

AN EVALUATION OF

THE LITERATURE

ON PATHOLOGY AND MEDICINE

IN ORAL DISEASE

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PATHOLOGY AND MEDICINE IN ORAL DISEASE.

It is the duty of the oral surgeon to diagnose and treat pathological lesions of the oral cavity. Since his field is but a small part of the body, it can be expected that his knowledge of the lesions which occur there will be detailed and exact. But in treating the mouth and jaws, he must not develop a narrow perspective; he must remember that he is assisting in maintaining the health of the whole human organism. The purpose of this review, then, is to emphasise that the oral surgeon's role is that of a ^{member of a} team working together, each with a special ability but having some conception and understanding of the whole problem. Hence, it is not expected that the oral specialist be a general physician; but it is reasonable that his background should be broad.

As all surgeons should be keen students of the mechanisms of inflammation, Part I, of this review is devoted to that subject. Part II, deals with systemic conditions which have oral manifestations, or which influence the oral surgeon's work.

A Bibliography is included with each chapter. For references to either text-book or journal the following pattern is used:-

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J. Sullivan
March 1957

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Chapter VII..... 201 - 208.

SYSTEMIC CONDITIONS PROVIDING ADDITIONAL
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P A R T 1.

INFLAMMATION AND INFECTIONS OF THE ORAL CAVITY.

Fundamental concepts of inflammation and inflammatory conditions of the Mouth.

A complete understanding of the tissue changes which accompany and accrue from traumatic injury, surgical procedures, infection and the various irritants is fundamentally essential for the oral surgeon. Therefore the general principles of the disturbances of the circulation and inflammation are described in some detail before dealing with inflammatory conditions of the mouth.

In dealing with the subject, the principle reference text is the 6th edition of Sir Robert Muir's "Text Book of Pathology," revised by Professor D. F. Gappell of the University of Glasgow. This excellent and detailed text is in itself a critical analysis, wherein every effort is made to induce its readers to ponder the unsolved mysteries of pathology. To compare opinions and discuss conclusions, reference will also be made to other works where necessary. The most recent information is not yet available in text book form and facts have been drawn from various forms of professional literature.

CHAPTER 1.

DISTURBANCES OF THE CIRCULATION.

Muir commences his chapter on "Disturbances of the Circulation" by describing and defining changes in a localised area. These are:--
Arterial or active hyperaemia:-- an increased blood flow in a particular area, due to dilatation of the arterioles and accompanied by a rise in pressure which causes the dilatation of a greater number of capillaries. It is important to note that active hyperaemia follows the artificially induced ischaemia of bloodless operations and haemorrhage may spring from unligated small vessels. Should the localised anaemic condition be allowed to continue too long, damage to capillary walls may result in a heavy loss of plasma.

Chapter 1. Cont'd.

Capillary dilatation:- usually rapidly follows mechanical, chemical or thermal irritation. Ultra violet rays, and some other irritations however, bring a slower, more chronic response, possibly leading to complete stasis. In these cases the damaged capillary walls do not recover, necrosis and thrombosis will follow and circulation can never be restored. Necrotic ulcerations in the palate are occasionally seen following the use of heavy injections of local anaesthetic with adrenalin. Pressure and vaso-constriction caused by the adrenalin produces an ischaemia for a period long enough for the tissue cells to die from lack of nutrition. In the more transitory types of capillary hyperaemia, recovery is complete.

Mention must be made here to the Lewis H-substance, closely resembling histamines, which is liberated from the cells of certain sensitive individuals, whose skin wheals easily. These individuals, however, are not abnormally sensitive to histamine, but this ready release of H-substance, and its effect upon the capillaries is believed to be associated with anaphylactic shock.

Local venous congestion is due to a mechanical obstruction to blood returning from any part of the body. The obstruction may be a thrombus, tumour or aneurysm. Reference is made later to the role of thrombus formation in cavernous-sinus thrombo-phlebitis.

However, it may be mentioned here that over-enthusiastic post-damming of full upper dentures by the Terrell technique (Dental Convention, 1951) will cause venous obstruction of the palate, resulting in congestion with a blue colouration of the mucosa.

General venous congestion is discussed later under systemic conditions which concern the oral surgeon.

Oedema or Dropsy. These are practically synonymous terms referring to "excessive accumulation of fluid in the connective tissue spaces or serous sacs of the body." Of interest is the term 'anasarca,' describing oedema of the skin and subcutaneous tissues.

The fluid in oedema is characteristic of that of ordinary lymph, but with a lower protein content and a lower specific gravity (1,006 to 1,012). The accumulation of these dropsical fluids

Chapter I. Cont'd.

known as transudates interferes with tissue nutrition, thereby lowering resistance to bacterial infection. Oedema maybe local or general.

In as much as a knowledge of the general oedemas provide a background for differential oral diagnosis, they are here mentioned:-

Cardiac Oedema usually following chronic venous congestion, typically presenting with dropsy in the extremities due to the influence of gravity.

