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EDITORIAL

The human mind and drug therapy

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Historically, it has been repeatedly observed that in controlled clinical drug trials, patients treated with placebos showed some improvement in their condition. The alleviation of symptoms following placebo therapy, ranged from 25% to 35%. It was also noted that those who improved had implicit faith in the doctor and optimism as regards outcome of therapy[1].

In the early 20th century a French pharmacist named Emile Coue observed that patients who were consuming apparently innocuous patent medicines, were rapidly relieved of their ailments. This was more so, if they had faith in the efficacy of the medicines prescribed[2]. This observation convinced Coue of the power of the mind in the healing process. He qualified as a psychotherapist in 1910 and promoted the technique of auto suggestion. He used to get his patients to repeat morning and evening "everyday in every way, I am getting better and better ". He published books on the method, and toured USA and Europe in a publicity campaign. In spite of considerable opposition from the medical fraternity of the West, the method nevertheless gained popularity and was known as **Couesism** - the new way. A limerick too was composed.

- There was an old doctor called Coue
- Who said to his patients 'J'ai vous
- To cure all your ills,
- Without any pills,
- You just think yourself better
- And get well at will.

The French Academy of Medicine objected to Coueism on the basis that the effects of auto-suggestion may deter, or even prevent patients from resorting to scientific treatment. Coue died of pneumonia in 1926.There is no record however as to whether he was treated with drugs or auto-suggestion for the disease.

Coueism is practised even today, and new editions of Coue's books are available.

Coue was of the view that the patient's imagination was stimulated by the prospect of the cure promised by the medicine, and this stimulated the imagination which brought about a cure. Neither the drug nor the therapist contributed to the result According to Coue it was the stimulus to the imagination that mattered, and not the 'conscious' will. An analogy to this is ,that one cannot consciously make saliva to flow. However if one imagines or pictures a delicious meal or item of food, then saliva begins to flow .and the " mouth waters", illustrating the influence of the imagination on the secretion of saliva.

It is well known too, that the choice of colour of a tablet or capsule can enhance the pharmacological effect. Drug manufacturers exploit this fact in marketing their products.

There have been instances where patients who had said that they cannot take "Disprin" because they develop abdominal pain. These same patients, however tolerated aspirin tablets , but were not told that they were receiving aspirin. This is indicative of a possible mental component in the development of symptoms. The Yogis in certain parts of India are able to control physiological functions like breathing, heart rate and pain purely by exercise of will power.

There is little doubt therefore as to the role of the human mind in producing therapeutic drug effects. Nevertheless the scientific basis of drug therapy, and the rational use of drugs should never be underestimated in patient care. The conditioning of the patient's mind prior to the commencement of therapy would certainly enhance the therapeutic effect produced. In order to do this the prescriber must win the confidence of the patient by taking pains to explain the need for, the action of and also the adverse effects that could arise, and also the high probability of obtaining a cure or relief of symptoms.

The foregoing perhaps illustrates in some way the effect of MIND over MATTER, and the need to focus on psycho-somatic medicine in the new millenium.

References

1. Rowe R. Placebos, psychotherapy and product perception - all in the mind. Drug Discovery Today. 2001; 6(21): 1075-6
2. Inglis B Self diagnosis and medication methods, ancient and modern. Royal Soc. Health J. 1977; 97: 156-158

LEADING ARTICLE

Sri Lanka Dental Journal 2001 30(2) 3-10

Infections in dental practice and risk management

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Galle

Introduction

"U.S. Hospital Needle Pricks Top 1,000 a Day" (CDC Reuters, 2000)
"Each year 300 to 400 health care workers die of hepatitis B infection in USA"
(J. Inf. Diseases, 1994)
"AIDS is a worldwide epidemic with 60-70 million infected"(CDC; MMWR 2000)
"Tuberculosis kills 2 million people each year" (WHO fact sheet No. 104, April 2000)

The unique nature of most dental procedures, instrumentation and patient care settings may require specific strategies aimed at preventing transmission of pathogens between dental health care workers (DHCWs) and their patients. Risks of transmission of infections between health care workers and patients in dental practices have been studied in great detail, publicized and created the much needed awareness among the dental practitioners. Although the principles of infection control remain unchanged, new technologies, materials, equipment and data require continuous evaluation of current infection control practices in managing such risks. Recommended infection control practices are applicable to all settings in which dental treatment is provided.

History of infection control

Infection control (IC) procedures are not a new phenomenon resulting from the Human Immunodeficiency Virus (HIV) infections and the epidemic it has caused. As early as 1952, the American Dental Association made the earliest recommendations and recognized the limitations of chemical agents. These were reviewed later with the emerging HIV and Acquired Immune Deficiency Syndrome (AIDS) epidemic, and methods to eliminate microorganisms in a dental practice emphasized pre cleaning and heat sterilisation [1].

In 1978, procedures for reducing contamination and cross contamination in dental offices were recommended. These procedures identified patients 'at risk' such as haemophiliacs, percutaneous drugs users and male homosexuals were based on patient's health status once identified. These procedures were termed isolation precautions and included most infection control procedures practiced today [2].

In the early 1980s, speculation about a "transmissible agent" resembling hepatitis B Virus (HBV) being involved in the transmission of AIDS was hypothesized[3]. This led to the recommendations of special precautions based on blood and body fluid isolation, when treating known AIDS patients and those in high-risk groups.

In 1986 the first dental specific infection control recommendations were published [4]. These were extended to all patients, to be used routinely, recognizing the need for health care workers to consider all patients as potentially infected with HIV and other blood borne pathogens. In 1987 the term "universal precautions" (UP) was first applied to the universal blood and body fluid precautions that replaced previous isolation procedures [5].

Mechanisms of exposure

Dental patients and DHCWs may be exposed to a variety of microorganisms via blood, oral or respiratory secretions. These microorganisms include hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, cytomegalovirus (CMV), herpes simplex virus (HSV) types 1 and 2, M. *tuberculosis,* staphylococci and streptococci. Other viruses and bacteria specifically infecting the upper respiratory tract may be transmitted in the dental operatory through several routes. These routes are direct contact with blood, oral fluids, or other secretions, indirect contact with contaminated instruments, operatory equipment or environmental surfaces or contact with air borne contaminants present in either droplet spatter or aerosols of oral and respiratory fluids.

Infections via any of these routes require the presence of all three links of the "chain of infection", which are a susceptible host, a pathogen with sufficient infectivity and numbers to cause infection, and a portal of entry in the host. Effective infection control strategies aim at breaking one or more of these links in the chain thereby preventing infection [6].

Guidelines for a safe practice

Universal precautions should be adopted in all instances of contact with a patient's blood, body fluids or mucous membranes to minimize transmission of infection between the dental health care worker and the patients [7].

a. Barrier precautions guidelines [8]

Hand washing should be done

* before and after each patient contact
* after removing gloves
* immediately after contact with blood, body fluids and mucous membranes

Gloves should be worn when there is anticipated contact with

* blood, mucous membranes and non intact skin
* soiled objects and surfaces

Non sterile gloves are appropriate for examinations

Single use gloves should not be washed repeatedly and reused

(washing of gloves causes undetectable holes to appear)

Other barrier techniques

* Surgical masks (impervious) should be worn when
  - there is a possibility of being splashed on the face
  - working in close proximity to a patient who is coughing
* Protective eye wear and face shields should be worn when
  - there is a possibility of splashes
  - DHCW has acne or dermatitis
  - preparing a tooth with high speed handpiece
  - polishing a crown
* Laboratory coats should
  - always be worn
  - kept in the work place
  - water impervious aprons should be worn when there is anticipated soiling with blood and body fluids

b. Safe handling and disposal of needles and other sharp instruments (e.g surgical blades etc.)

* Use with the sharp end pointed away * Pick up one at a time * Do not recap but use the 'scoop' technique * Unsheathed needle should not - get contaminated contribute to unintentional needle pricks	* Disposable sharps , needles, cartridges - do not bend before disposing - dispose into closable, puncture-resistant , biohazard container * Containers should be accessible and close to the work area
Reusable sharps * should be discarded into disinfectant * Utility gloves should be worn when cleaning and decontamination of reusable sharps	

c. Handling biopsy specimens

A sturdy container with a secure lid should be used to place biopsy specimens taking care to avoid contaminating the outside. If the outside gets contaminated, it should be cleaned and disinfected or the entire container should be placed in an impervious bag.

When extracted teeth are used in an educational setting, they should be handled while wearing gloves and removed of all soft tissue and debris by scrubbing with detergent and water. They should be stored in fresh hypochlorite (household bleach diluted 1:10 in tap water) [6].

d. Controlling environment contamination

Environmental surfaces that are difficult to clean or decontaminate (e.g. light handles, hand-operated controls, X-ray unit head, etc.) should be covered with an impervious material and changed between patients using a gloved hand. Rubber dams should be used appropriately when high-speed evacuation is being done. By positioning the patient correctly, environmental contamination can be avoided [8].

e. Safe disposal

Personal protective equipment such as masks, gloves, goggles, aprons have to be removed before leaving the laboratory or the patient care sites and disposed of safely depending on whether they are disposable items or they are to be reused. Disposable drapes should be put in the trash container.

Used linen should be placed in linen bags at the point of origin. Wet linen should be enclosed in impervious or plastic bags and then placed in the linen bag.

Solid waste such as paper products, cotton supplies should be discarded into the trash container after each patient. Contaminated disposable items have to be decontaminated prior to disposal or placed in a biohazard container for incineration.

Liquids that are infective should be disposed of in a proper sewer system. However, caution should be exercised when emptying, to avoid splashes and spills [8].

f. Sterilisation & Disinfection

Dental instruments that are reusable are categorized according to their risk of transmitting infection, nature of its use and body sites where they are used. (see box)

Critical	Semi critical	Non critical
* Penetrate soft tissue or bone * Sterilised after each use	* Contact with oral tissues * Sterilisation or high level disinfection	* Come into contact with intact skin * Intermediate or low level disinfection

Methods

Used instruments are kept in a suitable disinfectant till they are cleaned. Thorough cleaning with soap and water or detergent and using gloves is a prerequisite before disinfection or sterilisation. The instruments are then disinfected or sterilised depending on their heat stability and category. Moist heat, dry heat or chemical vapour is used for heat stable instruments. They are then packaged and stored. Sterilisation cycles should be monitored regularly using chemical indicators and or biological methods. Critical instruments that are heat labile should be subjected to cold sterilisation, making sure that the instruments are kept completely immersed for 10 hours [9].

Intra oral dental materials such as impressions, fixed and removable prostheses, orthodontic appliances etc. should be cleaned and disinfected before manipulation and before placing in the mouth. Guidelines from the manufacturer regarding their stability to heat and chemical disinfectants should be followed. An intermediate level of disinfection that is also "tuberculocidal " is preferable [10].

The dental unit and its immediate environment should be cleaned daily. Counter tops and unit surfaces should be cleaned and disinfected using chlorine (1/4-cup bleach to one gallon of water). Phenolic and iodophor disinfectants are also appropriate. Floors and walls can be cleaned with detergents or low level disinfectants [11](see box)

Chemical disinfectants and sterilants

Low level	Medium level	High level
- phenolic e.g. chloroxylenol, hexachlorophene - quaternary ammonium compounds e.g. zephiran - diguanides e.g chlorhexidine (savlon)	- phenolics e.g. sudol, hycolin - iodophors e.g. betadine - chlorine containing compounds - alcohol e.g. 70% ethyl or isopropyl - diguanides e.g chlorhexidine (hibisol)	- gluteraldehyde 2% formaldehyde

Risk through aerosols generated by a high speed dental drill

Aerosols are invisible particles that are less than 10 microns in diameter. They remain airborne indoors for a time. There is no clear evidence of cross infections occurring of blood borne pathogens that may be aerosolised during the use of a high-speed dental drill. However in the event of this possibility occurring effective barrier precautions outlined above will suffice to prevent infection [12].

Three factors are said to determine the occupational risk of acquiring HIV and HBV infections. They are the prevalence of the infection in the populations served, the risk of needle stick exposures per year and the risk of seroconversion from a needle stick exposure. The risk of seroconversion from a needle stick injury is more than 30% from a HBV e antigen positive patient and 0.2% from a HIV positive patient [13].

Specific Diseases - HBV and HIV

Prevalence in Sri Lanka

HBV	HIV
1980's - 0.02% (National survey) 1992 - 2.5% (Gampaha district) 1993 - 0.9% (Kandy, Hambantota & Kalutara)	People living with HIV/AIDS(estimated) - end of 1999 – 7500 - end of 2000 – 8500 Reported HIV/AIDS cases - End 2000 – 358 (National AIDS and STD Control Programme)

Transmission of HBV

Three hundred to four hundred HCWs die each year in the United States due to HBV infections and of these more than 200 are occupationally acquired. The high-risk groups among HCWs are the dentists, oral surgeons and orthopaedic surgeons. In 1970 before the hepatitis B vaccine was widely used, 13.6% of HCWs showed evidence of previous exposure. In 1992 evidence of HBV infection is reported as 9% in dentists, 21% in oral surgeons, 15% in orthopaedic surgeons and 3-5% among the general public [14].

The possibility of transmission of blood borne infections from DHCWs to patients is considered to be small. Reports published from 1970 to 1987 indicate nine clusters in which patients were infected with HBV, associated with treatment by an infected DHCW [15,16]. Since 1987 there have been no reports of transmission of HBV from dentists to patients. This is probably a reflection on effective vaccination, adoption of UP or incomplete reporting.

Transmission of HIV

Reports of occupationally acquired HIV infections in the USA up to June 1998, list 114 possible cases of which 51 have been documented. Forty-five of 51 resulted from percutaneous exposures (41 hollow bore needles, 2 broken glass vials, 1 a scalpel), 5 of 51 from mucocutaneous exposures to blood and 1 of 51 resulted from both. Seven of the possible cases were in DHCWs. But there were none in the documented cases [17].

Transmission of HIV to six patients from an infected dentist was reported in 1990 [18].

