

THE PLASMA LEVELS OF DEHYDROEPIANDROSTERONE SULPHATE, ANDROSTERONE SULPHATE, CORTISOL AND TRANSCORTIN IN CHINESE, INDIAN AND MALAY MALES

By D. Y. Wang, R. D. Bulbrook and K. Shanmugaratnam

In previous publications (1, 4, 15, 16) we have suggested that endocrine abnormalities may be implicated in the aetiology of cancer of the nasopharynx in African men.

The Chinese have the highest world incidence of nasopharyngeal cancer (12, 13). The incidence in Malays, despite gross under-reporting, is also significantly high. The Indians, however, have a low risk, the incidence of this cancer being no higher than in Western populations. In view of certain genetic similarities between the Chinese and the Malays and the fact that it is difficult to conceive of any environmental factor that is shared by these groups but not the Indians in Singapore, genetic factors would appear to be of greater aetiological significance. If genetically-determined endocrine abnormalities are important in the genesis of nasopharyngeal cancer, it might be expected that there would be patent differences in endocrine status between the Chinese and the Malays on the one hand and the Indians on the other.

This paper reports an investigation of the levels of plasma dehydroepiandrosterone sulphate (DS), androsterone sulphate (AS), cortisol and transcortin in Chinese, Indian and Malay men in Singapore.

METHODS

- (a) *Chemicals*: All reagents were of analytical quality and solvents were redistilled before use. Sephadex LH20 was obtained from Pharmacia Ltd. Cortisol-4- C^{14} (20mc/mM), cortisol-1,2- 3H (2000mC/mM) and acetic anhydride- 3H (100mC/mM) were purchased from The Radiochemical Centre, Amersham.
- (b) *Subjects*: Plasma was obtained between 8.30 a.m. and 11.30 a.m. from males resident in Singapore. Most of the subjects were ostensibly normal healthy medical students, laboratory workers or blood donors. The remainder were hospitalized subjects from

an orthopaedic ward. Of the normal subjects studied there were 20 Chinese (age range 20-41 years), 18 Indians (age range 22-41 years) and 18 Malays (age range 20-42 years). The orthopaedic patients were 7 Chinese (age range 36-61 years), 4 Indians (age range 37-50 years) and 2 Malays (ages 45 and 48 years). The patients with nasopharyngeal cancer were 4 Chinese, ages 49, 54, 58 and 56 years.

Heparin was used as an anti-coagulant. Plasma was stored at -70° . The plasma samples were packed with solid carbon dioxide, flown to London and stored again at -20° until assayed.

- (c) *Determination of plasma AS and DS*: The levels of AS and DS in plasma was determined by the gas-liquid chromatographic method of Wang, Bulbrook, Thomas & Friedman (17), with the modification that celite partition chromatography was replaced by chromatography on Sephadex LH20 (14).
- (d) *Determination of plasma cortisol*: The plasma levels of cortisol were determined using the double-isotope technique described by James & Fraser (10). C^{14} Cortisol was used to measure recovery and H^3 —acetic anhydride was used for acetylation.
- (e) *Transcortin levels*: The percentage of cortisol bound to plasma proteins was determined by equilibrium dialysis. This involved the dialysis of 8 ml. of isotonic saline against 1 ml. of diluted plasma (1:4 v/v of plasma and isotonic saline) at $37^{\circ}C$. (18)

RESULTS

- (a) *Normal Subjects*: The plasma AS, DS, cortisol and transcortin levels in normal Chinese Indian and Malay men are shown, plotted against age, in Figures 1 to 4. There are no differences between the levels of these parameters in the three races. There was no correlation between any of these steroid