Renal Oedema presenting suddenly in the early stages of acute nephritis with characteristic swelling in the ankles and facial tissues, especially around the eyes.

Cachectic Oedema in many chronic wasting diseases. It is interesting or
Dropsy. to note that a fall in plasma protein favours the

formation of transudates, and indeed the term "famine oedema" was used during two Great Wars.

Local Oedema. The various forms of local oedemas may result from a wide range of causes and conditions; obstructed veins and lymphatics, the bites of poisonous insects and reptiles, poisoned wounds and pustules, mechanical, chemical and thermal injuries.

Lewis's H-substance, already mentioned is associated with the formation of these oedemas.

Angio-neurotic Oedema. Possibly resulting from nervous disturbances, allergies or hereditary factors -- will be discussed in detail later.

Haemorrhage Is here considered only in relation to the multiple haemorrhages or petechiae which are associated with various general conditions. In inflammatory and other conditions, red corpuscles may escape through unruptured capillary walls by a process known as diapedesis. This type of haemorrhage may result from:-

a. Acute infections - Septicaemia.

Scarlet Fever.

Yellow Fever.

Chapter 1. Cont'd.

- b. Blood discrasias:- pernicious anaemia.
leukaemia.
haemorrhagica purpura.
- c. Chemical :- phosphorus.
- d. Vitamin deficiency:- vitamin K.
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CHAPTER II.

THE PATHOLOGY OF ACUTE EARLY INFLAMMATION AND METHODS FOR ITS CONTROL.

Montgomery defines inflammation as a 'cellular reaction of tissues to harmful stimuli'.⁽¹⁾ The process however is so complex and consists of so many phases that such a simple definition cannot suffice. In somewhat more detail than Montgomery, Muir traces the history of experient^ms and thinking on inflammation from Cobbenheins studies emphasising^{is} the effect of tissue damage, to Metchnikoff's work recognising the importance of bacteria and cellular reactions.⁽²⁾ Certainly, the modern concept is that inflammation is in the main a series of defensive reactions, but as will be demonstrated, the reactions sometimes defeat themselves and can benefit by assistance from the surgeon with well timed incisions, irrigation and thermotherapy.

In consequence of this statement, a clear understanding of the many processes of inflammation must form the solid background of a competent surgeon's technique.

The classical signs of inflammation given by Celsus are "Rubor," "Dolor," "Tumor" and "Calor," to which may be added function, "functio laesi," and the processes may be induced by injury, infection, chemical and other irritants, radiation and thermal changes.

Inflammation is described under two main headings, acute and chronic, the former being mainly exudative and the latter, proliferative in type. Intermediate conditions are noted, and frequently acute inflammation may progress through a sub-acute stage and become chronic. On the other hand, chronic or sub-acute lesions may exacerbate into acute conditions.

Acute Inflammation.

The initial sign of acute inflammation is active hyperaemia, sometimes following a momentary vascular contraction. The blood flow accelerates, an increased number of capillaries function, some capillary dilatation resulting directly from arteriolar activity, but much of it being an independent response of the capillaries themselves.

Chapter 11 Cont'd.

At this stage is the first escape of protein containing fluid from the vessels, the large protein molecules exert an increased osmotic pressure in the tissue spaces and encourage further exudate from the vessels. The area swells slightly and becomes redder. Shortly there follows a slowing down of the capillary blood flow bringing a further increased exudate of lymph (exudative), the leucocytes marginate from the centre of the blood vessels and 'pavement' the endothelium linings, which appears to become "sticky." Soon now, emigration of neutrophil leucocytes occurs, when these white cells extrude themselves through the vessel walls by a process known as diapedesis. At the same time as the extra-vasation of lymph and diapedesis of leucocytes there occurs some escape of red blood cells.

Concurrently with these vascular changes, significant reactions take place in the tissue cells themselves which enlarge, change form and become actively phagocytic. Fibrocytes enlarge, increase in cytoplasm, separate from their fibres and become fibroblasts; endothelial cells and histiocytes from the reticulo-endothelial systems become detached to ingest bacteria, cell debris and red corpuscles. The principle cells in acute inflammation are polymorpho-nuclear neutrophil leucocytes which appear almost immediately, followed some twelve to twenty-four hours later by the mononuclear cells which are derived from the monocytes of the blood and from tissue cells or histiocytes. The exudate contains plasma proteins, albumin, globulin and fibrinogen which forms a fibrin barrier and helps to contain the infection.

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The surgical significance of some of the events in the chain of reactions so far described in acute inflammation can now be considered.

Chapter II Cont'd.

Inflammation and control methods cont'd.

As described by Muir the high protein lymph exudate is mainly beneficial as it dilutes the chemical irritants, and carries anti-bacterial substances and opsoning which facilitate phagocytosis. However these substances are rapidly expended in the presence of bacteria and the exudate then becomes an ideal culture medium. Consequently, it is beneficial to encourage the flow of fresh exudate by establishing drainage or by irrigating open infected wounds with hypertonic saline solutions. The fresh exudate thus formed, flushes away many bacteria and carries with it ^a new supply of anti-bacterial substances.