Managing occupational exposure to potentially contaminated body substances (19)

* Wash area, give first aid
* Report incident soon
* The source patient (if known) is tested (after informed consent) for HIV and , hepatitis B
* If the source patient is proved to be infected, the exposed person has baseline tests and is counselled on the potential for transmission
* If hepatitis B contact has occurred in an unvaccinated person, hepatitis B immune globulin and a primary vaccine course are given. Others are given a booster vaccine dose.
* If there has been a definite parenteral exposure to HIV (16), anti retroviral prophylaxis is offered, preferably within a few hours. Counselling is also desirable.
* During the follow up period of 12 weeks, the exposed person is advised to protect sexual partners, avoid pregnancy, blood donation and report any febrile illness.
* Repeat HIV antibody test at 6 and 12 weeks
* Ensure appropriate documentation of incident, test results and follow up

Tuberculosis

Tuberculosis (TB) kills 2 million people each year. Factors that have caused increased concern are a worldwide epidemic gone out of control and the emergence of multi drug resistant strains. The prediction is that 1 billion more, will be infected by year 2020 and 70 million will die[20]. Transmission occurs due to exposure to airborne droplets coughed up by patients with active pulmonary TB.

Groups at higher risk for TB include prison inmates, homeless people, IV drug users, alcoholics, elderly persons in nursing homes, people infected with HIV, contacts of active TB patients, people from endemic countries such as ours.

Health care facilities are divided into 5 levels of risk: minimal, very low, low, intermediate and high depending on whether TB patients are treated or not. It is important to categorise dental practices in the country based on such guidelines taking into consideration that the notification rate of TB is 37.6 per 100,000 and 7157 new cases were reported in 1999 [21]. Dental practices in the country should develop written protocols for screening patients for active TB and dental care should be deferred but not refused for those with suspected TB. By referring them to appropriate medical facilities, they can be rendered noninfectious in 3 weeks by medication. When treated, they can receive dental care in private offices. Emergency dental care should be done in facilities with proper engineering controls and TB isolation rooms. Dental employees should have initial baseline TB screening when hired.

Vaccines for DHCWs

It is recommended that employers make hepatitis B vaccination available without cost to all their employees who may be exposed to blood or other infectious materials. Antibodies to hepatitis B surface antigen should be checked after the 3 doses of the vaccine, since the rates of hypo responders in the country is 15%. DHCWs are also at risk for exposure to and possible transmission of other vaccine preventable diseases; accordingly vaccination against measles,

mumps, rubella and tetanus may be appropriate for DHCWs [22].

Conclusion

In efforts to protect both patients and DHCWs studies should address surveillance, risk assessment, evaluation of measures to prevent exposure and of post exposure prophylaxis. This could lead to development of safer and effective medical devices, safe work practices and personal protective equipment that are acceptable to DHCWs, are practical and economical and do not adversely affect the patient.

Even though at the present time the prevalence of HBV and HIV appears to be low in the country, one cannot be complacent. The time is ripe to adopt strict measures to prevent cross infection in any medical setting, more so in busy dental practices. A safe dental practice requires the highest level of infection control, a clear understanding of the risks and adherence to strict standards and techniques. Each dental facility should develop a written protocol for instrument reprocessing, operatory clean up and management of injuries. There should be regular monitoring of sterilisation procedures. DHCWs must immunise themselves and check their antibody levels where relevant. Training in infection control strategies and continuous updates should be part of continuing professional development of all DHCWs. There is always room for improvement but no room for compromise.

References

1. Agents and methods for sterilization or disinfection of dental instruments. in Accepted Dental Remedies. 17th edition. American Dental Association, Chicago IL,1952.
2. Council on Dental Materials and Devices, Council on Dental Therapeutics: Infection control in the dental office, Journal of the American Dental Association 1978;97:673-677.
3. Centers for Disease Control and Prevention: Acquired immune deficiency syndrome (AIDS): Precautions for health-care workers and allied health care professionals. Morbidity and Mortality Weekly Report 1982;31(43):577-580.
4. Centers for Disease Control and Prevention: (CDC) Recommended infection -Control practices for dentistry. Morbidity and Mortality Weekly Report (MMWR)1986;35(15):237-242.
5. Centers for Disease Control and prevention: Recommendations for prevention of HIV transmission in health-care settings. MMWR 1987; 36 (2S).
6. CDC. Recommended infection control practices for dentistry. MMWR . 1993; 28 :3-4.
7. CDC Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other blood borne pathogens in health -care settings. MMWR 1988;37:377-87,387-8.
8. Universal Precautions Policy "Infection Control Manual, Grady Health System ". June 1994.
9. Favero MS, Bond WW. Sterilization, disinfection and antisepsis in the hospital. In Manual of Clinical Microbiology, 5th ed. Washington DC American Society for Microbiology 1991; 183-200.

10. CDC. Guidelines for prevention of transmission of HIV and HBV to health care and public safety workers. MMWR 1989;38 (S6): 1-37.

11. Rutala WA. APIC guidelines for selection and use of disinfectants. Am J of Infection Control 1990; 18:99-117.

12. Miller RL. Characteristics of blood containing aerosols generated by common powered dental instruments. Am Ind Hyg Assoc J 1995;56(7):670-6.

13. Gerberding JL. Incidence and prevalence of HIV, HBV, hepatitis C virus and cytomegalovirus among health care personnel at risk for blood exposure: final report from a longitudinal study. J Infect Dis 1994; 170: 1410-1417.

14. Cardo DM, Bell DM. Blood borne pathogen transmission in health care workers: risks and prevention strategies. Infect Dis Clin North Am 1997;11:331-336.

15. CDC. Hepatitis B among dental patients-Indiana MMWR 1985;34:73-5.

16. Levin ML, Maddrey WC, Wands JR et al. Hepatitis B outbreak traced to an oral surgeon. JAMA 1974;228:1139-40.

17. CDC. Case control study of HIV seroconversion in health care workers after percutaneous exposure to HIV infected blood-France, United Kingdom and United States. MMWR 1995;44:929-933.

18. CDC. Investigation of patients who have been treated bu HIV infected health care workers-United states MMWR 1993;42:329-31.

19. Gerberding L . Management of occupational exposure to blood borne viruses. N Eng J Med 1995; 332:444-451.

20. WHO Fact Sheet No. 104, April 2000.

21. Annual Health Bulletin, Ministry of Health Services, 1999.

22. CDC. Immunization recommendations for health care workers, Atlanta GA: CDC division of Immunization, Center for prevention services 1989.

REVIEW ARTICLE

Sri Lanka Dental Journal 2001 30(2) 11-17

Evaluation of the reliability of common cell proliferation parameters

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Introduction

Fast growing tumours have been shown to be deeply invasive and are known to have a poorer prognosis, compared with slow growing tumours[1]. Even though both cell proliferation and cell death (apoptosis) are equally important in tumourgenesis, more attention has been focused on cell proliferation than apoptosis. Literature reveals that great deal of time and effort have been spent by the researchers in studying and measuring cell proliferation. The significance of such measurements in tumour diagnosis and determining their prognosis has been reviewed[1,2]. Experimental evidence suggests, that the degree of cellular proliferation within a tumour gives an estimate of their biological behaviour[3]. Numerous independent studies have indicated that the degree of cell proliferation is a potentially important tumour marker of unique prognostic relevance in the study of human cancers[4,5,6]. Further, this assessment of proliferative status has been demonstrated to be a powerful prognostic indicator in breast, ovarian, lung and bladder cancer, non-Hodgkin's lymphoma and neuroblastoma[1,4,5,6].

With the realisation of the prognostic significance of cell proliferation in malignancies, more and more attention was focused on cell proliferation assessment methods without which consistent results could not be obtained. However, in assessment of cell proliferation divergent results have been observed even with the same set of tumours when different methodological approaches were employed. It has therefore not been possible to perform comparative studies successfully even between the same types of tumours. Therefore, it would be valuable to evaluate the different methodological approaches and their pitfalls as well as the reliability of representativeness of the proliferation fraction of them, before selecting a method for assessment of cell proliferation.

Literature reveals, that various methods have been used in the past to assess the cell proliferation or the proportion of cells that are in the proliferative compartment of the cell cycle.

These methods include:

- Counting the mitotic figures
- Flow cytometry
- Thymidine/Bromodeoxyuridine labeling of cells in S phase
- AgNOR technique and
- Immunohistochemical detection of PCNA/ Ki67 nuclear proteins.

The practical applications of these methods in the study of cell proliferation, are reviewed by Warnakulasuriya and Johnson[7].

The aim of the present review is to discuss the salient features of above methods and evaluate their reliability as indicators of cell proliferation in brief.

Counting mitotic figures

Assessment of cell proliferation by counting mitotic cells on conventionally stained histological sections using light microscopy is the most convenient, and therefore the most widely used method. A considerable disadvantage of this method is that it identifies only dividing cells,

which are in the mitotic phase of the cycling cell population. Mitotic phase is relatively short compared to other phases of the cell cycle in oral epithelia and extends from less than an hour to a maximum of two hours. Delay in fixation of tissues, size of the specimen[8] and all other methodological problems including non-random selection of counting fields, inconsistent criteria for the identification of mitotic figures, produce results that are unreliable[9]. The similarity of the light microscopic appearance between apoptotic cells and the cells which are in mitosis also has an impact on assessment of mitotic count as a proliferative index. Above all these, the subjective nature of this measurement cannot be ignored. However, mitotic count is the most widely used parameter of cell proliferation, as of both cost effectiveness of this investigation, which is performed only on routinely used H&E sections and the practical simplicity of it.

Flow cytometry

Flow cytometry has been used successfully and quite frequently to assess the cell proliferation in both fresh as well as formaline-fixed tissues. This is an automated technique in which a cell suspension prepared from the sample of tissue is employed. Using the capacity of some dyes to bind to DNA in a stoichimetric manner, the DNA content known as its ploidy status will be determined in comparison with some standard reference values. The S phase content and the proliferative activity can also be obtained by this technique with the help of advance mathematical models. However, physical distraction of the tissue architecture is one of the disadvantages in the technique, so that spatial relationship of cellular sub-populations is lost and possible inclusion of an admixed non-neoplastic cells in the sample[10]. Application of mathematical assumptions and involvement of advanced apparatus make the method further arduous. Nonetheless the information obtained by this method is objective and represent measurements on very large number of cells compared to most of the other techniques.

Thymidine/Bromodeoxyuridine labelling

Another approach to assess cell proliferation is calculating the labelling index by measuring the proportion of tumour cells, which are in the DNA synthesis (S) phase of the cell cycle. Labelling index is quantified on the basis of nucleic acid precursor incorporation into synthesizing DNA using tritiated thymidine ([^{3}H]dT) or bromodeoxyuridine (BrdUrd). Since the S phase of cell cycle is longer than the M phase, labelling index fraction is always larger than the mitotic count and therefore supposedly more reliable. One of the pitfalls in this technique is that the labelling index derived both from *in vivo* and *in vitro* incubation measures only the number of cells in the S phase, but not the actual compartment size of the growth fraction of the tissue. Introduction of double labeling technique proposed by Warnakulasuriya *et al*[11] , helped to overcome this drawback. However, the labelling index makes only the cells, which are in the synthetic phase of the cell cycle and not the total proportion of cells which are in the cell cycle[10]. These labelling methods also require fresh tissues for *in vitro* incubation with the label[11] or need to be administered *in vivo* before obtaining a biopsy suitable for study[12]. Requirement of *in vitro* administration of bromodeoxyuridine, further restricted, the wide usage of this method medico-legally. Inability to use the technique on archival tissues was also an obvious barrier in the procedure.

AgNOR technique

AgNOR technique has also been used to evaluate the cell proliferation in tumour tissues[13,14]. By this technique, nuclear organizer regions (NORs) would be demonstrated by means of the argyrophilia of their associated proteins[15] (AgNORS). Nuclear organizer regions are segments of DNA which are thought to be playing a role in RNA transcription [16]. The AgNORS are visualized as black dots within the nucleus and the mean AgNOR count for 50 or 100 cells is calculated. Their number (per nucleus) has been shown to be correlated with the rate of ribosomal

RNA transcription cell proliferation and DNA ploidy. The AgNOR technique is readily accessible and can be used on archival tissues but the significance and practical application of it, require a deep consideration. Giving different AgNOR counts for the same tumour due to heterogeneous nature of neoplasia is one of the disadvantages in the technique. Observation of higher AgNOR counts at the oxygenated margin of breast carcinomas compared to the hypoxic centre has been an added evidence for this finding. A lack of clear-cut differentiation in the range of AgNOR counts that distinguish between malignancy from benign, dysplastic and sometimes normal would be one of the obvious disadvantages in the technique[17]. Discrepancies in the AgNOR counts of cells in the different stages of the cell cycle in the same tumour, makes the technique further unreliable[10,18].

Immunohistochemical detection of PCNA/Ki67 nuclear proteins

Immunohistochemical detection of PCNA has been investigated as a marker of cell proliferation by a number of authors [19,20]. PCNA is a nuclear protein which is involved in DNA synthesis and functions as an auxiliary protein for DNA and cell cycle associated molecule, DNA polymerase d. Number of comparative studies have shown no correlation between PCNA immunoreactivity and other indices of cell proliferation, for example, S phase fraction (BrdUrd) and Ki67 immunostaining [17,21] . This might be an indication of the unreliability of PCNA as a marker of cell proliferation. However, present experimental findings that analyse the biological nature of the protein supplies adequate amount of evidence in this regard. It has been shown that the PCNA protein has a long half life (20 hours) resulting in staining persisting in cells which have recently left the cell cycle[22,23] so that the proliferation fraction assessed by PCNA represents not only the cells which are in the cell cycle but also quiescent cells or G0 cells.