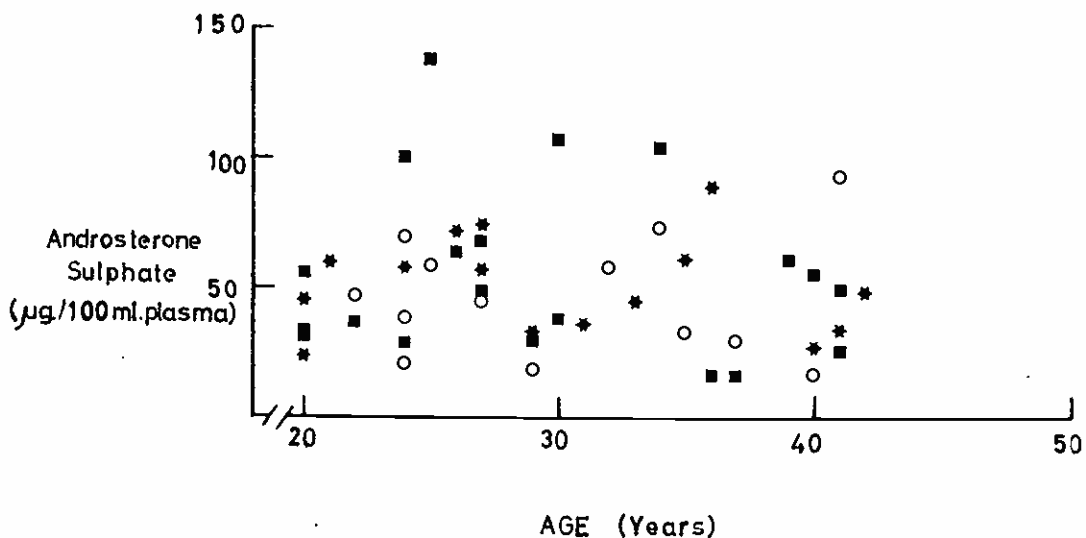


Fig. 1. Plasma level of androsterone sulphate against age. The amount of androsterone sulphate is expressed as androsterone.
 ■ = Chinese ○ = Indian * = Malay

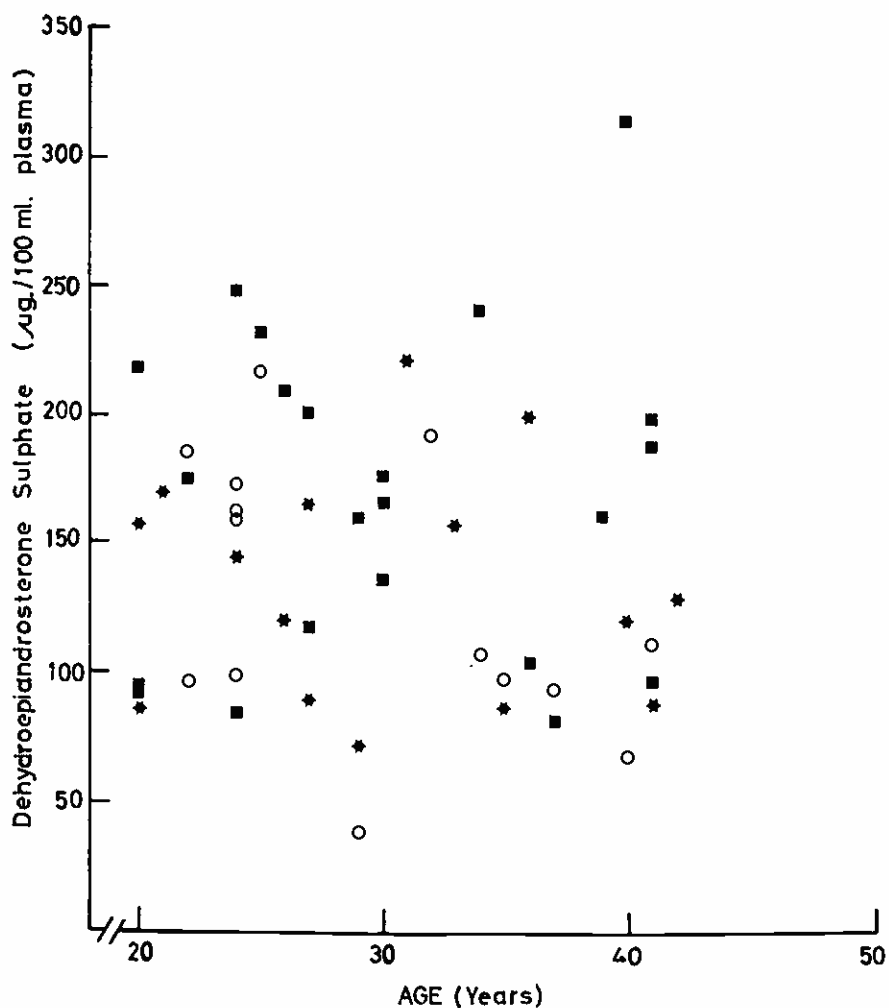


Fig. 2. Plasma level of dehydroepiandrosterone against age. The amount of dehydroepiandrosterone sulphate is expressed as dehydroepiandrosterone.
 ■ = Chinese ○ = Indian * = Malay