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In aseptic surgery on non-infected lesions, post-operative or traumatic wounds, inflammation is undesirable. As no bacteria should be present, the defensive qualities of an inflammatory exudate are unnecessary and its accumulation leads only to oedema with associated pain from pressure on nerve endings.

To avoid unnecessary trauma in these cases operations should be carried out with sharp sterile instruments, using sufficiently large flaps to avoid unnecessary damage, leaving all bony margins smooth and trimmed and being careful that no bone fragments or tissue debris are left in the surgical field. Neglect of any of these precautions will lead to useless inflammatory oedema and stasis.

"It is evident from pathologic process of inflammation that we must induce hyperaemia in septic conditions and retard hyperaemia in aseptic conditions."⁽³⁾ This statement contains the essence of thinking when thermo-therapy is being instituted. The application of heat or cold is usually applied by hydrotherapy. Following aseptic surgery ice packs or cold compresses are applied as soon as possible, being used for periods of twenty to thirty minutes every hour.⁽⁴⁾ Cold penetrates the tissues more effectively than heat and by inducing vasoconstriction of the capillary vessels, reducing blood and lymphatic flow prevents unwanted inflammation. With cold, local metabolic action is reduced and is contra - indicated.

Chapter 11 Cont'd.

should infection develop. Heat is applied in infective conditions to encourage a greater hyperaemia and its use will be discussed in greater detail in the treatment of infections.

The practice of precise surgical techniques, aseptically carried out in a dried sterilised field and followed by intelligent thermotherapy has proved its merits to graduates from University of Sydney. However it is proposed to discuss the use of anti-inflammatory agents recently being employed to control post-operative oedema. At the same time the opportunity will be taken to deal with the effectiveness of some of these agents in various inflammatory diseases.

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ANTIHISTAMINICS.

As mentioned earlier, Lewis originally described the release of a histamine-like H-substance which is related to shock and many of the vascular changes of inflammation. Histamine itself is produced from the amine-acid, histidine and is formed in damaged tissue. (5) It is liberated by the mucosa of the stomach, possibly assisted by putrefactive processes of the intestinal bacteria, circulated in the blood stream and is stored in the body cells to be released in surgical and anaphylactic shock, by trauma, insulin shock, bacterial toxins and snake venom. ~~Histamine increases vasodilation and stimulates pain, toxins and snake venom.~~ Histamine increases vasodilation and stimulates pain, increases capillary permeability and consequently the resultant oedema.

At an international symposium on "The Mechanism of Inflammation" held in Cannada in 1953, Ungar stated that histamine could be released without cell damage and perhaps is liberated by an enzymatic mechanism. (6) He thought it likely that serofibrinokase acts on the enzyme precursor, profibrinolysin contained in the blood to produce fibrinolysin which then attacks the protein to which histamine is attached releasing it from its cell. Histamine is thus one of the "mediators" of inflammation.

Chapter 11 Cont'd.

Antihistaminics. Cont'd.

The rationale of the use of antihistamines following aseptic surgery is therefore easy to see. Recently many oral surgeons have used antihistamines to control inflammation following surgery and to treat difficult chronic inflammations of the mouth. Johnson and Jakubs described the use of antihistamine, benadryl, 1c.c. of which was injected intramuscularly daily for four days following bilateral ostectomy of the mandible.⁽⁷⁾ Hyaluronidase (vide infra) and antibiotics were used in conjunction with this therapy. Silverman and Maslansky^{M^S Maslansky} have reported the use of anti-histamines to control post-operative oedema.

Szmyd reports a 'double blind' control experiment on five hundred patients using placebos for 50% and antihistamine capsules for the remainder.⁽⁸⁾ Following surgery, he noted no significant difference in post-operative oedema, pain or trismus but with antihistamines, nausea was reduced and drowsiness increased. It is noteworthy however, that the antihistamine was administered by capsules per oris, whereas many other reports are based on the results of intramuscular injections.

For some time, antihistamines have proved their worth in the treatment of allergic states, travel sickness, asthma and small burns, being especially useful in the treatment of drug allergies (procaine, novocaine, penicillin, suphonilamedes, insect bites.)

Their use may have merit in the treatment of angio-neurotic oedema, acute rhinitis, food allergy, anaphylactic shock, serum sickness, pruritus, vasomotor rhinitis, light erythema, idiopathic neuralgias and some of the resistant forms of stomatitis where the aetiology is not certain, but may be of an allergic nature.

The most common side effect is drowsiness or somnolence. This of course is not undesirable prior to the administration of anaesthesia or the performance of surgery. Customary sedative premedication can be adjusted accordingly. It is undesirable where the patient will shortly have to perform tasks requiring accuracy such as driving an automobile. Other undesirable effects may

Chapter 11. Cont'd.ANTI-HISTAMINICS. Cont'd.

include gastric upset, fleeting joint pains and dryness of the mouth. Their prolonged use retards healing.