The value of PCNA Index as a proliferative marker has further been questioned after revealing the association between expression of the protein and DNA repair[24]. The presence of PCNA protein in non-cycling normal keratinocytes *in vivo* after mild ultraviolet exposure and demonstration of involvement of PCNA in DNA repair in a cell free model of DNA damage provided the experimental evidence needed to establish this. Other experimental factors such as type of antibody employed, nature of the fixative used, the time of fixation and the immunohistochemical technique employed also have an effect on the results if they are not properly standardized. Overexpression of PCNA antigen, in tumour adjoining normal tissue cells which are subjected to the effect of growth factors, has also been observed in a number of experiments[25,26]. This piece of evidence reflects that the growth factors may induce the expression of PCNA in cells which do not enter S phase[22]. This also further questions the purity of proliferation fraction, assessed by PCNA.

The immunohistochemical detection of Ki67 nuclear protein has become more popular as a technique as well as a quantitative measure of cell proliferation, because of relevant advantages over the other cell proliferation assessment methods discussed earlier. A close association of the protein expression with that of proliferative compartment of the cell cycle has been reported. However, the definite function of the protein is still unknown. Cell cycle analysis studies have revealed that Ki67 proliferation associated antigen is expressed in all active phases of the cycle namely G_1, S, G_2 and M but not in G_0 or quiescent cells[27].

Even though various studies demonstrated the potential prognostic significance of Ki67 proliferation marker, acceptance of it as a valuable tool was limited for almost a decade (till 1991) due to the fact that the antigen defined by this antibody could not be characterized. Eventually Gerdes *et al*[28] had been able to identify a 1095 base pair (bp) partial clone, by immunoclonal screening of a lgt 11 human cDNA expression library which encode the epitope of Ki67 nuclear

protein. The location of the gene was also determined (10q25) with the help of *in situ* hybridization technique using this as a probe[29]. With the identification of the partial DNA structure of the Ki67 antigen, Key *et al,* developed a new monoclonal antibody equivalent to Ki67 using bacterially expressed cDNA containing 62 base pair repetitive elements encoding for Ki67 epitope[30]. Development of genetically engineered new monoclonal antibodies solved the problem of the application of Ki67 monoclonal antibody to formalin-fixed, paraffin-embedded material, which until then had been restricted only to fresh tissues. However, antigen unmasking using the microwave pretreatment of the paraffin sections became a compulsory step in the protocol used for these antibodies[31].

One of the main advantages of Ki67 proliferation antigen is that it is not expressed in the non-cycling cells as a result of the short half-life of the protein[32] (1 hour or less). Short half-life may probably be due to the presence of numerous proline-glutamic acid serine-threonine motifs in the protein, which facilitate rapid catabolism[33]. Development of both KiS5 antibody against Ki67 molecule which recognises the overall growth fraction and KiS2 antibody against a 100 kd proliferation specific nuclear protein which expressed exclusively in the cell cycle phases S, G_2 and M, marked a further step in the field cell proliferation.[34,35] By obtaining the ratio of Ki-S2 to Ki-S5, it has been able to discriminate the overall growth fraction from fraction of cells in S through M phase of the cycle. The ratio which denotes as the cycling fraction may vary widely in neoplastic cell populations, thus represent the relative cell fraction in the cycle compartment after the G_1/S transition, the complementary value corresponding to the relative percentage of cells in G_1.

However, when employing this method, a further set of practical problems, have to be taken in to consideration. These are the different degrees of tissue conservation and fixation resulting in heterogeneity in the pattern of staining, under staining, or false negative staining results. The heterogeneous nature of cell proliferation even within the tumour, makes it important to use large biopsies and to immunohistochemically assess serial sections at different levels of the same tumour to overcome the intra tumour heterogeneity. In the case of assessing the results with counting method, the number of cells, which need to be counted to obtain a representative sample is not yet clearly defined. Counting over 500 tumour nuclei is generally accepted as a minimum requirement [36]. Absence of expression of Ki67 nuclear protein has been observed in nutritionally deprived cells[37] and therefore special care should be taken to avoid the involvement of necrosed areas. The most important question to be answered is 'Does the mean Ki67 index really represent the proliferative compartment of the tumour?. Most of the studies assumed that cells in all the phases of the cycle namely G1, S, G2 and M are evaluated, in the assessment of cell proliferation by means of immunocytochemistry. However, it has been shown in another study, that cells which are in the early G_1 phase could have been excluded from the estimate due to the insufficient threshold of Ki67 protein in the cells to be detected immunohistochemically[27]. However, compared to the whole cell cycle the early G_1 phase cells that may or may not have been included in the estimated mean value, would be proportionately very small. On the other hand Scott *et al* (1991) have shown that immunohistochemical measurement of Ki67 may slightly over estimate the proliferative fraction of tumours[23]. On the other hand, by using immunohistochemistry, we assess the fraction of proliferation cells or the state of cell proliferation and not the rate of cell proliferation. A tumour with a slow cell cycle could have many cells in cycle with high mean Ki67 index but still have a relatively slow proliferation rate. A tumour with a short cell cycle could be highly proliferative but could have few cycling cells resulting in a low mean Ki67 index[38]. This shows that the assessing the rate of cell proliferation would be more informative than the state of cell proliferation even though obtaining

such measurement is rather difficult. However, as the true picture of the rate of proliferation of a tumour is not independent of apoptosis or programmed cell death, both will have to be assessed in obtaining a meaningful answer. This makes the task more difficult.

Conclusion

The reliability, of the common methods that have been used in the past to assess the cell proliferation and their identified short comings, as well as the nature of the biological process behind these procedures were briefly discussed. The evidence presented clearly indicates the need for a good understanding and broad science based knowledge of all aspects in cell proliferation other than methodological detail before deciding on a suitable proliferative marker in research or clinical studies. Evidence based, knowledge is further useful for accurate interpretation of results while the quality of the results can be improved with the optimisation of the selected method.

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References

1. Tubiana M and Courdi A. Cell proliferation kinetics in human solid tumours: relation to probability of metastatic dissemination and long term survival. Radiotherapy Oncology; 1989;15: 1-5.
2. Hall PA, Richards MA, Gregory WM, D'Ardenne AJ, Lister TA, Stansfeld AG. The prognostic value of Ki67 immunostaining in non-Hodgkin lymphoma. Journal of Pathology 1988; 154: 223-235.
3. Sledge GW, Eble JN, Roth BJ, Wuhrman BP, Fineberg N and Einhorn LH. Relation of proliferative activity to survival in patients with advance germ cell cancer. Cancer Reseach 1988; 48: 3864.
4. Kreipe H, Alm P, Olsson H, Hauberg M, Fischer L, Parwaresch R. Prognostic significant of a formalin resistant nuclear proliferation antigen in mammary carcinomas as determined by the monoclonal antibody Ki-S1. Amarican Journal of Pathology 1993b; 142: 651-657.
5. Rudolph P, Alm P, Heideberecht H-J, Bolte H, Ratjen V, Baldetorp B, Ferfo M, Olsson H, Parwaresch R. Immunohistochemical proliferative marker Ki-S2 as prognostic indicator for lymph node-negative breast cancer. Journal of National Cancer Institute 1999; 91: 271-278.
6. Rudolph P, Alm P, Olsson H, Heidebrecht HJ, Ferno M, Baldetorp B, Parwaresch P. Concurrent overexpression of p53 and c-erbB-2 correlates with accelerated cycling and concomitant poor prognosis in node negative breast cancer. Human Pathology 2001; 32:311-319.
7. Warnakulasuriya and Johnson NW. Importance of proliferation markers in oral pathology. In: Seifert G (ed) Current topics in Pathology 1996; 90: 147-177.
8. Cross SS, Start RD, Smith JHF. Does delay in fixation affect the number of mitotic figures in processed tissue. Journal of Clinical Pathology 1990; 43: 597-599.
9. Baak JPA. Mitosis counting in tumours. Human Pathology 1990; 21: 683-685.
10. Quinn CM, Wright NA. The clinical assessment of proliferation and growth in human tumours: evaluation of methods and applications as prognostic variables. Journal of Pathology 1990; 160: 93-102.
11. Warnakulasuriya KAAS. Cell proliferation of human oral mucosa. PhD thesis (1976), University of Glasgow.colorectal carcinomas measured *in vivo*.

12. Rew DA, Nilson, Taylor I, Weaver C. Proliferation characteristics of human British Journal of Surgery 1991; 78: 60-66. 12.
13. Hirsch SM, DuCanto BA, Caldarelli DD, Hutchinson JC, Coon JS. Nucleolar organizer regions in squamous cell carcinoma of the head and neck. Laryngoscope 1992; 102: 39-44.
14. Piffko J, Bankfalvi A, Ofner D, Rasch D, Joos U and Schmid KW. Standardized AgNOR analysis of the invasive tumour front in oral squamous cell carcinomas. Journal of pathology 1997; 182: 450-456.
15. Ploton D, Menager M, Jeannesson P, Himber G, Pigeon F, Adnet JJ. Improvement in the staining and the visualization of the argyrophilic proteins of nuclear orgernizer region at the optical level. Journal of Histochemistry 1986; 18: 5-14.
16. Alperts B, Bray J, Lewis J, Raff M, Roberts K, Watson JD. Molecular biology of the cell. New York and London 1983; 624-626.
17. Warnakulasuriya and Johnson NW. Nuclear organiser region (NOR) distribution as a diagnostic marker in oral keratosis, dysplasia and squamous cell carcinoma. Journal of Oral Pathology and Medicine 1993; 22: 77-81.
18. Quinn CM and Wright NA. The usefulness of clinical measurements in cell proliferation in gynecological cancer. International Journal of Gynecological Pathology 1992; 11: 131-143.
19. Shin DM, Voravud N, Ro JY, Lee JS, Hong WK, Hittleman WK. Sequential increase in proliferative cell nuclear antigen expression in head and neck tumouregenesis: a potential biomarker. JNCI 1993; 85: 971-978.
20. Welkoborsky HJ, Hinni M, Dienes and Mann WJ. Predicting recurance and survival in patients with laryngeal cancer by means of DNA cytometry, tumour front grading, and froliferation markers. Annals of otology Rhinology Laryngology 1995; 104: 503-510.
21. Jones AS, Roland NJ, Caslin W, Cooke TG, Cooke LD and Forster G. A comparison of cellular proliferation marker in squamous cell carcinoma of the head and neck. Journal of Laryngology Otology 1994; 108: 859-864.
22. Hall PA, Hart I, Goodlad R, Coates PJ, Lane DP. Expression of proliferating cell nuclear antigen in non cycling cells. Journal Of Pathology 1992; 168: 97A(abstract).
23. Scott RJ, Hall PA, Haldane JS, Van Noorden S, Price Y, Lane DP and Wright NA. Comparison of immunohistochemical markers of cell proliferation with experimentally determined growth fraction. Journal of Pathology 1991; 165: 173-178.
24. Shivji KK, Kenny MK and Wood R. Proliferation cell nuclear antigen is required for DNA excision repair. Cell 1992; 69: 367-374.
25. Hall RJ, Buckley CH, Gullick WJ, Fox H, Williams J, Wilcox FL. Prognostic value of epidermal growth factor receptor expression in cervical carcinoma. Journal of Clinical Pathology 1993; 46: 149-153.
26. Ottavio L, Chang CD, Rizzo MG, Petralia S, Travali S and Baserga R. The promoter of the proliferating cell nuclear antigen (PCNA) gene is active in serum-derived cells. Biochemmical Biophysical Research Commununication 1990; 169: 509-516.
27. Gerdes J, Lemke H, Wacher H. Hschwab U, Stein H. Cell cycle analysis of a cell proliferation associated human nuclear antigen defined by the monoclonal antibody Ki67. Journal of Immunology 1984; 133: 1710-1715.
28. Gerdes j, Li L, Schluter C, Duchrow M, Wohlenberg C, Gerlach C, Stahmer I, Kloth S, Brandt E, Hans-D Flod. Immunobiochemical and molecular biologic characterization of the cell proliferation-associated nuclear antigen that is defined by monoclonal antibody Ki67. American Journal of Pathalogy 1991; 138:867-873.
29. Fonatsch C, Duchrow M, Rieder H, Schluter C, Gerdes J. Assignment of the human Ki67 gene (Ki67) to 10q25- qter. Genomics 1991; 11: 476-477.

30. Key G, Becker MHG, Baron B, Duchrow M, Schluter C, Flad H-D and Gerdes J. New Ki67-equivalent murine monoclonal antibodies (MIB-1) generated against bacterially expressed parts of the Ki67 cDNA containing three 62 base pair repetitive elements encoding for the Ki67 epitope. Laboratory Investigations 1993; 68: 629-636.
31. Shi S-R, Key ME, Kalra KL. Antigen retrieval in formalin- fixed paraffin-embedded tissues: an enhancement method for immunohistochemical staining based on microwave oven heating of tissue sections. Journal of Histochemistry and Cytochemistry 1991; 32: 219-229.
32. Bruno S, Darzynkiewicz Z. Cell cycle dependent expression and stability of the nuclear protein detected by Ki67 antibody in HL-60 cells. Cell Proliferation 1993; 25: 31-40.
33. Rogers S, Wills R and Rechsteiner M. Amino acid sequences common to rapidly degraded proteins: the PEST hypothesis. Science 1986; 234: 364-367.
34. Heidebrechi HJ, Buck F, Haas K. Monoclonal antibodies Ki-S3 and Ki-S5 yield new data on the Ki67 proteins. Cell Proliferation 1996; 29: 413-425.
35. Heidebrechi HJ, Buck F, Steinmann J. Novel proliferation associated nuclear protein specifically restricted to cell cycle phases S, G2, M. Blood 1997; 90: 226-233.
36. Brown DC and Gatter KC. Invited review-monoclonal Ki67: its use in histopathology. Histopathology 1990; 17: 489-503.
37. Baisch H and Gerdes J. Simultaneous staining of exponentially growing versus Plateau phase cells with the proliferation associated antibody Ki67 and propidium iodide: analysis of flow cytometry. Cell Tissue Kinetic 1987; 20: 387-391.
38. Sarbia M, Bittinger F, Porschen R, Dutkowski P, Torzewski M, Willers R, and Gabbert HE. The prognostic significance of tumour cell proliferation in squamous cell carcinomas of the oesophagus. British Journal of Cancer 1996; 74: 1012-1016.

