ORAL PRECANCEROUS CONDITIONS IN PENINSULAR MALAYSIA*

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INTRODUCTION

SOUTH-EAST ASIA has the highest frequency of oral carcinoma in the world because of the popularity of oral habits such as betel-quid chewing, smoking and the drinking of alcohol. Although the mouth is easily accessible for direct and detailed clinical examination and changes in the colour and or texture of the oral mucosa can be clinically and histologically diagnosed as precancerous conditions, nevertheless it is regrettable to note most of our oral cancer patients seek treatment at a very late stage. The size of the oral cancer and cervical lymph node metastasis at the time of diagnosis and treatment are two important factors that determine the long-term survival of oral cancer patients.

There is a high frequency of correlation of precancerous conditions with oral carcinoma. Ramanathan *et al.* (1975) in a study of 75 oral cancer patients reported that leukoplakia was present in 61% of Indian males, 47% of Indian females, 44% of the other males and 25% of the other females. Submucous fibrosis occurred exclusively in Indians in the above quoted study. It was reported in 32% of the Indian males and in 10% of the Indian females.

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* This paper was presented in the symposium on "DIAGNOSIS AND TREATMENT OF ORAL CARCINOMA" of the Plastic Surgery Section of the 51st General Scientific Meeting of the Royal Australian College of Surgeons and held in Kuala Lumpur on 10th May, 1978.

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Cancer prevention is better than cancer treatment. Oral carcinoma in a vast majority of patients is preventable (Ramanathan, 1977). The World Health Organization Expert Committee for the Histopathological Nomenclature and Classification of Oral Precancerous Consitions has spelt out histological gradings which will allow for the prompt treatment of oral precancerous conditions at the earliest phase of epithelial dysplasia. A programme aiming to diagnose oral precancerous conditions promptly and to treat them even before they develop into carcinoma can be regarded as a cancer prevention scheme. This plan can be regarded as a health programme of national importance if it could be extended to cover our entire population. As a first step towards this objective a National Registry of Oral Precancerous Conditions was established in December 1974 by a National Council and whose chairman is Dr. Abdul Rahman bin Awang, the Director of Dental Services of Malaysia.

MATERIAL AND METHODS

This study was based on the records of the National Registry of Oral Precancerous Conditions and maintained by the Department of Stomatology, Institute for Medical Research, Kuala Lumpur. The period covered was from 1st April 1967 up to 31st October 1977. All patients diagnosed with (1) homogeneous leukoplakia (Fig. 1); (2) speckled leukoplakia (Fig. 2); (3) lichen planus; (4) submucous fibrosis (Fig. 3 and 4); (5) erythroplakia (Fig. 2) and (6) smoker's keratosis and with or without biopsies were registered in the National Registry. The definitions of the above mentioned oral precancerous conditions have been given elsewhere (Ramanathan *et al.*, 1973). They conform with the definitions outlined by the WHO Expert Committee on Oral Precancerous Conditions.

Where biopsies were available the premalignancy index (PMI) scores adopted by the WHO Expert Committee on Oral Precancerous Conditions were applied. The PMI scores are divided

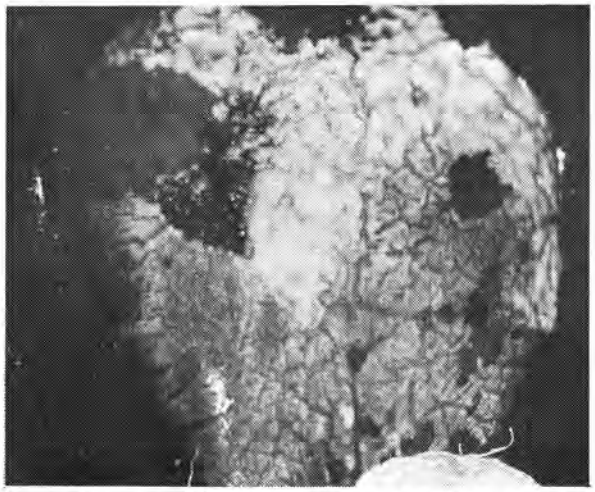

Fig. 1. Shows a homogeneous leukoplakia of the tongue having a uniform white appearance.