In all antihistamine treatment, it is advisable to commence with small doses which may be gradually increased if the individual reaction is not adverse. Single oral doses last about five hours only, so that they should be repeated three to four times daily. (9)

Some of the available antihistamines are:-

CHLORPHENIRAMINE MALEATE.

Syn:- Piriton Maleate.

Dosage:- Adults, 2 to 4 mg. orally T.I.D.
Children 1 to 2 mg. " "

May also be used for injection.

PROMETHAZINE HYDROCHLORIDE. ('Phenergan.')

A very soluble white powder.

Dosage:- Adults, 25 to 100 mg. orally per diem.
Children,
0 to 2 yrs. 10 to 20 mg. per diem.
2 to 5 yrs. 15 to 25 mg. " "
5 to 10 yrs. 25 to 50 mg. " "
Intramuscularly 12 to 50 mg. (2 c.c. of 2.5% soln.)
Intravenously 12 to 50 mg. (rarely used.)

In ointment form is valuable to reduce oedema and ease pain from insect bites.

MEPERAMINE MALEATE. ("Anthisan") ("Phenergan").

A Dosage:- Adults, up to 300mg. each dose — 1.0 grams daily.

Dosage:- per oris.

Children 0 - 1 year 25 to 75 mg. per diem.
" 1 - 2 " 37 to 100 mg. per diem.
" 2 - 4 " 50 to 125 mg. per diem.
" 3 - 4 " 75 to 200 mg. per diem.
" 4 - 7 " 100 to 250 mg. per diem.
" 7 - 14 " 250 to 400 mg. per diem.

Injections of meperamine maleate are not commonly used.

Chapter. 11 Cont'd.
ANTI-HISTAMINICS. Cont'd.

p-Aminosalicylate of 1-phenyl-lpyridyl-(2)- 3dimethyl-aminopropane.
 ("Evil").

Dosage:- per oris.

Adults and children over 10, 25 to 50 mg. T.I.D.

By injection..... 25 to 50mg. (1 to 2 c.c.
 in ampoules.)
 one to two times daily.

Young Children..... 12 to 25 mg. one to two times
 daily.

Injections should be made intramuscularly or intravenously very SLOWLY.

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A. C. T. H. CORTISONE AND HYDROCORTISONE.

In 1949, Hench, Kendall, Slocumb and Polley described to the world the use of pituitary and adreno-cortical hormones in the treatment of rheumatoid arthritis. Since that time the relation of these hormones to growth, repair and inflammation have opened new fields for study and it is natural that dental literature should contain an increasing number of references to them. In the main, oral surgeons have directed their attention to experiments with these endocrine substances in:-

1. Amelioration of recalcitrant pathological conditions manifesting themselves in the face and mouth.
2. Therapy in temporo-mandibular arthralgias.
3. The control of undesirable inflammation following surgery.

In 1956, in the Sept. issue of "Oral Surgery, Oral medicine and oral Pathology," Douglas and Kresberg give an excellent review of the literature on these drugs. (10)

A.C.T.H., an abbreviation for adrenocorticotrophic hormone, is one of the main tropic hormones secreted from the anterior lobe of the pituitary gland. It is probably derived from the basophil or beta cells when the body is under physical mental or emotional stress, and sympathetic nervous stimulation causes the adrenal medulla to release adrenalin which circulates, stimulates the hypothalamus which in turn stimulates the pituitary gland to liberate A.C.T.H.

Chapter 11 Cont'd.

Carried by the blood stream, this hormone causes the adrenal cortex to produce glucocorticoids, principally cortico-sterone and cortisone. Also derived from the cortex of the adrenal glands, the mineralocorticoids, principally desoxycorticosterone and sex hormones (androgens and oestrogens) are not so sharply stimulated by A.C.T.H. (11,12.)

Now, the function of the individual cortical hormones is not yet fully understood, but it is certain that cortisone, hydrocortisone and their compounds exert an anti inflammatory reaction. Recently, Dougherty and White have shown that A.C.T.H. cortisone and hydrocortisone cause a fall in the number of lymphocytes and eosinophils. Vally Menkin in 1954, showed that hydrocortisone acted at a cellular level, the cells being prevented from releasing the normal chemicals of inflammation.

The following is a list of cases where cortical hormone therapy may be instituted. (13)

1. All cases of unwanted inflammation after surgery.
 - a. Preventing scar formation from external incisions. (Griswald.)
 - b. Prevention of oedema following aseptic surgery on uninfected lesions.
2. Acute traumatic inflammation -- sprains and strains.
3. Arthritis of temporo-mandibular joint -- injections of 15 mg. of hydrocortisone at intervals until the condition clears.
4. Pemphigus Vulgaris -- 300 to 500 mg. of cortisone daily for 3 to 5 weeks then gradually reducing dosage, or 10 mg. delta cortisone daily for three months.
5. Erythema multiforme -- 200 mg. cortisone daily for 4 to 8 weeks.
6. Lupus erythematosus (Orban and Wentz) -- 100 to 200 mg. of cortisone daily for 10 to 14 days followed by a minimal maintenance dosage.
7. Periarthritis nodosa -- 150 to 200 mg. of cortisone daily for three weeks then 50 to 75 mg. daily for 3 to 4 months.
8. Bell's Palsy (Moss, Walters and Walters) 300 to 400 mgs. daily for three weeks; then 50 to 75 mg. daily for 3 to 4 months.