CLINICAL UPDATE

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Oral mucosal white lesions – An update

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Introduction

Oral mucosa appears white when there is excessive keratin formation, epithelial hyperplasia, reduced vascularity in the underlying tissue, intracellular oedema or accumulation of whitish material on the surface of the mucosa. There are a number of aetiological factors for oral mucosal white lesions. White lesions may be a localized problem in the oral cavity or a manifestation of a systemic illness. There is a considerable misunderstanding and confusion about white lesions that all the white appearing lesions are sinister especially interpreted as "leukoplakias". Hence, it is of utmost importance to identify those lesions precisely.

This article discusses a spectrum of white lesions in the oral mucosa.

A. Developmental white lesions

a. White sponge naevus (WSN)

This is a rare autosomal dominant condition first described in the early 20th century [1]. Lesions of WSN are asymptomatic and affect several mucosal sites including oral, oesophageal, vulval and vaginal mucosa [2,3]. These lesions first appear before puberty as snow-white, somewhat thickened with spongy consistancy affecting extensively the oral mucosa leaving very little normal tissue. However, the attached gingiva is generally spared[4]. Histopathologically the epithelium is thickened with marked acanthosis and parakeratosis. The parakeratotic layer is oedematous which lead to "basket weave" appearance.

The diagnosis is straightforward and usually established by characteristic clinical features. Biopsy is confirmatory. Differental diagnosis of w.s.n includes pachyonychia congenita, hereditary intraepithelial dyskeratosis, Darier's disease and acquired diseases such as candidal infection . There is no specific treatment needed due to the asymptomatic and benign nature of the disease.

b. Dyskeratosis congenita

This is a rare condition which appears to be inherited as an autosomal recessive , x- linked characteristic [4,5]. The disease is characterized by oral white lesions, nail dystrophy and pigmentation of the skin.

Oral lesions appear in childhood and basically the palate and tongue are affected. The lesions appear as erosions or blisters which are followed by the accumulation of white patches. These lesions show severe dysplasia regardless of the clinical appearance. There is no treatment for this condition. However, it is mandatory to carryout careful periodic examination to monitor possible malignant transformation [6].

c. Benign intraepithelial dyskeratosis (Witkop's disease)

This is a rare highly penetrant condition transmitted as an autosomal dominant nature [3]. This disease appears at very early stages of life (within 1st year) as oral white lesions and bulbar conjunctivitis. Commonly affected oral sites are buccal, labial and commisural mucosae, floor of the mouth, lateral surface of the tongue, gingivae and palate. These lesions remarkably mimic white sponge naevus and hence adequate history and biopsy are mandatory in establishing the diagnosis. No treatment is needed due to its self limiting, benign nature and no malignant transformation.

d. Keratosis follicularis (Darier's disease/Darier white disease)

This condition is transmitted as an autosomal dominant characteristic. However, many cases may appear sporadically or due to mutations. The disease is manifested as skin as well as oral lesions. The oral involvement appear when skin lesions become extensive. The preferred oral sites are gingivae and palate although any site could be involved. A characteristic feature of the lesion is the appearance of small white papules.

It is important to differentiate this condition from smokers palate, condyloma accuminatum. These lesions do not show any malignant predisposition. However, treatment with vitamin A analogues has been used effectively [3, 5].

e. Pachyonychia Congenita

This is an extensively rare condition which is transmitted as an antosomal dominant manner. This is characterized by thickening of nails, hyperkeratosis, hyperhydrosis of the palms and soles. This disease appears in the oral cavity as a whitish thickening of the oral mucosa [5]. There is no treatment available.

f. Fordyce's spots

Fordyce's granules are ectopic sebaceous glands of which the origin is thought to be developmental. They appear as multiple aggregations commonly on the buccal mucosa and lip vermilion. Lesions are asymptomatic and often identified by routine oral examination. This condition is fairly common affecting approximately 80% individuals [3]. Some patients may develop cancer phobia for this condition. There is no treatment needed except reassurance in cancerphobic patient.

B. Reactive lesions

Chronic low-grade trauma of physical or thermal nature can give rise to keratosis or hyperkeratosis presumably as a protective mechanism.

g. Frictional Keratosis

Sharp edges of teeth, ill fitting dentures, chronic cheek biting can lead to hyperkeratosis. Hence such lesions are related to the site of irritation, as an example the buccal mucosa in relation to a sharp edge of a posterior tooth (Figure 1). A careful history and examination help in arriving at the diagnosis. Removal of the suspected aetiological factor would resolve the problem. It is important to differentiate these lesions from leukoplakia. Hence, any lesion which do not respond to local treatment or suspicious lesions should be biopsied [3, 7].

h. Smokers Palate

Smokers palate is a condition associated with pipe smokers and reverse smokers. The mucosa of the posterior hard palate and the soft palate are affected. Lesion has a characteristic appearance of white nodular excrescences with a red dot in the

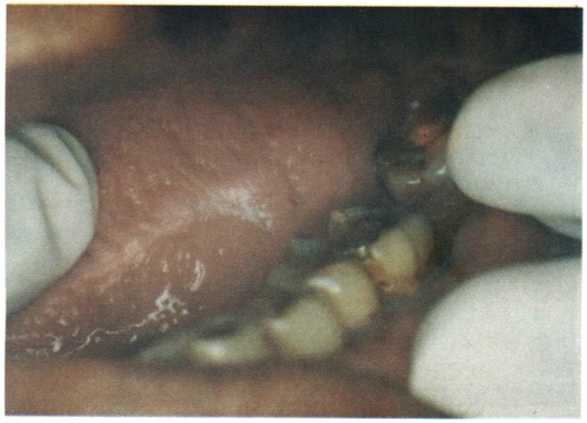

Figure 1. Frictional keratosis. Note the sharp cusp of the first molar tooth

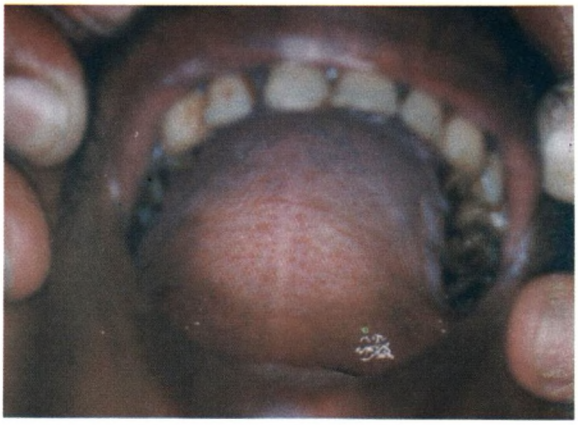

Figure 2. Smoker's palate

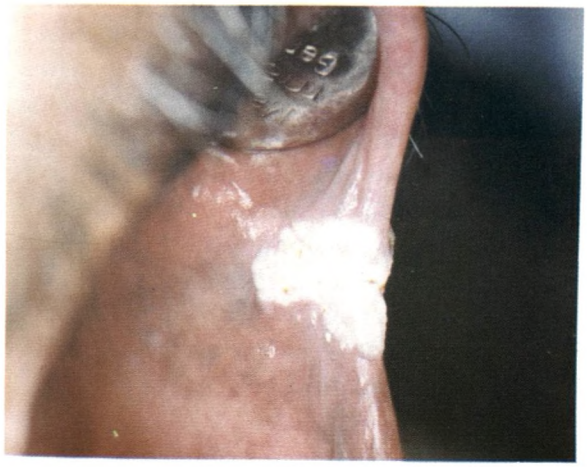

Figure 3. Chronic hyperplastic candidosis on the left commisure

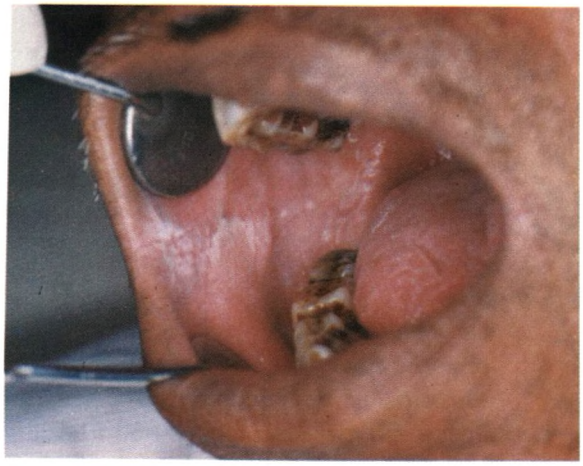

Figure 4. Homogenous leukoplakia on the right buccal mucosa

middle (Figure 2). The mucosa is white due to hyperkeratosis while nodular elevations are due to cystic dilation of the ducts of minor salivary gland. The heat together with combustion products of tobacco is supposed to be responsible for this lesion [8]. This lesion is known to be premalignant.

C. White lesions due to infections

(i) Viral infections

i. *Hairy leukoplakia*

Hairy leukoplakia (HL) is a white patch with corrugated or "hairy " surface occuring typically at the lateral borders of the tongue. This condition was first described in 1984 among homosexual men in San Francisco [9]. HL is a manifestation of HIV infection which progress to AIDS. However, it is also seen in immuncompromised patients other than HIV such as bone marrow transplant patients [10]. It is important to differentiate this lesion from leukoplakia. This lesion does not pose any malignant potential[10].

j. Koplik's spots

Koplik's spots generally precede the skin lesions of measles by 1-2 days. These lesions in the mouth appear as an erythematous macules with a white necrotic center.

(ii) Fungal infections

k. Candidosis

Oral candidosis is a relatively common opportunitistic mycotic infection in man. This organism is a predominant commensal in the oral cavity and about 50-60% healthy individuals carry candidal species in their mouths [11]. Oral candidosis manifests in different ways such as white lesions, red lesions and a mixture of white and red lesions.

l. Acute pseudomembrânous candidosis (Thrush)

This condition produces a characteristic white or creamy slightly elevated patch which can be rubbed off leaving a raw erythematous base [12]. Pseudomembranous candidosis is unusual in otherwise healthy individuals. Hence, an underlying predisposing factor such as AIDS should be sought if thrush is identified[10]. Furthermore, neonates and also elderly patients can have this infection. Diagnosis is usually clinical and presence of a large number of candida like hyphae or pseudohyphae in smears from the lesion and heavy yield of candida species in cultures of the lesion [12]. Appropriate anticandidal agents and elimination of predisposing factors are the mainstay of management.

m. Chronic hyperplastic candidosis

Chronic hyperplastic candidosis shows either homogenous or nodular white patches in the oral mucosa (Figure 3). This lesion is generally seen in descending order in the commissrue, buccal mucosa, palate and tongue [13]. In this condition candidal hyphae are frequently found to be invading the epithelium rather than colonizing on the surface[14]. The aetiology of this condition was subjected to debate and multifactorial aetiology has been proposed such as smoking, alcohol consumption. Furthermore, superinfection of already present homogeneous leukoplakia may lead to candidal leukoplakia together with above mentioned perdisposing factors[13].

n. Chronic mucocutaneous candidosis

Chronic Mucocutaneous Candidosis (CMC) is a group of rare heterogenous conditions characterized by candidal infection in the oral cavity skin and nail

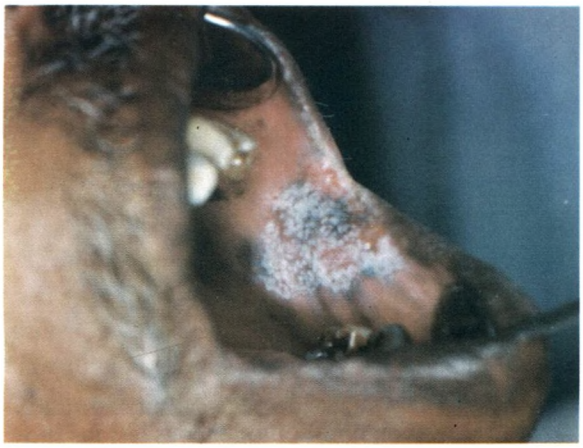

Figure 5. Non-homogenous leukoplakia on left commisure

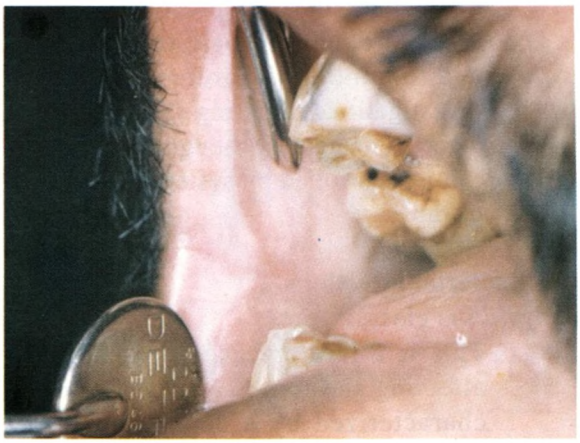

Figure 6. Oral submucous fibrosis

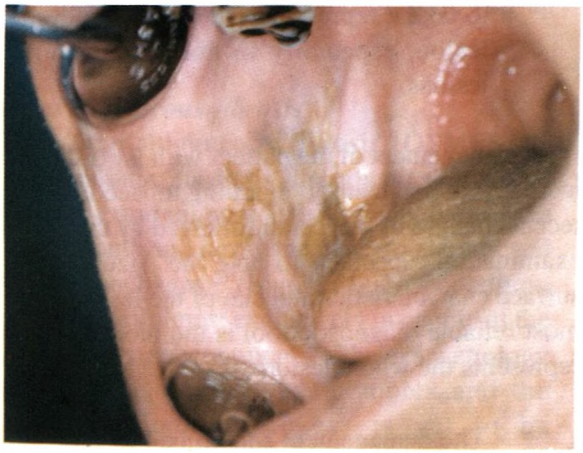

Figure 7. White lesion due to snuff

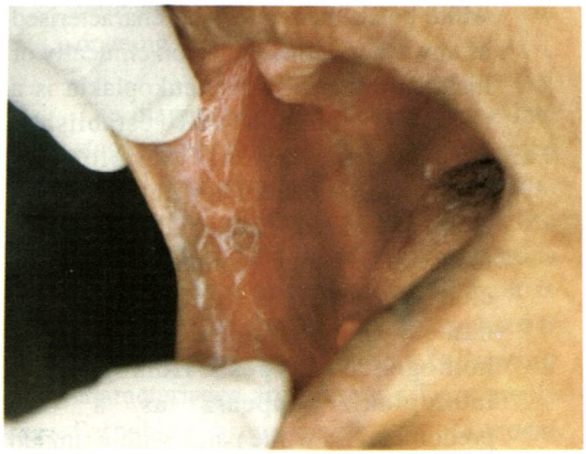

Figure 8. Oral lichen planus. Note the reticular pattern

beds[15]. The disease starts as pseudomembranous type followed by skin and nail involvement [3]. CMC is considered to be a phenotypic presentation of a spectrum of immunologic, endocrinologic and immune disorders. Hence, investigations targeting the underlying defect is mandatory though the condition can be controlled by systemic antifungal therapy [11, 16].