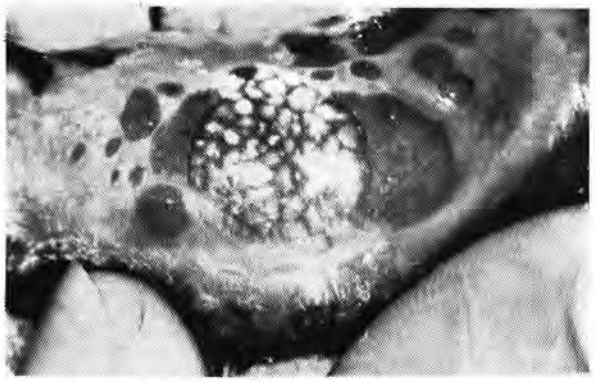

Fig. 2. Shows a Speckled leukoplakia in the centre of the lower lip. Red atrophic areas are interspersed with white hyperothokeratotic or hyperparakeratotic patches. Several erythroplakias of varying sizes and consisting of well-defined, fiery red patches can be seen at the periphery of the speckled leukoplakia.

Fig. 3 & 4. Shows submucous fibrosis involving the lips, cheeks and soft palate and giving a blanched appearance of the oral mucosa. There is limited opening of the mouth. The fibrous bands are better palpated than seen.

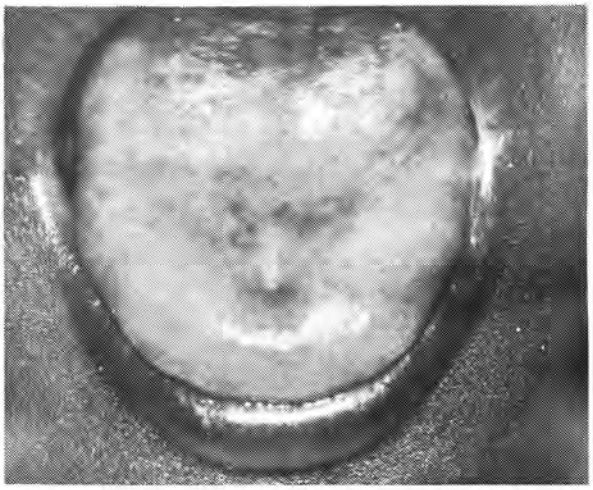

Fig. 5. Shows submucous fibrosis presenting as a bald, shiny tongue. A homogeneous leukoplakia is also present.

into the following four grades based on (1) changes in the individual cells and (2) in the interrelationship of one cell to another i.e. stratification, viz:

(a) — There is no evidence of future malignancy in the material examined.

(b) — There are some changes, such as mild atypia, but I do not think that malignancy is impending.

(c) — There is sufficient change (e.g. atypia) to make this lesion worrying. It should be eliminated if possible.

(d) — This is little short of carcinoma-in-situ.

A more detailed account of the operation of the National Registry of Oral Precancerous Conditions has been reported elsewhere (Ramanathan and Ng Kok Han, 1978). In all 194 patients were registered. PMI scores were recorded in 145 patients.

FINDINGS AND DISCUSSION

Just like oral carcinoma (Ramanathan and Lakshimi, 1976) there is a predominance of Indian patients (72%) with oral precancerous conditions (Table 1). Like oral carcinoma precancerous conditions of the mouth would also seem to be closely related to oral habits. The peak age incidence was between 51 — 60 years (40%). The three patients below 20 years of age comprised of a 13-year-old Indian boy with lichen planus, a 15-year-old Indian boy and a 16-year-old Malay girl with submucous fibrosis.

The distribution of the oral precancerous conditions were (1) homogeneous leukoplakia (51.2%), (2) lichen planus (16.1%), (3) submucous fibrosis (15.2%), (4) speckled leukoplakia (11.9%), (5) erythroplakia (2.8%) and (6) smoker's keratosis (2.8%). Seventeen patients (8.8%) had two oral precancerous conditions. Of the patients with two oral precancerous conditions, the Indian female formed the largest group (59%). Of these 17 patients 76.5% had submucous fibrosis and leukoplakia (Fig. 5). In Malaysia so far no case of submucous fibrosis has been reported in the Chinese and Malay male. However, submucous fibrosis has been reported in Chinese living in Taiwan and Papua-New Guinea. (Su, 1954; Barnes, 1975).

Table II shows the distribution of oral precancerous conditions by race, sex and premalignancy index (PMI) scores. In 76 patients (47%) immediate surgical treatment was indicated because of their histological features of epithelial dysplasia. The peak age incidence of the PMI scores of (**c**) — 56% and (**d**) — 43% was also between the ages of 51 — 60 years. All the PMI scores of (**d**) and about 80% of the PMI scores of (**c**) occurred in the Indians.