Chapter 11 Cont'd.

A.C.T.H. Cortisone and Hydrocortisone. Cont'd.

9. Shock-discussed later.
10. Lichen Planus.
11. Aphthous Stomatitis.

Fischer had varying success in treating the following conditions with 2.5% hydrocortisone ointment:-

- a. Active leukoplakia.
- b. Glossitis.
- c. Allergic cheilitis.

It has also been used for:-

- a. Desquamative gingivitis.
- b. Erythematosis.

Amesbury utilised hydrocortisone ointment in 430 cases of exodontia where immediate dentures were inserted and reported the following effects:- (14)

- a. Dramatic relief from pain which was more rapid after general anaesthesia than after local anaesthesia, regardless of the anaesthetic agent used.
- b. Suppression of the inflammatory process.
- c. Prompt healing of traumatised tissue.
- d. Almost total absence of offensive odours.

Contra-indications against the use of A.C.T.H. and Glucocorticoids.

1. Peptic Ulceration:-

When glucocorticoids are given over a long period, almost symptomless peptic ulcers, difficult to diagnose, may form. Routine therapy should include the administration of aluminium hydroxide gel and a previous history of peptic ulceration usually contra indicates treatment.

2. Hypertension and Psychological conditions:-

In normal patients the central nervous system is stimulated giving a feeling of well-being. However, in patients of unstable mental background, a careful watch should be made for signs of over-anxiety, agitation and melancholia. The literature is somewhat

Chapter 11. Cont'd.

contradictory on this point, Dobbs, for example, suggesting its use in wartime emotional distress, angio-neurotic oedema and in practically all instances of crisis. Clearly, more research is needed into these aspects of cortical hormone therapy.

3. Thrombo-embolic conditions:--

Prolonged administration may lead to an increased tendency to thrombus formation. Therefore the use of glucocorticoids is contraindicated and during therapy a careful check should be made for any signs of cavernous thrombo-phlebitis.

4. Diabetes Mellitus:--

Glucocorticoids facilitate carbohydrate absorption and hinder its catabolism and may therefore produce 'cortisone diabetes.' In addition, there is decreased response to insulin, so that hormone therapy in diabetes is most unwise and in normal patients a daily test for hyperglycaemia and glycosuria should be made. The diet should be low in fats and carbohydrates.

5. Osteoporosis, Malnutrition, Cachexia and Senescence.

Protein synthesis is inhibited and its breakdown is increased by cortical hormones leading to a negative nitrogen balance, osteoporosis and muscular wastage. Therefore, the use A.C.T.H., cortisone or hydrocortisone should be withheld where any of the above conditions already exist. Diet during treatment should be high in first class proteins and androgens administered to stimulate protein production. The tendency to osteoporosis may be modified by the use of oestrogen but experiments in this field are in a very early stage. (15)

6. Glomerulo-nephritis:--

Sodium retention is increased and may be manifested by an increase in weight in blood pressure. There may be a reduced urinary output, especially where renal function is already impaired. A low salt content is advised and two to three grains of ammonium chloride taken daily.

7. Convulsive and Cardiac Disorders:--

Excessive loss of potassium salts may have an adverse effect on the above conditions and should be balanced by the administration of

Chapter II. Cont'd.

two to six grams of potassium chloride daily. Androgen also assists potassium retention.

In general, any of the signs and symptoms of Cushing's syndrome (pituitary basophilism) should indicate a cessation of glucocorticoid therapy. However, it is generally wise to taper off treatment gradually to allow the natural adrenocortical functions to resume and androgen should be administered for a further one or two weeks.

At present, it can be stated that adjuvant glucocorticoid therapy offers hope in the many oral diseases formerly resistant to treatment. As there is still much to learn of the action and side effects of these hormones, it is wise to proceed cautiously, and have the patient thoroughly medically checked. It seems reasonable to assume that use of 2 . 5% hydrocortisone ointment will be free of undesirable side effects and that the dosage used in injections for temporomandibular arthralgia is unlikely to cause untoward reactions. When this treatment is used, the hydrocortisone, being insoluble is diffused over as large an area as possible, endeavouring to use one needle puncture only. For the first day there is increased pain, but as the hormonal anti-inflammatory properties take effect there is relief. (16 & 17)

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TRYPSIN.