(iii) Bacterial infections

o. Syphilitic glossitis

This is a rare precancerous condition affecting the tongue [17]. The lesion is characterized by a depapillated area probably due to obliterative endarteritis which leads to circulatory insufficiency. Atrophic tongue is vulnerable to irritants such as tobacco, alcohol etc. leading to the development of keratotic areas [18]. Syphilitic glossitis may lead to carcinoma of the dorsum of the tongue [19].

D. Premalignant lesions and conditions

p. ***Leukoplakia***

Leukoplakia is defined as a predominantly white patch that cannot be characterised as any other definable lesion clinically or histopathologically [17]. Leukoplakia is a relatively common well established precancerous lesion. Aetiology of leukoplakia is either idiopathic or related to use of tobacco. Leukoplakia according to its morphology (colour and surface characteristics) is divided into two: namely the homogeneous and non-homogeneous types. Homogeneous leukoplakia appears as a thin predominantly white patch with wrinkled or corrugated surface having similar consistency throughout the lesion (Figure 4). Non-homogeneous lesion shows white or white and red with irregular surface [20] (Figure 5).

q. Poliferative verrucous leukoplakia

Poliferative verrucous leukoplakia (PVL) is a white patch with a verrucous surface which shows a strong tendency to transform into malignancy [21]. PVL begins as a simple keratotic patch but becomes clinically aggressive and multifocal. It is generally resistant to all forms of treatment.

Histopathology of leukoplakia may vary from hyperkeratosis to carcinoma in situ. In general the homogeneous leukoplakia shows little evidence of dysplasia. However, non-homogeneous lesions show more severe degrees of dysplasia and sinister outcome [7,20]. It is important to establish the diagnosis by biopsy and histopatholgical evaluation. It should include whether dysplasia is present or not and if present the degree of dysplasia hence the presence of dysplasia carry an increased risk of malignant transformation[20].

In this context it is of utmost importance to take a representative sample from the lesion, especially in non-homogenous lesions.

Management of the patient with PVL should include detailed history regarding tobacco habits, recent changes of the lesion followed by thorough examination especially to note the size, colour, surface characteristics and site of the lesion. The most reliable diagnostic tool is the biopsy which represents the whole lesion.

The management should be based on the clinical and histopathological features. The first line of treatment is directed at eliminating the possible causative factors – for example tobacco habits. The second line of treatment is either to keep the lesion under observation or to remove.

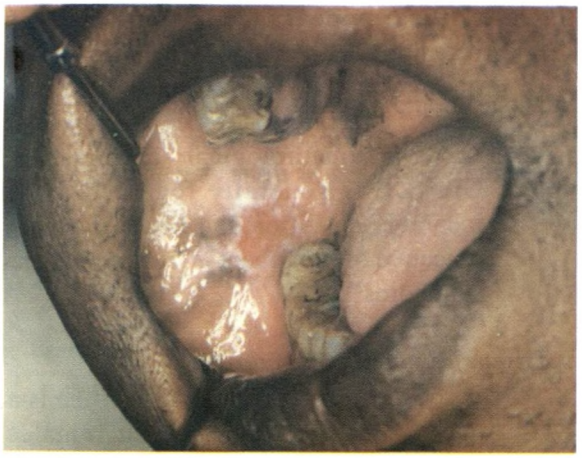

Figure 9. Discoid lupus erythematosus

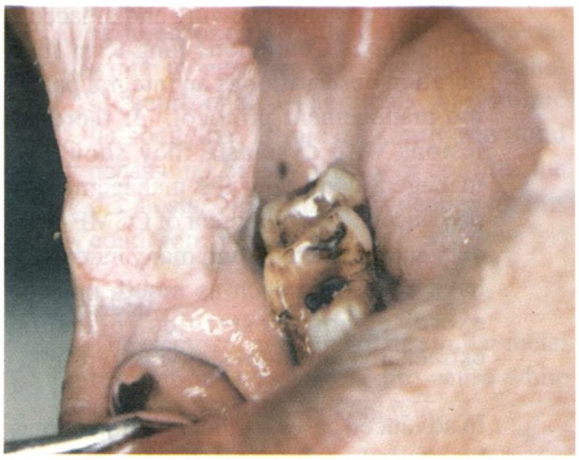

Figure 10. Squamous cell carcinoma

Lesions which show up hyperkeratosis or mild dysplasia can be kept under observation. If there are changes suggestive of malignant transformation, during the close observation period a biopsy should be repeated. Severe dysplastic lesions should be removed. All patients who had undergone surgery also should be followed up carefully [22].

q. Oral submucous fibrosis

Oral submucous fibrosis (OSMF) is a chronic, insidious, disabilitating disease of the oral mucosa affecting any part of the mouth and rarely the pharynx, larynx and oesophagus [23] (Figure 6). This condition occurs almost exclusively in people of the Indian subcontinent [24]. The exact etiology of this condition is complex and the pathological process is yet to be understood. However, the role of arecanut chewing habit as an aetiological factor has been established[25,26].

At the early stages the affected individuals experience burning sensation and inability to tolerate spicy food. Furthermore, they experience dryness in the mouth, alteration of taste and hypersalivation. With the advancing disease the mucosa becomes pale and stiff leading to inability in opening the mouth[27,28].

The diagnosis of the disease at the late stages is not difficult due to the presence of all the stigmata of the disease. However, at the early stages the characteristic features of palpable fibrous bands are not present. Therefore, it is recommended that OSMF be diagnosed if one or more of the following characteristics are present. They are 1. Palpable fibrous bands, 2. Mucosal texture feels rough or leathery, 3. Blanching mucosa with histopathological features characteristic of OSMF (atrophic

epithelium loss of rete ridges and juxta epithelial hyalinization)[29].

In the long term management quitting the habits of arecanut chewing and tobacco is mandatory. Continuous long-term short duration observation is an integral part of the management protocol. If there are lesions with dysplasia they should be managed along with the management of precancers. The treatment of OSMF is not very successful although many modalities have been tried such as mouth opening exercise, cortocosteroids, placental extracts,hyaluronidase, chymotrypsin[30].

In advanced cases surgical treatment may be needed such as bilateral temporalis myotomy or coronoidectomy [25]. Intra-lesional injection of interferon gamma together with stretching exercises appear to have a significant therapeutic effect [31,32].

E. White lesions related to smokeless tobacco

Smokeless tobacco is a popular form of tobacco used as snuff or chewing forms particularly among adolescents [33]. Both forms of smokeless tobacco can cause white lesions in the mouth. However, snuff appears much more likely to cause oral lesions than chewing[3], while dysplasia is more likely to occur in tobacco chewers[7]. The lesion is usually associated with the site where the tobacco is placed. The affected area generally shows a wrinkled or granular surface[3] (Figure 7).

Discontinuation of the habit in most instances would resolve the problem. To develop malignancy a long-term exposure is necessary .

F. Dermatological conditions

r. Lichen planus

Lichen planus (LP) is relatively a common mucocutanous condition affecting 1-2% of the population[3,34]. Clinically oral lesions may appear in various combinations of reticular, plaque like, bullous, atrophic and erosive forms [35] (Figure 8). Although, it is not difficult to diagnose the lesion on clinical appearance, plaque like LP resembles leukoplakia which commonly occurs on the dorsum of the tongue. Hence, the confirmation of the diagnosis needs histopathological examination. Oral LP is generally regarded as an incurable condition and hence the main objective of treatment is to minimize the symptoms[36].

s. Discoid lupus erythematosus

Discoid lupus erythematosus (DLE) is a disease of the middle aged females affecting the skin. However, oral lesions may be accompanied by skin lesions. The buccal mucosa, gingiva and vermilion are the most commonly affected oral mucosal sites. Lesions appear as erythematous or erosive areas often surrounded by white striae radiating from the periphery (Figure 9). Lesions are indistinguishable from oral LP unless biopsied . DLE is considered to be a precancerous condition and hence attention has to be paid in view of preventing malignant transformation[17].

G. Benign and malignant tumours

t. Squamous cell papilloma

Squamous cell papilloma is a benign tumour originating from the epithelium. Human papilloma virus (HPV) has been regarded as the aetiological factor. This lesion could occur in any part of the oral mucosa with a predilection to the junction between hard and the soft palate. The lesion is usually pedunculated with a papiliferous suface with a whitish colour. The lesions are generally asymptomatic. It can be easily treated with surgical excision or laser oblation [37].

u. Squamous Cell Carcinoma / Verrucous carcinoma

Squamous cell carcinoma may appear as a white patch or a growth (Figure 10). Furthermore, a carcinoma may appear in a pre-existing white lesion such as leukoplakia. Verrucous carcinoma usually presents as an exophytic growth and the surface may show up features of keratosis which appear white.

H. Other exophytic growths

v. Verruca

Verruca vulgaris is caused by HPV. Lesions usually appear in the oral mucosa due to autoinnoculation from affected fingers [38]. Verracae generally appear as warty or smooth surface papules. They appear as white exophytic lesions commonly occuring on lips or commisures. Lesions can be removed surgically by laser or cryotherapy.

v. Condylomata

This infectious lesion characteristically occurs in anogenital region. However, oral mucosa also may be involved. This lesion is aetiologically related to HPV sub types 6 and 11 [37]. These lesions are commonly seen on the tongue or palate in patients with sexually transmitted disease or in immunocompromised patients[7]. Treatment is generally by surgical excision using laser, cryosurgery or scalpel excision.

I. Miscellaneous

w. Leukoedema

This generalized buccal mucosal condition is a variation from the normal. The aetiology of this condition is not yet known. It is an asymptomatic condition and hence found in routine clinical examination. Clinical appearance is characterized by diffuse filmy or milky white, and when the mucosa is stretched the opaque changes dissipate. This condition is seen commonly in dark skinned people, although leukoplakia, white spongy naevus, hereditary benign intraepithelial dyskeratosis may mimic leukoedema. Clinical examination and occasional biopsy will help confirm the diagnosis. No treatment is needed for this condition.

x. Galvanism

The electrical potential of dissimilar metal restorations was believed to cause white lesions similar to leukoplakia.

y. Chemical burns

The most common burn of the oral mucosa is due to aspirin which usually occurs when patients keep aspirin in the buccal sulcus in relation to an aching tooth. Lesions due to chemical burns usually appear as a white patch with sloughy mucosa. History would suggest the possible aetiology and hence diagnosis is straightforward. Lesion is self limiting but antiseptic mouthwashes such as 0.2% chlorhexidine my be beneficial.

z. Skin grafts

Skin grafts in the mouth may appear white or creamy in colour. Margin is regular in outline and show hair in some grafts. This may be mistaken for leukoplakia.

Conclusion

White lesions in the mouth are due to a diverse array of causes. Some of the white lesions may carry a significant health problem especially due to its aggressive nature such as malignancy.

Identification of white, potentially malignant lesions is of utmost importance in view of prevention of malignant transformation. Furthermore, some

white lesions may pose unneccessary cancerphobia in patients. Hence, careful attention is needed in managing patients with oral mucosal white lesions.

A. Developmental	a.White sponge naevus b. Dyskeratosis congenita c. Benign intra epithelial dyskeratosis d. Keratosis follicularis e. Pachyonychia congenita f. Fordyce's spots
B. Reactive	g. Frictional keratosis h. Smokers palate
C. Infective (i) Viral (ii) Fungal (iii) Bacterial	i. Hairy leukoplakia j. Koplik's spots k. Acute pseudomembranous candidosis l. Chronic hyperplastic candidosis m. Chronic mucocutaneous candidosis n. Syphilitic glossitis
D. Premalignant lesions and conditions	o. Leukoplakia p. Oral submucous fibrosis
E. White lesions associated with smokeless tobacco	
F. Dermatological conditions	q. Lichen planus r. Discoid lupus erythematosus
G. Benign and malignant tumours	s. Squamous cell papilloma t. Squamous cell carcinoma /Verrucous carcinoma
H. Other exophytic growths	u. Verrucae v. Condylomata
I. Miscellaneous	w. Leukoedema x. Galvanism y. Burns z. Skin grafts

References

1. Whitten J B. The electron microscopic examination of congenital keratoses of the oral mucous membrane. Oral Surg 1970; 29(1): 69-83.
2. Busen N, Htompkin M. Perianal white sponge nevus in a Hispanic female: A case study. The internet journal of advanced nursing practice 4 (2) 2001. (http ://www.icaap.org/iuicode).
3. Regezi J A, Scuibba JJ. Oral pathology – clinical and pathologic correlations. 3rd edition. Philadelphia: Saunders 1999; 83-121.
4. Cawson R A, Binnie W H, Eveson J W. Colour atlas of oral disease – clinical and pathologic correlations. 2nd edition.London. Mosby 1994; 12.2 .