The commonest sites for oral precanceous conditions were (1) buccal mucosa (65%), (2) tongue (13%) and (3) labial commissures (9%). The labial commissures (85%), tongue (47%) and the buccal mucosa (43%) had the most ominous precancerous histological features. Like-wise the most ominous precancerous histological features — PMI scores of (**c**) and (**d**) — seen in the various oral precan-

Table I

Distribution of patients with oral precancerous conditions by race, sex, and age groups

AGE GROUP IN YEARS	MALAYS		CHINESE		INDIAN		TOTAL		TOTAL	PERCENTAGE
	M	F	M	F	M	F	M	F		
0 — 10	—	—	—	—	—	—	—	—	—	
11 — 20	—	1	—	—	2	—	2	1	3	1.6%
21 — 30	1	—	3	2	7	8	11	10	21	10.8%
31 — 40	2	2	2	3	6	9	10	15	25	12.9%
41 — 50	4	1	3	1	12	14	19	18	37	19.0%
51 — 60	4	3	4	2	31	31	41	36	77	39.7%
61 — 70	4	—	5	1	11	5	20	6	26	13.4%
71 — 80	—	1	1	—	1	—	2	1	3	1.6%
81 — 90	—	—	—	—	1	—	1	—	1	0.5%
UNKNOWN	—	—	—	—	1	—	1	—	1	0.5%
TOTAL	15	8	18	9	72	67	107*	87**	194	100%
PERCENTAGE	7.7%	4.2%	9.3%	4.6%	37.1%	34.5%	55.1%	44.9%	100%	

* — 2 males of other races; ** — 3 females of other races.

Table II

Distribution of oral precancerous conditions by race, sex and premalignancy index (PMI) Scores

PRECANCEROUS CONDITIONS	MALE a b c d	FEMALE a b c d	MALE a b c d	FEMALE a b c d	MALE a b c d	FEMALE a b c d	TOTAL	PERCENTAGE
HOMOGENEOUS LEUKOPLAKIA	2 4 6 —	— — 1 —	1 3 1 —	1 — 1 —	6 14 18 5	3 12 8 3	90*	56.6%
SUBMUCOUS FIBROSIS	— — — —	— — — —	— — — —	— — — —	2 3 6 1	3 4 5 3	27	17.0%
SPECKLED LEUKOPLAKIA	— — — —	— — — —	— — 1 —	— — — —	— 4 5 2	3 1 6 1	23	14.5%
LICHEN PLANUS	1 — — —	1 1 — —	3 — — —	3 1 — —	3 — — —	1 — — —	15**	9.4%
ERYTHROPLAKIA	— — — —	— 1 — —	— — 1 —	— — — —	— — — —	— — 2 —	4	2.5%
TOTAL	3 4 6 —	1 2 1 —	4 3 3 —	4 1 1 —	11 21 29 8	10 17 21 7	159	100%
PERCENTAGE	13 (8.2%)	4 (2.5%)	10 (6.3%)	6 (3.7%)	69 (43.4%)	55 (34.6%)	100%	

* Others — Female — 1(b)

** Others — Female — 1(b)

cerous conditions were: (1) erythroplakia (75%), (2) speckled leukoplakia (65%), (3) submucous fibrosis (56%) and (4) homogeneous leukoplakia (48%).

Oral submucous fibrosis is an important precancerous condition in Indians. The cause of submucous fibrosis is unknown. There is also no known treatment for this condition. Submucous fibrosis is also challenging to manage for quite often leukoplakia supervenes and multiple oral carcinomas develop. Often there seems to be a wide field of cancerization in submucous fibrosis.

Submucous fibrosis seems to be the Asian version of sideropenic dysphagia (Plummer-Vinson syndrome; Paterson-Kelly syndrome) seen in Caucasians. In fact these two conditions are no more than two different spectra of one broad and common entity just like the obverse and reverse of one and the same coin. As suggested earlier (Ramanathan *et al.*, 1975) Behcet's syndrome, periadenitis mucosa necrotica recurrens (PMNR) and recurrent aphthous ulcers (RAU) again appear to be different spectra of this one broad and common entity. The latter conditions probably are progressively milder clinical expressions. Wray *et al.* (1975) and Sapiro (1977) have demonstrated iron, folic acid and vitamin B12 deficiencies in patients with recurrent aphthous ulcers. In all the above stated conditions iron deficiency and vitamin B complex deficiency appear to be important causative factors.