In a preliminary report, Paul and Naplicic describe the results obtained when one dose of 0.5 c.c. (2.5 mg.) of trypsin was injected intramuscularly for eighteen patients requiring apicectomies. Controls were used. Their observations were that inflammation was reduced and that the only side effect, pain at the site of the intramuscular injection, was not evident when the gluteal muscle was chosen. (18)

Trypsin is an enzyme which stimulates the natural production of enzymes, reverses and prevents the signs of inflammation. In addition it augments thrombolysis.

Chapter II Cont'd.HYALURONIDASE.

This is an almost non-toxic enzyme found in bacteria such as streptococci, snake venoms, spermatozoa and Luckes. Capable of hydrolysing mucopolysaccharides such as hyaluronic acid, it facilitates the spread and absorption of antibiotics and local anaesthetic in the tissues. In traumatic inflammation hyaluronidase has been used to hasten absorption of transudates and blood. Care should be taken that infection is not present as its dissemination would be greatly hastened.

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PART 1. CONT'D.CHAPTER III.THE PATHOLOGY OF LATER STAGES OF INFLAMMATION.Later Stages of Acute Inflammation.

When the ^hphagocytes have been mobilised to a site of infection or irritation the inflammation may be arrested before there is much tissue destruction. The exudate if absorbed, by the the lymphatics, enzymes bring about lysis of the fibrin barrier, tissue debris is digested by the mononuclear cells, and the leucocytes return to the blood stream. This is resolution. (1)

In infections, the typical inflammatory reaction described may vary according to the predominant type of bacteria. For example, staphylococcus aureus, possessing an enzyme staphylo-coagulase coagulates the plasma in the exudate, forms a fibrin clot and generally these infections are localised. Streptococcus haemolyticus, however, releases fibrinolysin which dissolves the fibrin barrier and also possesses an enzyme, hyaluronidase and streptokinase which by acting with the hyaluronic acid of the tissue spaces help to disseminate the infection. (2) Hector and others report using this enzyme where rapid dissemination of a drug is required. (3) It is mentioned here to emphasise that it should not be used as an adjuvant in the presence of infection. By reason of its hyaluronidase, streptococcus spreads more widely in the tissue than staphylococcus and is thus commonly isolated from cellulitis. Other organisms do not evoke the typical response of polymorphs, whilst in some cases overwhelming infections are actually accompanied by a leucopenia. Whether the phagocytes succeed in overcoming the infection in time to allow resolution to take place depends on the number, type and virulence of the organisms present, the nutrition, natural and acquired immunity of the host and the site of the lesion. Nutritional factors are also important.

When the irritant or infection is not completely removed, the continued destruction of tissue cells and leucocytes causes suppuration, the liquefied mass of destroyed cells being present as pus.

Chapter III. Cont'd.

LATER STAGES OF ACUTE INFLAMMATION Cont'd.

Menkin states that pH of the exudate is lowered at this time and that when the pH drops to 6.7 the granular cells cannot survive. Whether this is confirmed or not, the fact is that the polymorphonuclear leucocytes (microphages) are destroyed in suppuration, and are gradually replaced by macrophages (non-granular cells.) It is certain that toxins and enzymes are important in causing the cell-destruction of suppuration.⁽⁴⁾ During this period of cellular change there is a continuing emigration of polymorphonuclear cells and their enzymes continue to digest the tissues. The continued accumulation of polymorphs is due to the chemotactic substances from the bacteria. Because tissue has been destroyed a complete return to normal is impossible. In the abscess cavity now formed resistant dead tissue may form a slough, which when removed facilitates healing.

As the suppurative process slows down, a reactive proliferation of surrounding connective tissue cells form a "pyogenic membrane." If the abscess is small the pus is absorbed when finally sterile leaving a small cicatrix. Larger abscess cavities should be opened and evacuated to leave a minimum of fibrosis on healing. They may 'point' and themselves discharge onto the surface.

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CATARRHAL INFLAMMATION.

This is a term applied to inflammation of the epithelial surfaces and is associated with damage and desquamation. When located on the membranes mucous an increased secretion dilutes the irritant. The secretion may be mucinous or largely aqueous and is at first clear, but as leucocytes emigrate it assumes muco-purulent characteristics. Epithelial cells may separate, to be replaced by young cells which in turn are desquamated. In adjacent tissues are seen the usual signs of inflammation. If resolution does not take place, chronic catarrhal inflammation ensues characterised by structural changes which will not return to normal. Underlying connective tissue cells proliferate to form granulation tissue and the mucous membrane itself

Chapter III. Cont'd.

Catarrhal Inflammation. Cont'd.

ultimately becomes atrophic. The ducts of mucous glands may be occluded to form cysts.

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THE GENERAL EFFECTS OF INFECTION.

Apart from their local effect of tissue cell damage, toxins enter the blood stream to produce toxaemia and act on the thermoregulatory brain centre to cause an elevation of body temperature (pyrexia.)