5. Shafer W G, Hine M K, Levy B M. A text book of oral pathology. 4th edition. Philadelphia. Saunders 1983: 824-825.
6. Ogden G R, Chisholm D M,. Dyskeratosis congenita: Report of case and review of literature. Oral Surg Oral Med Oral Pathol 1988; 65: 586-591.
7. Scully C, Porter S. Orofacial disease: update for dental team. Dental update 1999; 20:123-129.
8. Rossie K M, Guggenheimer J. Thermally induced "nicotine"stomatitis: A case report 1990; Oral Surg Oral Med Oral Pathol 1990; 70 : 597-599.
9. Greenspan D, Greenspan J S, Conaut M, Peterson V, Silverman S Jr De Souza Y. Oral "hairy" leukoplakia in male homosexuals: evidence of association with both papilloma virus and herpes group virus. Lancet 1984;ii: 831-834.
10. Greenspan D, Greenspan J S. HIV related oral disease. Lancet 1996; 348: 729-733.
11. Samaranayake L P, Lamey P J. Oral candidosis – clinicopathological aspects. Dental update 1988; Jul / Aug 227-231.
12. Holmstrup P, Samaranayake LP. Acute and AIDS related oral conditions. In: Samaranayake L P, Mac Farlane T W (eds) Oral candidosis. Wright. London,1990;153-183.
13. Walker D M, Arendorf T. Candidal leukoplakia, chronic multifocal candidosis and median rhomboid glossitis. In: Samaranayake L P, Mac Farlane T W (eds) Oral candidosis. Wright. London,1990;184-199.
14. Lynch D. Oral candidosis. Oral Surg Oral Med Oral Pathol 1994;78: 189-193.
15. Porter S R Scully C. Chronic mucocutaneous candidosis. In: Samaranayake L P, Mac Farlane T W (eds) Oral candidosis. Wright. London,1990;200-212.
16. Bryan M G, Libow L. Chronic mucocutaneous candidosis. E Medicine Journal 2001; 2(6) (http://www. emedicine.com/derm)
17. Pindborg J J,Reichart P A, Smith C J, van der Wall I. WHO Histological typing of cancer and precancer of the oral mucosa. 2nd ed. New York. Springer 1997.
18. Prabhu S R, Bhutani L K, Shetty J N. Bacterial infections due to spirochetes. In: Prabhu SR, Wilson D F,Daftary D K, Johnson N W (eds) Oral diseases in the tropics. Oxford University press. Delhi, 1993: 215- 251.
19. Brightman V J. Diseases of the tongue. In: Lynch M A, Brightman V J, Greenberg MS (eds) Burket's Oral medicine – diagnosis and treatment. 9th edition. Lippincott. Philadelphia, 1994: 240 –300.
20. Axell T, Pindborg JJ, Smith C J, van der Wall I. Oral white lesions with special reference to precancerous and tobacco related lesions: conclusion of an international symposium held in Uppsala, Sweeden J Oral Pathol Med 1996; 25: 49-54.
21. Hansen L S, Olson J A, Silverman S jr. Proliferative verrucous leukoplakia. Oral Surg Oral Med Oral Pathol 1985; 60: 285-298.
22. Daftary D K, Murti P R, Bhonsle R B, Gupta P C, Metha F S, Pindborg JJ. Oral precancerous lesions and conditions of tropical interest. In: Prabhu SR, Wilson D F,Daftary D K, Johnson N W (eds) Oral diseases in the tropics. Oxford University press. Delhi, 1993: 402- 428.
23. Borle R M, Borle S R. Management of oral submucous fibrosis. J Oral Maxillofac Surg 1991; 49: 788-791.
24. Pindborg JJ, Murti P R, Bhonsle R B, Gupta P C, Daftary D K, Metha FS. Oral submucous fibrosis as a precancerous condition. Scand J Dent Res 1984; 92: 224-229.
25. Canniff J P, Harvey W, Harris M, Oral submucous fibrosis: its pathogenesis and management. Br Dent J 1986; 160: 429-434.
26. Maher R, Lee A J, Warnakulasuriya KAAS, Lewis J A, Johnson N W. Role of arecanut in the causation of oral submucous fibrosis: A case control study in Pakistan. J Oral Pathol Med 1994; 23:65-69.
27. Pindborg JJ, Chawla TN,Srivastava A N, Gupta D, Mehrotra M L. Clinical aspects of oral

submucous fibrosis. Acta Odont Scand 1964; 22: 679-691.

28. Johnson N W, Maher R, Trivedly C, Warnakulasuriya S. The clinical features and pathology of oral submucous fibrosis. Meeting report. Oral Diseases 1997; 3: 276-291.
29. Zain R B, Ikeda N, Gupta P C, Warnakulasuriya KAAS, Shresta P, Axell T. Oral mucosal lesions associated with betel quid, areca nut and tobacco chewing habits: consensus from a workshop held in Kualalumpur, Malaysia, Nov 25-27, 1996. J Oral Pathol Med 1999; 28: 1-4.
30. Gupta D, Sharma S C. Oral submucous fibrosis- A new treatment regimen. J Oral Maxillofac Surg 1988; 40:8
31. Harris M, Haque M F, Meghji S. Treatment of oral submucous fibrosis. Meeting report. Oral diseases 1997;3: 290-291.
32. Haque M F, Meghji S, Harris M. Immunohistochemistry of Oral submucous fibrosis – pre- and post inteferon gamma treatment. Meeting report. Oral diseases 1997;3: 289-290.
33. Connolly G N, Winn D M, Height SS, Henningfield J E, Walker B, Hoffman D. The reemergence of smokeless tobacco. N Engl J Med 1986; 314:1020- 1027.
34. Eisen D, Lynch P D. The mouth: Diagnosis and management. Missoury. Mosby 1998: 149-152.
35. Anderson J O. Oral lichen planus – a clinical evaluation of 115 cases. Oral Surg Oral Med Oral Pathol 1998; 25 : 31-44
36. Silverman S, Gorsky M, Lozata – Nur F Giannottic. A prospective study of findings and management in 214 patients with oral lychen planus. Oral Surg Oral Med Oral Pathol 1991; 72:625-670.
37. Regezi J A, Scuibba JJ. Oral pathology – clinical and pathologic correlations. 3rd edition. Philadelphia: Saunders 1999: 160-175.
38. Cawson R A, Binnie W H,Eveson J W. Colour atlas of oral disease – clinical and pathologic correlations. 2nd edition.London. Mosby 1994; 13.3 .

RESEARCH ARTICLE

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Premature termination of orthodontic treatment by patients in hospital practice in Sri Lanka

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Abstract

Introduction: *In a state funded orthodontic service with shortage of manpower which result in the inability to pay adequate attention during case selection could lead to failure of identifying patients who may discontinue treatment prematurely. As the failure to complete treatment is one of the greatest risks of orthodontic treatment, the expected benefit of treatment in a state funded hospital is doubtful.* ***Objective:*** *The objective of the present investigation was to find out the rate of discontinuation and the nature of patients who have terminated orthodontic treatment prematurely, in order to take precautions to reduce the drop out rate in the hospital practice.* ***Materials and Methods:*** *The sample studied consists of records of 100 consecutively started orthodontic patients treated by a specialist. The relevant factors such as the patient's age, gender, distance traveled, extraction pattern, type of appliance used and the severity of the malocclusion were recorded. The study casts of all the cases were scored using PAR index (Peer Assessment Rating) to determine the severity of malocclusion.* ***Results:*** *The discontinuation rate of the sample was found to be 26%. The comparison of completed and discontinued groups revealed that the discontinuation rate was not related to the severity of the malocclusion (Mean PAR score for completed group was 34.69 and for discontinued group was 32.46). The rate of discontinuation was also not related to the age, gender, distance traveled, and to the extraction pattern. Discontinuation rate was greater in patients treated with removable appliances (55%) compared to those treated with fixed appliances (11.7%) (P<.05)*

Key words : *Discontinuation of treatment, orthodontic patients*

Introduction

The aim of orthodontic treatment is to provide improved function by correction of occlusal irregularities in order to create greater resistance to disease and also to improve facial appearance of the individual. Improved facial appearance will in turn contribute to the mental as well as physical well being of the individual. Even though improvement of the health is considered as the main objective of orthodontic treatment there is very little evidence in recent literature justifying orthodontic treatment on dental health grounds[1,2].Therefore the benefits of orthodontic interventions have to be balanced against treatment risks and cost in order to safeguard the individual from orthodontic procedures, that are of little benefit or even harmful. It is also equally important to avoid unnecessary treatment to prevent exhaustion of limited economic resources available in the health care system of a developing country like Sri Lanka.

The risks of orthodontic treatment include the possible tissue damage, increased susceptibility to dental disease and partial or complete failure to accomplish goals of orthodontic treatment. Failure

to accomplish goals of orthodontic treatment is mainly due to inaccurate diagnosis which leads to underestimation of constraints of skeletal discrepancies which are beyond orthodontic interventions for successful correction of the malocclusion. The mismanagement of space and anchorage requirement, faulty technique and poor patient compliance also play a major role in the failure of treatment. All the above factors other than patient compliance are within the control of the orthodontist. Even if meticulous attention is given during orthodontic diagnosis, treatment planning and use of treatment mechanics, if the patient fails to complete the course of treatment, expected goals of the orthodontic treatment could not be achieved leading to failure of treatment.

Failure to complete treatment due to premature termination of treatment by the patient is one of the known risks of orthodontics which is well established in orthodontic literature[3]. Even though, orthodontic treatment is mainly provided by the state funded hospitals in Sri Lanka, a system of auditing quality of treatment and the cost effectiveness is not yet established.

The purpose of the present investigation was to estimate the rate of premature termination of orthodontic patients in hospital practice in Sri Lanka and to identify the nature of the patients who terminate treatment prematurely.

Materials and methods

The sample studied consists of one hundred consecutively started orthodontic patients who attended the Orthodontic Unit, Faculty of Dental Sciences, University of Peradeniya for treatment during the year 1994. All the cases were diagnosed and treated by a specialist. The hospital records of these patients were perused to determine the age of the patient, gender, distance traveled to the hospital, pattern of extraction of teeth and type of appliance used. Whether the patient continued the treatment until expected goals of treatment were achieved was also recorded.

The severity of the malocclusion was assessed using PAR (Peer Assessment Rating) index[4]. The concept of PAR index is to score the various occlusal traits which make up a malocclusion. The individual scores are summed up to obtain overall total representing the degree by which a case deviates from normal alignment and occlusion. The PAR index in summary applies a score to the following occlusal features when examining a set of study models.

- Upper labial segment -(1)
- Lower labial segment (1)
- Buccal segment relationship (1)
- Over jet - (6)
- Over bite (2)
- Center line (4)

The figure in the brackets represents the weightage given to each feature of the malocclusion. The weightages given in the index were derived from a validation exercise which had been carried out to reflect contemporary orthodontic opinion[5].

Pre-treatment study models of all patients included in the study were measured using the PAR ruler (Ortho-Care UK Limited) by the author. PAR score was calculated for each set of study model. After an interval of one month, randomly selected 26 sets of study models were measured as a validation exercise. Intra-examiner variability was assessed using Kappa statistics. The result obtained was 0.86. A Kappa value greater than 0.80 is indicative of very high level of agreement[6]. It would appear therefore that PAR index is highly reproducible.

Data analysis was done to estimate the rate of discontinuation and to identify the nature of the patients who terminated treatment prematurely using the variables age, gender, distance traveled to the hospital, pattern of extraction, type of appliance used and severity of the malocclusion.

Results

The total number of patient records examined was 100; 48 males and 52 females. The majority (79%) of the patients were below 15 years of age. The rate of discontinuation (premature termination by the patient) was 26%.

Table 1 shows the results of the Pearson Chi-Square test for the relatedness or independence of the variables.

Distribution of patients according to the gender with the rate of discontinuation is given in Table 2. The rates of discontinuation among males and females were 25% and 26.9% respectively. There was no statistical significance between the two groups. (Pearson Chi-Square value is 0.226 with a P value of 0.634).

Table 3 shows the distribution and the rate of discontinuation according to the age group. The group below 15 years of age showed a discontinuation rate of 31.7% and the group above 15 years showed a 50% rate of discontinuation . The difference between the two groups was not statistically significant. (Pearson Chi-Square value is 0.743 with a P value of 0 .389)

The distribution with the rate of discontinuation according to the distance traveled to the hospital is given in Table 4. Seventy nine percent of the sample lived within the radius of 20 km. The rate of discontinuation of those who lived within 20km. radius was 40% and those who lived beyond 20km. radius was 24%. There was no statistically significant difference between the continued and the discontinued groups in terms of the distance traveled to the hospital (Pearson Chi-Square value is 1.03 with a P value of 0.310).