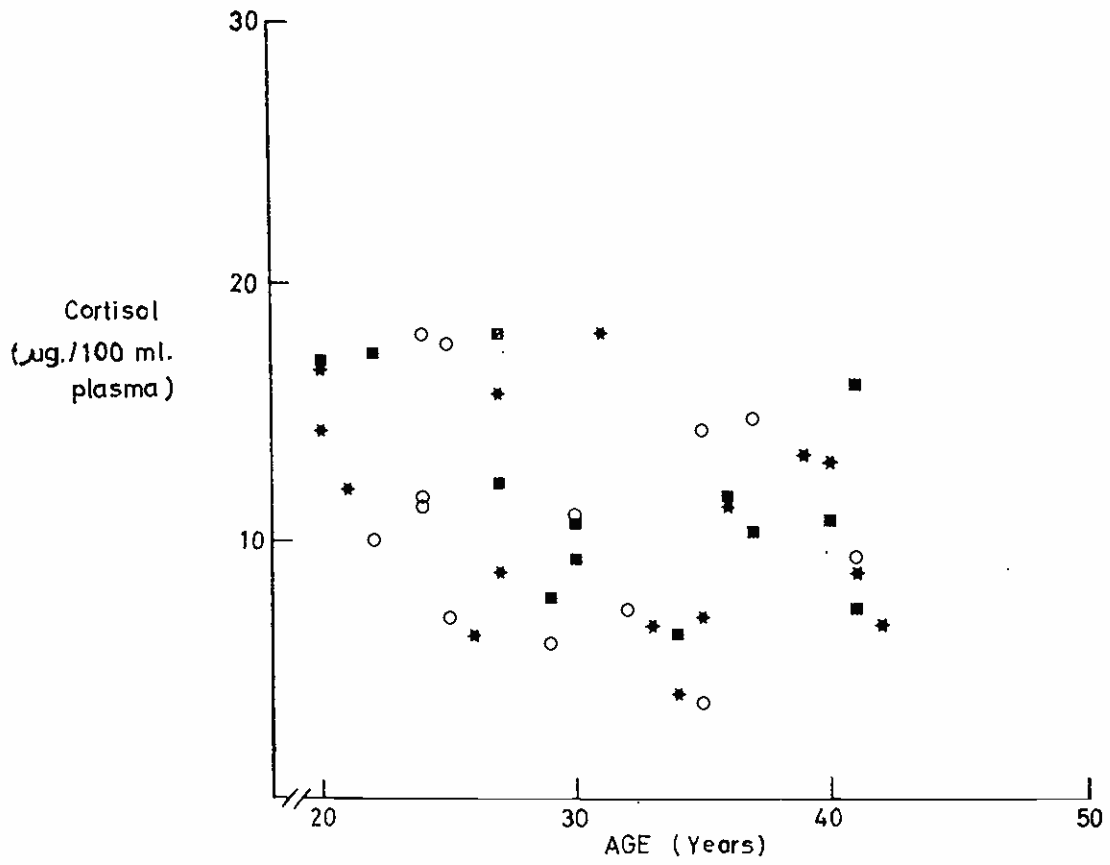


Fig. 3. Plasma level of cortisol against age.
 ■ = Chinese ○ = Indian * = Malay

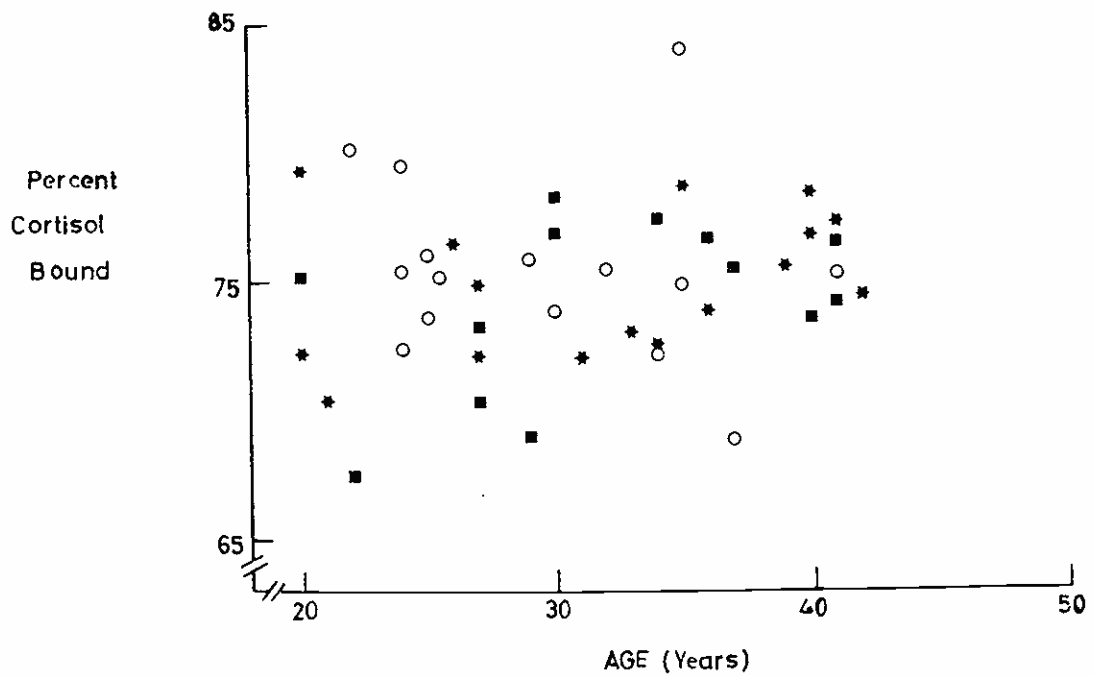


Fig. 4. The percentage of cortisol bound to plasma against age.
 ■ = Chinese ○ = Indian * = Malay

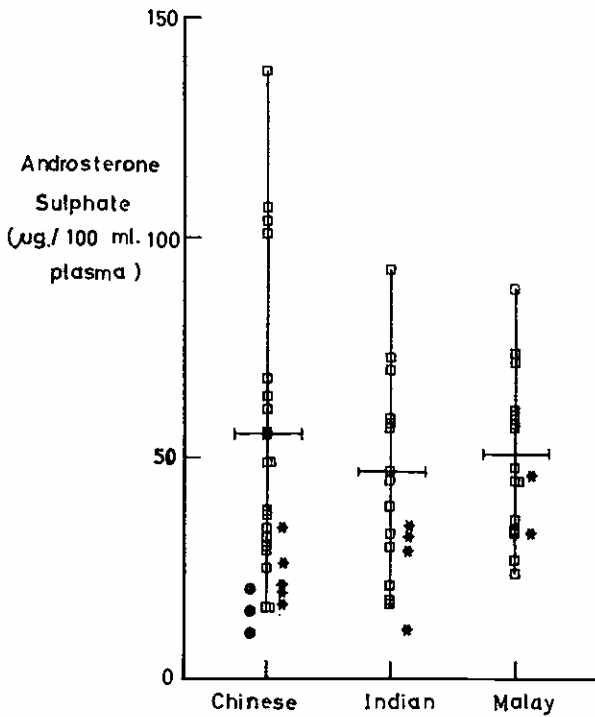


Fig. 5. Comparison of plasma levels of androsterone sulphate of Chinese, Indians and Malays. The amount of androsterone sulphate is expressed as androsterone.

□ = Normal ● = Nasopharyngeal cancer
★ = Orthopaedic patient

The mean age of the normal Chinese, Indian and Malay males was 29.6, 29.9 and 30.1 years, respectively.