The other significant general effect of inflammation is leucocytosis, wherein the number of white cells in the blood may increase to 25,000 per c.mm. or more. Usually this increase is mainly on the part of polymorphonuclear neutrophils, but this is not always so and a differential white cell count is often a valuable diagnostic aid. Leucocytosis is described more fully under "Blood," but it is relevant here to list the causes of the different types of leucocytosis and leucopaenia. (5) (6)

Causes of Leucocytosis.

- a. Acute infections. (especially coccal.)
localised — abscesses, infected wounds, osteitis, osteomyelitis, tonsillitis, appendicitis.
Generalised — rheumatic fever, diphtheria
- b. Complications in non infectious diseases (malignant neoplasms.)
- c. Intoxications — chemicals, drugs.
Metabolic intoxications (uraemia eclampsia.)
- d. Allergic responses (after initial leucopenia)
- e. Haemorrhage.
- f. Post operative response.
- g. Leukaemia.

Causes of Leucopenia.

- a. Specific infections — trypanosomiasis, chronic tuberculosis, typhoid and paratyphoid fever, undulant fever, measles, influenza, rubella, malaria, post febrile smallpox, dengue, kala azar, histoplasmosis.
- bb. Overwhelming infections — septicaemia, miliary tuberculosis.

Chapter 111. Cont'd.

CAUSES OF LEUCOPENIA. CONT'D.

- c. Debilitated states.
- d. Haemopoietic disturbances (especially splenic). Banti's disease (an anaemia with enlarged spleen and cirrhosis). Gaucher's disease (splenomegaly associated with splenic anaemia), aplastic anaemia, alekaemic anaemia, agranulocytosis, secondary metastatic deposits in the bone.
- e. Chemicals — Amidopyrine, sulphonilamides, salts of heavy metals, benzol.
- f. Radiant energy.
- g. Early allergic responses.
- h. Acute traumatic shock.
- i. Widal's haemoclastic crisis.
- j. Anaphylactic Shock.
- k. Acute Pneumonia in alcoholics.

CAUSES OF LYMPHOCYTOSIS.

- a. Specific infections — infectious mononucleosis, pertussis, exanthemata, especially mumps, chronic tuberculosis, secondary and congenital syphilis.
- b. Convalescence from acute infections.
- c. Lymphocytic leukaemia.
(Relative lymphocytosis in leucopenia and exophthalmic goitre.)

CAUSES OF EOSINOPHILIA.

- a. Allergic responses — asthma, angioneurotic oedema, hay fever.
- b. Pemphigus, herpetic dermatitis and other dermatologic diseases.
- c. Specific infections — erythema multiforme, Scarlet fever.
- d. Haemopoietic disturbances — Hodgkin's disease, pernicious anaemia, chronic myeloid leukaemia, post-splenectomy.
- e. Irradiation.

CAUSES OF MONOCYTOSIS.

- a. Specific infections — tuberculosis, sub-acute bacterial endocarditis, typhus, brucellosis and such protozoal infections as malaria and Rocky Mountain spotted fever.

Chapter III. Cont'd.CAUSES OF MONOCYTOSIS. Cont'd.

- b. Hodgkin's disease.
- c. Monocytic leukaemia.
- d. Tetrachlorethane poisoning.

CAUSES OF BASOPHILIA. (6)

Note: in acute infections may disappear altogether.

- a. Chronic myeloid leukaemia.
- b. Polycythaemia vera.
- c. Cirrhosis of the liver.
- d. May be in early stages of Hodgkin's disease, chronic sinusitis, small-pox, and chicken-pox.

The third general deleterious effect of inflammation is due to the effects of toxins and varies greatly. For example, in tetanus and diphtheria there is severe intoxication and organs distant from the site of infection may be markedly affected. In localised infections, general toxæmia may not be severe. Regardless of the type, long standing infections cause degenerative changes in various organs due to an absorption of toxins over a long period. In these cases there occurs loss of weight, muscular weakness and anaemia. In general it can be stated that it is not the presence of the bacteria themselves, but rather their toxins which cause bodily reactions.

CELLS FOUND IN INFLAMMATORY CONDITIONS.1.....Polymorphonuclear Leucocytes. (Microphages.)

These cells are derived from the finely granular myelocytes of the bone marrow only. Mainly concerned in catarrhal inflammation and infections by the pyogenic organisms, — staphylococci, streptococci, pneumococci and coliform bacilli, they are actively amoeboid and phagocytic and possess proteolytic properties.

Normally, there is a reserve of polymorpho-nuclears at the periphery of the blood stream in the bone marrow and in leucocytosis the bone marrow increases to supply further polymorphs as they are required. Various bactericidal and opsonic substances appear to be derived from polymorphonuclear white cells. They are usually located around necrotic and degenerate material, even where there are no other inflammatory conditions.

Chapter III. Cont'd.

2.....Macrophages or non-granular wandering cells.