Submucous fibrosis appears to be an altered oral mucosa following a prolonged period of deficiency of iron and vitamin B complex. This altered oral mucosa appears to develop more easily a hypersensitivity to oral irritants such as spices, especially chillies and to the betel-quid, especially to the lime and tobacco components.

This rather limited study so far indicates that oral lichen planus, smoker's keratosis and keratosis in the floor of the mouth do not appear to be precancerous conditions in Malaysians as they have been reported in population studies elsewhere. This difference could be largely due to the different patterns of oral habits.

SUMMARY

A programme aiming to diagnose oral precancerous conditions promptly and to treat them even before they develop into carcinoma can be regarded as a cancer prevention scheme. The pathologist by applying the WHO Premalignancy Index (PMI) scores to biopsies can be of great guidance and value to both the surgeon and the patient. In 76 patients (47%) with oral precancerous conditions immediate surgical treatment was indicated because of their histological features of epithelial dysplasia. The labial commissures (85%), tongue (47%) and the buccal mucosa (43%) had the most ominous precancerous histological features. Likewise the most ominous precancerous histological features seen in the various oral precancerous conditions were: (1) erythroplakia (75%), (2) speckled leukoplakia (65%), (3) submucous fibrosis (56%) and (4) homogeneous leukoplakia (48%). Oral submucous fibrosis is an important precancerous condition in Indians. The cause of submucous fibrosis is unknown. There is also no known treatment. The author has speculated that submucous fibrosis is the Asian version of sideropenic dysphagia seen in Caucasians.This rather limited study so far has indicated that oral lichen planus, smoker's keratosis and keratosis of the floor of the mouth do not appear to be precancerous conditions in Malaysians.

ACKNOWLEDGEMENT

I wish to place on record my profound appreciation to Dr. Abdul Rahman bin Awang, the Director of Dental Services, Malaysia and Chairman of the National Council for the maintainence of the "National Registry of Oral Precancerous Conditions", all the National Council members, the Director, Institute for Medical Research, Kuala Lumpur and to the numerous colleagues throughout Peninsular Malaysia for their encouragement and valuable support in maintaining the National Registry of Oral Precancerous Conditions and in carrying out this preliminary study. I wish to also thank members of the WHO Expert Committee on Oral Precancerous Conditions for allowing me to apply the PMI scores in this study.

REFERENCES

Barnes, P. (1975) Submucous Fibrosis. *Papua New-Guinea Med. J.* **18**, 56 — 70.

Ramanathan, K., Tan Cheng Keat, Retnanesan, A., Canaganayagam, A. (1973) Oral Precancerous Conditions — Frequency in 1,648 Malaysians with Correlation to Oral Habits. *Dent. J. Mal. & Sing.* **13**, 11 — 21.

Ramanathan, K., Dharmalingam, S.K. and Perdaman Singh (1975) Frequency of Precancerous Conditions in 75 Malaysian Oral Cancer Patients. *Mal. J. Surg.* **1**: 29 — 38.

Ramanathan, K. and Lakshimi, S. (1976) Oral Carcinoma in Peninsular Malaysia — Racial Variations in the Indians, Malays, Chinese and Caucasians in "Cancer In Asia, Opportunities for Prevention, Detection and Treatment." Takeshi Hirayama. Editor. University of Tokyo Press, 27 — 36.

Ramanathan, K. (1977) Oral Carcinoma: Causes and Prevention. *Medical Progress.* **4:** 16 — 20.

Ramanathan, K. and Ng Kok Han (1978). The First Report of the National Registry of Oral Precancerous Conditions. Dept. of Stomatology Publication, Institute for Medical Research, Kuala Lumpur, January.

Sapiro, S.M. (1977). Folic Acid Deficiency Preceding Non-Tropical Sprue. *J. Oral Med.* **32,** 106 — 109.

Su I Pin (1954) Idiopathic Scleroderma of the Mouth. Report of Three Cases. *Ach. Otolaryngol.* **59,** 330 — 332.

Wray, D., Ferguson, M.M., Mason, D.K., Hutcheon, A.W., Dagg, J.H. (1975). Recurrent Aphthae: Treatment with Vitamin B12, Folic Acid, and Iron. *Brit. Med. J.* **2,** 490 — 493.