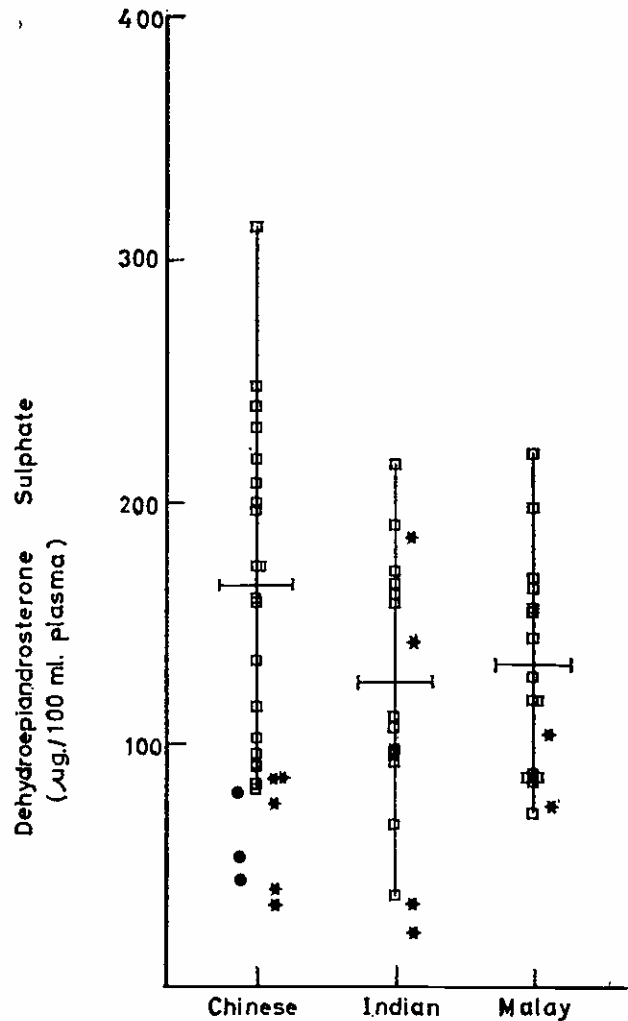


Fig. 6. Comparison of plasma levels of dehydroepiandrosterone sulphate of Chinese, Indians and Malays. The amount of dehydroepiandrosterone sulphate is expressed as dehydroepiandrosterone.

□ = Normal ● = Nasopharyngeal cancer
★ = Orthopaedic patient

The mean age of the normal Chinese, Indian and Malay males was 29.6, 29.9 and 30.1 years, respectively.

parameters and age, although the age range studied was limited to 20-40.

(b) *Hospitalized Subjects:* The levels of plasma AS, DS, cortisol and transcortin for hospitalized subjects and patients with nasopharyngeal cancer are shown in Figures 5 to 8. Age has not been taken into account since no correlation was found between the steroid levels and age. However, some caution is necessary since the mean age of the hospitalized and nasopharyngeal cancer patients was about 45 years, compared with 30 years for the normal subjects. The hospitalized group appears to have less AS and DS in their plasma than normal subjects. The four cancer patients studied also appear to have low plasma AS and DS and high cortisol levels.

DISCUSSION

The population of Singapore offers epidemiological advantages in a study of possible hormonal influences on the incidence of cancer of the nasopharynx. Since Chinese and Malay men have a predisposition towards this form of cancer which Indian men do not, it was of interest to measure some aspects of the endocrine environment in the three racial groups.

Our present results show that the levels of AS, DS, cortisol and the degree of plasma cortisol binding are the same in the racial groups studied. This is in contrast to earlier findings that both urinary and plasma oxosteroids in Kenyan Africans were generally lower than in British males (1, 4, 15, 16).

It follows, therefore, that the hypothesis that an abnormal steroid environment in a

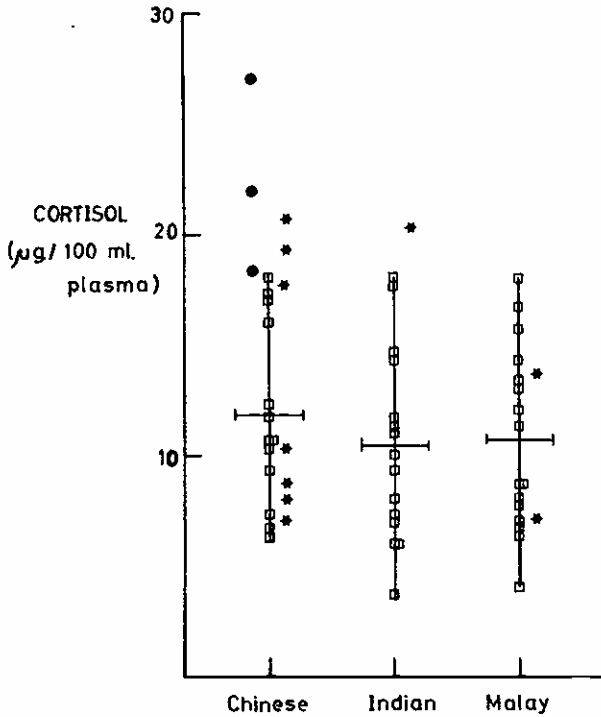


Fig. 7. Comparison of plasma levels of cortisol of Chinese, Indians and Malays.

