

Deviations in normal anatomy, pattern of growth, and abnormal sexual development are frequent reasons for suspecting endocrine disorders in pediatric patients. The clinical recognition of virilized genitalia manifested as labioscrotal fusion and clitoral hypertrophy warrants further evaluation since clitoral size is fully

developed by the twenty-seventh week of gestation. Androgen induced labioscrotal fusion results in an increase in anogenital distance.

It is therefore the purpose of this paper to provide normative data among full term neonates. Three hundred sixty four full term infants of 37-42 weeks gestational age were included in the study. No pregnancies were complicated by drug use or maternal illness. Anogenital distance determined were (1) Anus to fourchette (AF)-loser segment, (2) Anus to the base of clitoris (AC), and (3) Fourchette to the base of clitoris (FC)-upper segment. Using a caliper, the distances were measured in millimeters, twice by a single examiner. Twenty percent of the total population were measured by another author for interobserver reliability. The lower limit of measurement was 23 mm. The mean AF measured 24.59 mm ±0.002 while mean AC measured 51.33 mm ±0.0197, and mean FC measured 24 mm ±0.002. From these measurements, the FC/AC and AF/AC ratios were calculated to establish the relative length of each component distance. The ratio is 0.49-0.50 in the normal full term infants. AF is one-half of the total distance from anus to clitoris. If the ratio is greater than 0.50, it exceeds the 95% confidence limit for normal values and requires further endocrine evaluation.

ANTI-TB ACTIVITY OF SOME PHILIPPINE SPONGES USING DIFFERENT SCREENING ASSAYS

MELIZA T. TALAUE[1], SCOTT G. FRANZBLAU[2], GISELLE P. CONCEPCION[1] and GINA CARAAN-MANGALINDAN[1]

[1]Marine Science Institute, College of Science
University of the Philippines Diliman
1101 Quezon City

[2]Laboratory Research Branch, GWL Hansen's Disease Center,
Louisiana State University

Tuberculosis, magnified by the increasing incidence of TB with HIV infection and the emergency of multi-drug resistant strains, continues to be the world's leading cause of death from one infectious agent. The Philippines' diverse marine resources are a potential source of anti-TB compounds that can be screened by rapid, sensitive, and inexpensive anti-mycobacterial assays.

In this study, crude MeOH extracts of 53 Philippine sponges were assayed for anti-tuberculosis activity using BACTEC, agar dilution, disk diffusion, and Alamar Blue assays. In the BACTEC assay, three extracts were found to be active against the virulent strain of *Mycobacterium tuberculosis* (H37Rv) with a minimum inhibitory concentration (MIC) range of <15.62-3.25 μg/mL, and two were active against *M.*

avium (% inhibition 74.99 at 40 µg/mL). In the agar dilution assay, 11 extracts were active against H37Ra, an avirulent strain of *M. tuberculosis* with a MIC range of <15.62-250 µg/mL. In addition, tests using faster growing organisms such as *M. flavescens* and BCG yielded zones of inhibition measuring 5-15 mm. The results of the Alamar Blue assay of samples that demonstrated activity against H37Ra in the agar dilution assay indicated MICs that deviated ±1 dilution from those obtained from the agar dilution assay.

The results of these assays suggest that of H37Ra can be used as an alternative inoculum whose sensitivity is comparable to that of H37Rv. Also, Alamar Blue assay, being less expensive than BACTEC and more rapid and sensitive than both agar dilution and disk diffusion assays, can be used as a reliable primary screening assay for anti-tuberculosis activity.