Distribution of the patients and the rate of discontinuation according to the pattern of extraction is given in Table 5. Those who were treated with non extraction techniques showed a greater rate of discontinuation (48.4.%) when compared with those who were treated with extraction techniques (27.7%). The difference was not statistically significant.(Pearson Chi-Square value is 1.46 with a P value of 0.226)

Table 6 shows the distribution of the patients according to the type of appliance used. Sixty two percent (62%) of patients were treated with removable appliances and 38% patients were treated with fixed appliances. The rate of

Table 1. Results of Chi-Square Test for relatedness or independence

Variable	CalculatedX_2	TabulatedX_2	Degree of freedom	Alpha level	Minimum expected cell count	P value
Gender	.226	3.84	1	.05	11.96	.634
Age	.743	3.84	1	.05	5.46	.389
Distance	1.031	3.84	1	.05	8.06	.310
Extraction	1.464	3.84	1	.05	10.40	.226
Appliance	7.627	3.84	1	.05	9.88	.006

Table 2. Distribution and rate of discontinuation in terms of gender

Gender	Treatment continued	Treatment discontinued	Discontinuation rate
Male	48	13	26.9%
Female	52	13	25%
Total	74	26	

Table 3. Distribution and rate of discontinuation in terms of age group

Age group	Treatment Continued			Treatment Discontinued			Discontinuationrate
	Male	Female	Total	Male	Female	Total	
<15 years	30	30	60	9	10	19	31.66%
> 15 years	3	11	14	4	3	7	50%
Total	33	41	74	13	13	26	

Table 4. Distribution and rate of discontinuation in terms of distance to the hospital

Distance	Treatment Continued			Treatment Discontinued			Discontinuationrate
	Male	Female	Total	Male	Female	Total	
< 20 Km	23	26	49	11	9	20	40.9%
> 20km	10	15	25	2	4	6	24%
Total	33	41	74	13	13	26	

Table 5. Distribution and rate of discontinuation in terms of the pattern of extraction

Extractionpattern	Treatment Continued			Treatment Discontinued			Discontinuationrate
	Male	Female	Total	Male	Female	Total	
Extraction	20	27	47	7	6	13	27.65%
Non extraction	13	14	27	6	7	13	48.41%
Total	33	41	74	13	13	26	

Table 6. Distribution and rate of discontinuation in terms of the appliance used

Appliance	Treatment Continued			Treatment Discontinued			Discontinuationrate
	Male	Female	Total	Male	Female	Total	
Removable	19	21	40	9	13	22	55%
Fixed	14	20	34	4	0	4	11.76%
Total	33	41	74	13	13	26	

discontinuation of patients who were treated with removable appliances was 55% and of the group treated with fixed appliances the rate was 11.8%. The difference was statistically significant with Pearson Chi-Square value of 7.63 and a P value of 0.006. A greater rate of discontinuation was seen in the group treated with removable appliances when compared to those treated with fixed appliances.

The mean PAR score for the group who completed the treatment was 34.69(13.49) and for those who discontinued treatment was 32.46(11.62). There was no significant difference of the mean PAR score between the two groups (95% CI for difference, -3.67 to 8.13). The rate of discontinuation of the sample studied was not related to the severity of the malocclusion.

Discussion

The aims of the present study were to determine the rate of discontinuation of orthodontic patients and to identify the nature of the patients who terminated treatment prematurely. Clinical studies in Orthodontics are frequently reported as being consecutively treated but often this means consecutively completed. This automatically excludes the patients who fail to complete a course of treatment. Thus, a series of consecutively treated cases may be no more than a series of outstanding case reports[7] . The only valid way of assessing

the rate of discontinuation is to include all consecutively started cases. As the severity of the malocclusion was assessed measuring the pre treatment study models using the PAR ruler the sample of one hundred consecutively started cases were studied to reduce the measurement error.

The rate of discontinuation in the present study is 26%. Any discontinuation of orthodontic treatment is highly undesirable and every reasonable step should be undertaken to reduce its incidence as far as possible. The study reveals the nature of the patients who terminate treatment prematurely in hospital service in Sri Lanka.

The level of discontinuation in orthodontics is well documented in orthodontic literature. This has been extensively studied in British National Health Service. Schanshieff [8] has reported 25% of discontinuation rate. Others, Rose,[9] Haynes,[10] Cousins,[11] Haynes,[12] Brattstrom [13] and Shaw et al.[14] have reported varying levels of discontinuation rates. These levels have improved to a great extent after introduction of the strict quality control methods in British National Health Service. Eaton et al. [15] have reported 12.1% and 13.5% rates of discontinuation of patients who were treated by the clinicians with specialist qualification and without specialist qualification respectively.

In Sweden where most of the orthodontic treatment is provided by public health service, treatment is free for patients below 20 years of age provided that there is an acceptable orthodontic need for such treatment. As the treatment is easily available and free, the frequency of prematurely terminated cases might be expected to be higher than in countries where the treatment is paid by the parent. But rates of discontinuation reported were comparatively low in many studies. Brattstrom et al. [13] have reported 4% rate of discontinuation in cases treated over a ten year period.

The overall rate of discontinuation of the patients during active treatment in the present study is 26% which is a very high level of discontinuation when compared with the British and Swedish National Health Services which employ very strict patient selection criteria using Index of Treatment Need (IOTN) [16].

The rate of discontinuation (26%) in the present study is comparable with the results of Schanshieff [8] (25%), a study which has been carried out before introduction of indices of treatment need in British National Health Service. Twenty six percent of discontinuation rate found in the present study is considerably a greater rate of discontinuation when compared with the available manpower and resources in a developing country.

There is a wide variation of results according to the nature of the patients who have terminated treatment prematurely. Richmond and Andrews [17] have shown a greater rate of discontinuation among those who had mild malocclusions, who were treated with non extraction treatment using removable appliances. Eaton et al.[15] have found that the levels of discontinuation was age related and those who were below 18 years of age had a lower rate of discontinuation. Wilmot et al.[18] reported that a greater rate of discontinuation was seen in cases treated with removable appliances than in cases treated with fixed appliances.

Present study did not show statistically significant difference between the two groups who continued or discontinued treatment with regard to the age, gender, distance traveled to the hospital, extraction pattern and severity of malocclusion. Statistically significant difference was seen with regard to the type of appliance used for correction of malocclusion. Greater rate of discontinuation was seen in cases treated with removable appliances (55%) when compared with fixed appliances(11.76%) as in the study reported by Willmot[18].

In common with other studies, this study too indicated that when the appliances are removable from the mouth, treatment is more likely to be discontinued than when fixed appliances are used. Such patients have control of their appliances and can more easily discontinue treatment at their own will. Therefore, the factors like patient compliance and motivation which have not been considered in the present study need to be considered in future investigations to improve cost benefit of the orthodontic treatment in hospital practice in Sri Lanka.

References

1. Hunt O, Hepper P, Johnston C, Stevenson M, Burden D. Professional perceptions of the benefits of Orthodontic treatment .Eur J Orthod 2001 June; 23(3) 315-23.
2. McComb JL, Wright JL, Fox NA, O'Brien KD. Perceptions of the risks and benefits of orthodontic treatment. Community Dental Health 1996 Sep;13(3): 133-8.
3 Shaw WC, Richmond S Quality control in Orthodontics: Risk/Benefit considerations. British Dental Journal. 1991 Jan; 5:33-37.
4. Richmond S, Shaw WC, Roberts T, Andrews M. The PAR index (Peer Assessment Rating); method to determine the treatment outcome of orthodontic treatment in terms of improvement and standards. Eur J Orthod 1992;14:180-187.
5 Richmond S, Shaw WC, O'Brien KD, Buchanan B, Jones R, Stephen CD, et al. The development of the PAR index (Peer Assessment Rating); reliability and validity. Eur J Orthod 1992;14:125-139.
6 Landis JR, Kock GG, The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.
7 Jones MC. The Barry project-a three dimensional assessment of occlusal treatment changes in a consecutively referred sample; in incisors. British J Orthod 1990; 17: 1-19.
8. Schanshieff S. Committee of Enquiry into Unnecessary Dental Treatment. HMSO. London. ISBN 0 11 321051.
9 Rose JS. A thousand consecutively treated orthodontic cases: a survey. British J Orthod 1974; 1: 45-54.
10. Haynes S. Discontinuation of Orthodontic treatment in the general dental service in England and Wales 1972-1979. British J Orthod 1982; 152: 127-129.
11. Cousins AJ, Lewis HG, Vaider PH. Changes in Orthodontic treatment pattern within one orthodontic practice over a 15 year period. British J Orthod 1981; 8: 11-14.
12 Haynes S. Trends in the number of active and discontinued orthodontic treatments in the general dental service. 1964-1986/87. British J Orthod 1991; 18: 312-323.
13 Brattstrom V, Ingelsson M, Alberg E. Treatment coorperation in orthodontic patients. British J Orthod 1991; 18: 37-42.
14. Shaw WC, Richmond S, O'Brien KD, Brook P. Quality control in orthodontics: indices of treatment need and treatment standards. British Dental Journal 1991; 170: 107-112.
15. Eaton KA, Stephens CD, Heesterman RA. Discontinued orthodontic treatment in the general dental service and community dental service in England and Wales during the summer of 1991. Br J Orthod 1996; 23 (2): 125-8.
16 Brook PH, Shaw WC. The development of an index for orthodontic treatment priority. Eur J Orthod 1989; 11: 309-332.
17. Richmond S, Andrews M. Discontinued orthodontic treatment in the general dental service of England and Wales (1990-1991). Br J Orthod 1995; 22: 263-268.
18 Willmot DR, Dibiase D, Birnie DJ, Heesterman RA. The consultant orthodontic group survey of hospital waiting lists and treated cases. British J Orthod 1995; 22 (1); 53-7.

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Relational database management system for reporting histopathological data.

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Abstract

It has been an accepted fact that most of the hospitals in Sri Lanka do not have proper recording systems for both laboratory and clinical data. In the recent past this field has improved dramatically in a global scale, especially after the introduction of computers. The present system which was developed using Microsoft Access to send histopathology reports enables both pathologists and clinicians to gather information about their patients. Basically two data bases, namely personal and subsequent visit, have been coupled in order to include both histopathological and personal data in the system. The patient's data can be recalled by using various individual parameters such as patient's name, date of birth etc. Provision for statistical analysis in the package enhance the possibility of research and clinical audit.

***Key Words**: Pathology Reports, Microsoft Access, statistics*

Introduction

Reporting of data is one of the key areas in both research activities and in conveying laboratory findings to clinicians. Storage of medical data is a compulsory issue in developed countries for various reasons such as medico-legal purposes, patient follow-up and research etc. In developing countries such as ours the inadequate use of modern facilities has been a major drawback in data reporting systems. An organised data reporting system will certainly enhance the proper management of patients with the help of readily available follow-up data and all the relevant information regarding the patient. Medico-legal problems are not a main concern in our country at present but considering the likelihood of this particular problem the patient records should be kept for various time periods depending on the type of data.

The present data reporting system was designed in order to facilitate the function of diagnostic Oral Pathology reporting service in the Department of Oral Pathology, Faculty of Dental sciences, University of Peradeniya. The program was designed with the use of Microsoft Access database management system software. Therefore the objective of this study was to introduce a simple system of data reporting in the practice of histopathology. The new system has been in use for a period of almost one year with extreme success, overcoming the difficulties and shortcomings experienced with the previous conventional system using typewriters.

Method

The present system is composed of relational databases, which have been linked together. To run the present system certain hardware facilities are necessary. Preferably the computer should have windows 95, 98 or 2000 with MS office 97 or 2000.The hard disc capacity of 1GB or more and 166MHz or more clock speed will bring about a better performance. The specific requirements of the Pathologist was given a special emphasis as this data base has been designed for the Histopathology reporting service. Accordingly two databases were established as personal database and subsequent visit detailed database. The patient's personal details such as name, age, sex etc were included in the former whilst all the other information shown in Figure 1 were entered into the latter database.

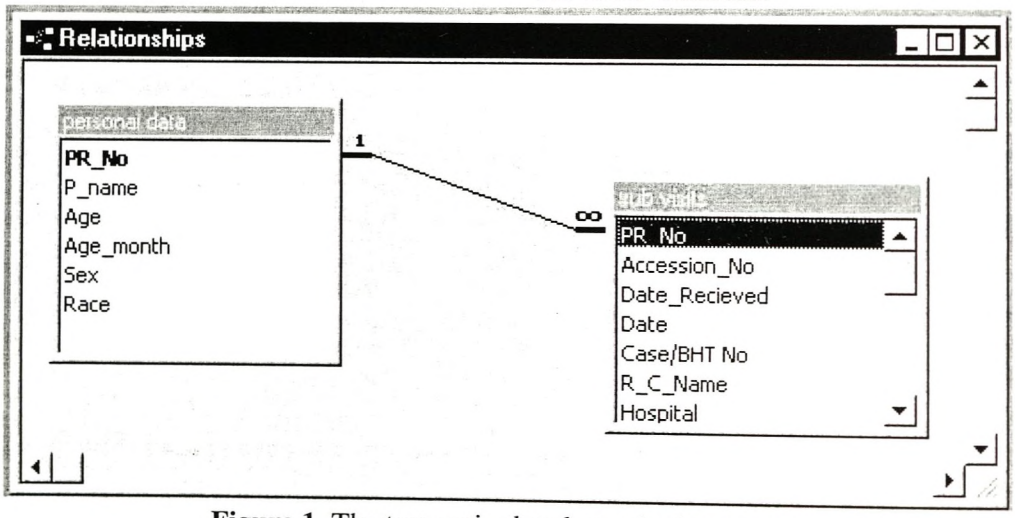


Figure 1. The two main data bases in the system

Each patient was given a personal identification number (PR No) which can be used to trace the patient during all subsequent visits. It is much easier if the clinicians mention the PR number of the particular patient in the request form when they send the biopsy. Another number that was given to each biopsy is called the accession number, which also helps to trace the individual case. But one patient can have several accession numbers if multiple biopsies have been carried out in the past. When the patient is recalled by the PR number all the accession numbers of the case appear on the screen.

All the diseases were labelled using internationally recognised numbering system known as SNOMED (Systematic Nomenclature of Medicine). According to this system, each anatomical site of the body and each disease has a specific number which certainly helps both the Pathologist and the clinician in various aspects.

The provision has been made in the system for simple statistical analysis.

The main menu of the program was designed in a very simple way including all the important sections of the program (Figure 2). It is easy to enter into the specific section of the program which the operator is interested in just by clicking the mouse.

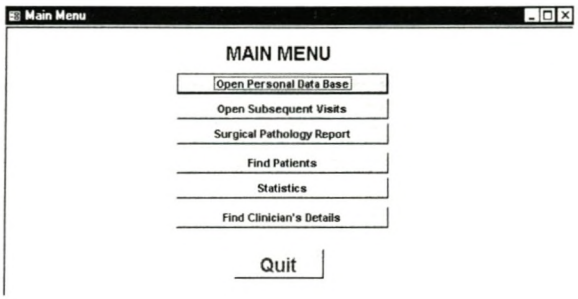


Figure 2. Main menu of the program

Entering data is straightforward as each individual parameter is given a separate cage. The details of the patient should be entered into both the personal database (Figure 3) and to the subsequent visit database (Figure 4).