□ = Normal ● = Nasopharyngeal cancer
★ = Orthopaedic patient

The mean age of the normal Chinese, Indian and Malay males was 31.8, 30.5 and 32.0 years, respectively.

particular population (as evidenced by low levels of plasma androgens) is a necessary factor in the genesis of nasopharyngeal cancer is untenable. African men in general show such an abnormality when compared with a population (British) in whom the incidence of the disease is lower. Chinese men do not, in that they have similar plasma levels to Indians in spite of a 20 fold higher incidence in the former population. In other words, plasma androgen levels may be identical in low and high-risk populations. Some further investigation of this point may be desirable. Steroid values in normal populations show a great deal of variability between subjects and the 95% limits may be very large (2, 3, 5-11, 14). It may be that the variability of steroid levels in normal Chinese males is greater than in Indians or Malays and that some very high or very low values may be found in the Chinese. It then might follow that the high-risk group in the Chinese population would be those at the ex-

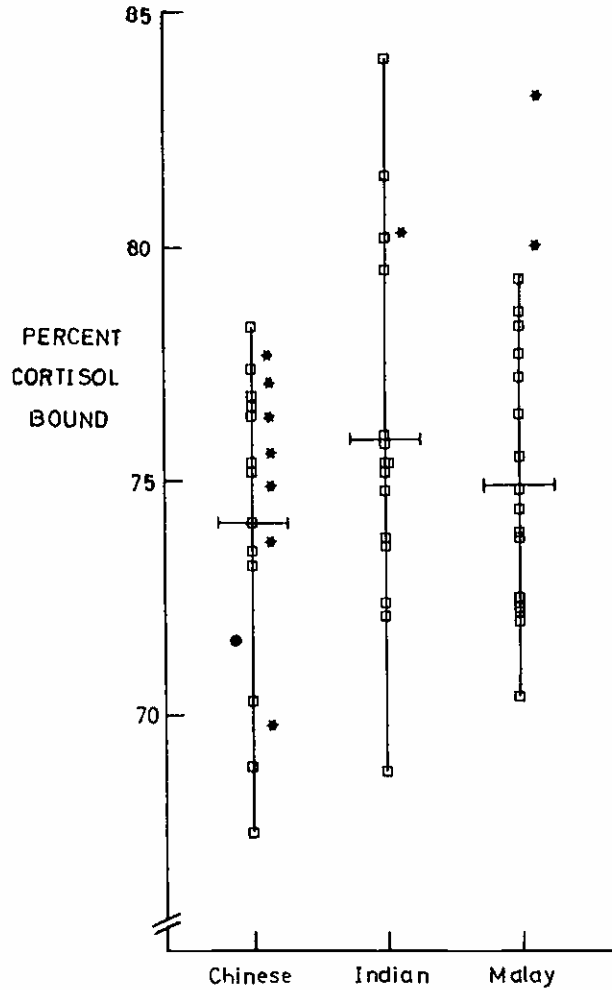


Fig. 8. Comparison of transcortin binding of Chinese, Indians and Malays.

□ = Normal ● = Nasopharyngeal cancer
★ = Orthopaedic patient

The mean age of the normal Chinese, Indian and Malay males was 31.8, 30.5 and 32.0 years, respectively.

treme lower end of the normal distribution. The data in Figures 5 and 6 indicate that this possibility is extremely unlikely. Some of the lowest values were found in Indians, in whom nasopharyngeal cancer is rare.

There is now the question of the hormonal status of patients with established nasopharyngeal cancer. Only four Chinese patients are included in this study and they are characterized by low androgen and high corticoid levels. The low androgen levels also occur in patients hospitalized for orthopaedic reasons and much more work is necessary to see whether the nasopharyngeal group are significantly lower than this particular control group. Nevertheless, the present results are in agreement with previous findings of low levels of plasma AS and DS in patients with nasopharyngeal cancer. It remains to be determined whether this abnormality is caused by or precedes the disease.

Bulbrook & Hayward (3) have postulated that hormonal abnormalities preceding the clinical appearance of breast cancer may be multidirectional and it will be necessary to investigate other hormonal factors in the racial groups in Singapore before rejecting the concept that the hormonal environment plays a part in the aetiology of nasopharyngeal cancer.

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