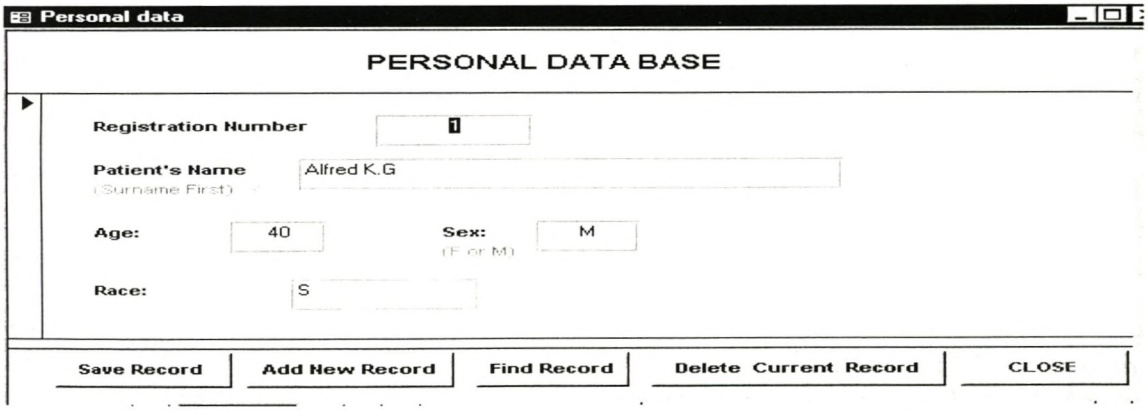


Figure 3. Personal data base

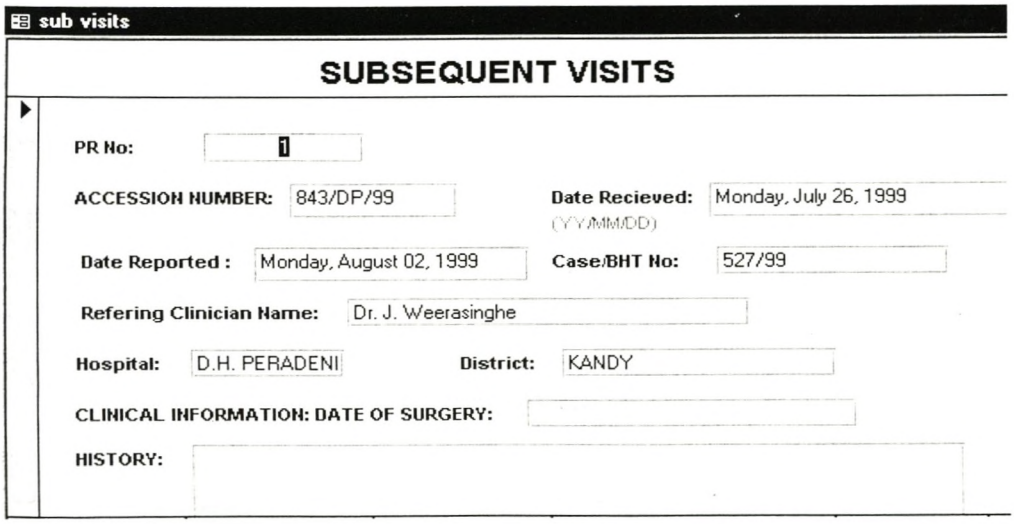
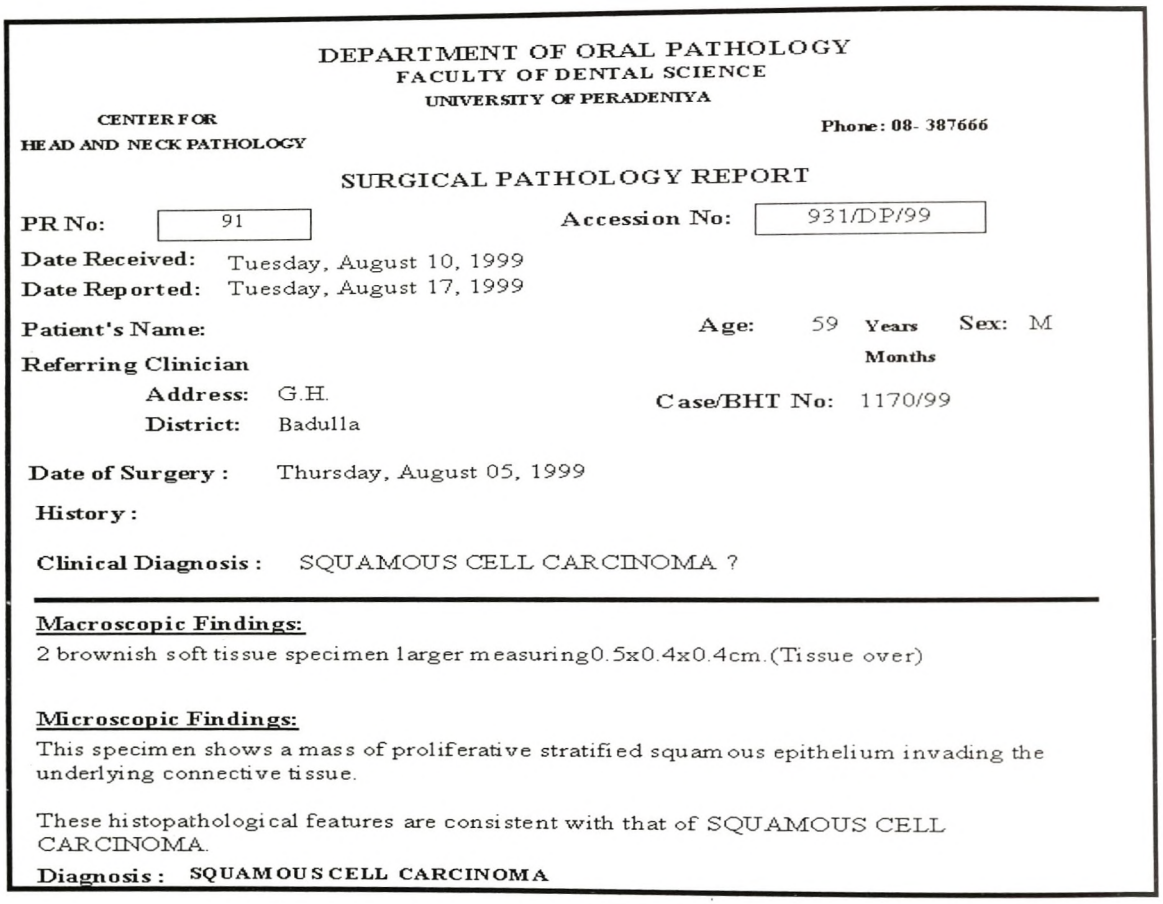


Figure 4. Data base for subsequent visits

The final report which is sent to the clinician is a very comprehensive but easily understandable one and the important information is highlighted in the report (Figure 5)



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SURGICAL PATHOLOGY REPORT

PR No: 91 Accession No: 931/DP/99

Date Received: Tuesday, August 10, 1999
Date Reported: Tuesday, August 17, 1999

Patient's Name: Age: 59 Years Sex: M
Months

Referring Clinician
Address: G.H.
District: Badulla

Case/BHT No: 1170/99

Date of Surgery : Thursday, August 05, 1999

History :

Clinical Diagnosis : SQUAMOUS CELL CARCINOMA ?

Macroscopic Findings:
2 brownish soft tissue specimen larger measuring0.5x0.4x0.4cm.(Tissue over)

Microscopic Findings:
This specimen shows a mass of proliferative stratified squamous epithelium invading the underlying connective tissue.

These histopathological features are consistent with that of SQUAMOUS CELL CARCINOMA.

Diagnosis : SQUAMOUS CELL CARCINOMA

Figure 5. Final report

Discussion

It is well known that reporting medical data in a clear and scientific way certainly improves the quality of both medical and dental services. The use of computer with the help of a simple program such as Microsoft Access will give the Pathologist and the Clinicians adequate details of their patients. An expert knowledge on computers is not necessary to run this program. There are numerous advantages of this program are:

1. Readily available data on patient's previous disease conditions. All previous records of the patient can be traced easily using the personal identification number (PR number). This will enhance the diagnostic accuracy of the subsequent biopsies from the same patient. Therefore the quality of the treatment will automatically be improved.
2. Easy access to data for research purposes.
3. The correction of reports before sending to clinicians is much quicker than using a conventional type writer.
4. Ability to maintain a register for various disease entities in the country according to international standards. All the disease entities can be compared with disease levels in other

countries because of the use of SNOMED system.

5. Provision has been made for statistical analysis of various parameters. The menu for the above function shows the possible entry points to the analysis (Figure 6).
6. This system has two ways of backing up data. Firstly it saves in the tape drive and secondly the data can be retrieved from the main server of the Hospital.
7. The system can be protected with a password.

A main limitation of this system is that MS Access is necessary to run the program since this is not a compiled program.

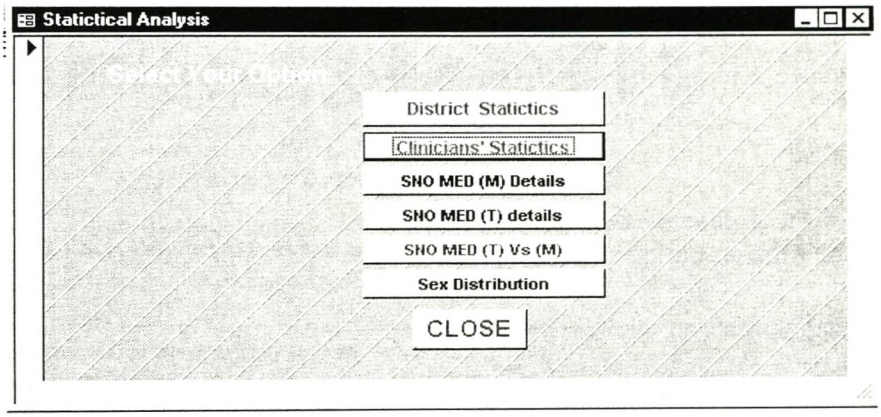

Figure 6. Menu for the statistical analysis

The following are some of the areas, which can be analysed statistically.

A. It is possible to compare the number of biopsies from different districts as the Department of Oral Pathology offers the service for most of the General Hospitals in the country. eg: Table 1 and Figure 7

District	No. of Patients
A	250
B	93
C	40
D	10
E	5
F	25
G	30
H	50
I	6
J	8
K	10
L	44
M	56
N	34
O	67

Table 1. Analysis according to districts

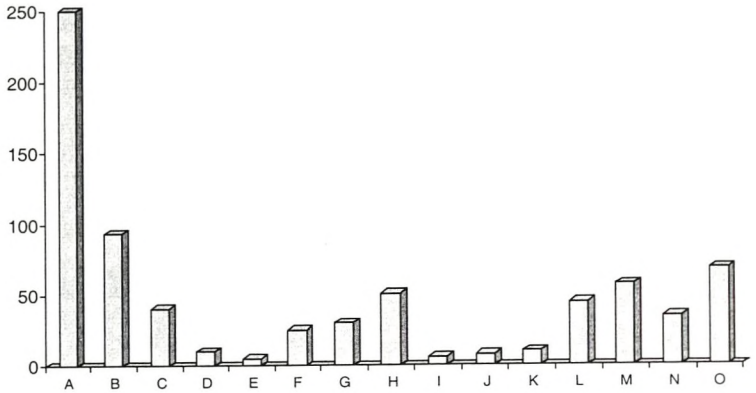

Figure 7. Analysis according to districts

B. The breakdown of patients according to the clinician for a given period of time can be calculated. eg: Table 2

Name of the Clinician	No of Patients Sent
Dr. A	56
Dr. B	67
Dr. C	88
Dr. D	12
Dr. E	45
Dr. F	35
Dr. G	66
Dr. H	75
Dr. I	202

Table 2. Number of biopsies according to the surgeon

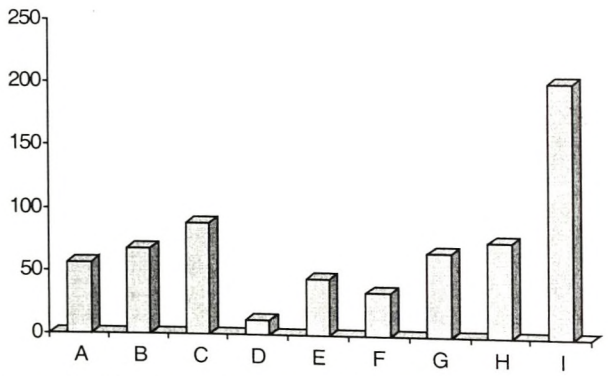

Figure 8. Number of biopsies according to the surgeon

C. The sex distribution for various diseases or number of male and female patients for a specific time period is available. eg: Figure 9

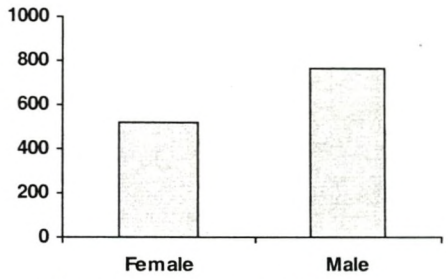

Figure 9. Gender distribution

D. Analysis according to SNOMED system gives very valuable information for research purposes and for comparison of various disease entities between countries. The use of the above system gives both the disease entity (M) and the specific site of the disease (T) which allows the pathologist or the clinician to identify specific diseases in specific sites for a given period of time.

References

1. Royal college of Pathologist report of the working party. The retention and storage of pathological records and archives. 1995

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1st to introduce a clinically proven toothpaste and toothbrush in Sri Lanka.

1st to launch fluoride toothpaste in Sri Lanka.

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1st to conduct islandwide dental support programmes for school children.

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1st to promote an International Dental Congress in Sri Lanka.

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