These cells are derived from several sources;- for example, the monocytes of the blood, and the histiocytes derived from the endothelial cells of the lymph and blood vessels. Metchnikoff claimed they were important in phagocytosis of damaged cellular tissue, protozoa, and some of the slow-growing bacteria. It is impossible in established conditions to decide upon the source for these macrophages or mononuclear cells and consequently Maximow described them as 'polyblasts.' He considered that these cells may ultimately become plasma cells or giant cells. Fibrocytes and histiocytes in inflammatory conditions also assume the round form of macrophages and become phagocytic.

LYMPHOCYTES AND PLASMA CELLS.

Accumulating mainly in chronic conditions, but occasionally being present in more acute inflammation, lymphocytes emigrate from the blood stream and possess feeble amoeboid and a minimum of phagocytic powers.

Plasma cells are larger than lymphocytes with more abundant protoplasm and basophil and with an eccentric nucleus possessing a coarse chromatin network. Weakly amoeboid and rarely phagocytic, they appear to be derived from lymphocytes and are seen in granulating wounds, sub acute and chronic inflammatory lesions. Their function is obscure, but is probably protective.

EOSINOPHIL LEUCOCYTES.

In normal health, their number in the blood stream varies, but larger numbers are present in the conditions listed above. The administration of A.C.T.H. acting through the hormones of the adrenal cortex appears to reduce the number of eosinophils, and in acute infections this mechanism is possibly responsible for the reduced number of eosinophils.

FIBROBLASTS.

Oval or spindle-shaped, fibroblasts are formed from ordinary fibrocytes. They appear in early inflammation, increase and become more active. They seem to be the only cells to form collagenous fibres.

Chapter III. Continued.GIANT CELLS.

Metchnikoff described the formation of multinucleated plasmoidal masses of great size and varying in form from the fusion of different types of cells. They contain numerous small nuclei which vary in form. Originating mainly from reticulo-endothelial cells, they may also be formed by connective tissue and epithelial cells. Giant cells are formed either by the amitotic division of single cell nuclei or by the fusion of several cells. They are found around material difficult to absorb, such as cholesterol crystals, cutgut and silk sutures, often in the vicinity of fatty and degenerated cells, and in chronic lesions, (tubercular, syphilitic and fungus infections.)

MAST - CELLS.

They are cells containing coarse basophil granules, which are composed largely of heparin and may be a source of this substance. It is possible but not certain that these cells are derived from the adventitial cells and are found in association with them.

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With the exception of the granular leucocytes whose source is definitely from the bone marrow and which change into no other type, the cells mentioned above may change from one form to the other, and in many cases their mode of formation is still doubtful.

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CHRONIC INFLAMMATION.

Cellular proliferation of fixed cells, the formation of new blood vessels and the presence of macrophages, plasma cells, lymphocytes and giant cells are the essential features of chronic inflammation. The reaction is typically productive rather than exudative. Chronic inflammation may exist as a sequel to acute conditions or with minor irritations, certain types of bacteria and small inoculations of organisms of low virulence, the inflammatory reaction may be chronic from the outset. All intermediate stages of inflammation may exist from acute to sub-acute and chronic, and one type may revert

Chapter 111. Cont'd.CHRONIC INFLAMMATION. Cont'd.

to the other with changes in resistance of the host, virulence of the organism, treatment and secondary infection.

Certain organisms such as tubercle bacilli and treponema pallidum characteristically produce chronic lesions. Mild irritants and some mild poisons produce similar reactions.

In the earlier stages of chronic inflammation the "connective tissue poliferation^r is comparatively cellular, the cells being spindle-shaped and the fibres scanty and fine. Later the collagenous fibres become denser and the number of cells decrease.

In addition to the cells mentioned above, 'foam cells', macrophages filled with globules of myelin fat are abundant in chronic granulomatous lesions (e.g. actinomycosis.) Foamy cells appear to be associated with degenerative changes.

Chronic inflammation is often associated with the formation of granulation tissue, which may be comparatively diffuse or form a localised tumour (gromuloma). Granulation is discussed further under 'repair.'

In organs, there is usually a permanent loss of specialised cells in chronic inflammatory lesions.

Fibrosis the typical feature of chronic inflammation, may result from other conditions:-- associated with atrophy where the blood supply has been deminished and in all forms of 'replacement fibrosis.'

REPAIR AND HYPERTROPHY.

In childhood, growth and cellular proliferation is active, but in the adult it exists only to replace wear and tear. Constantly the desquamative processes of mucous membranes and skin epithelium requires some cellular replacement, and the bone marrow is continually supplying new blood cells but in the tissues as a whole, 'tissue tension' restrains proliferation. This state of abeyance however, may change in the circumstances that are now mentioned.

REPAIR OF WOUNDS AND TISSUE DESTRUCTION.

In its simplest form repair takes place following incision with a sharp sterile knife. The cells in the neighbourhood of the breached

Chapter III. Cont'd.

Repair of Wounds and tissue destruction. Cont'd.

tissues proliferate to restore the 'breach in continuity.' When the edges of this wound are closely apposed the line of incision is sealed with an exudate of blood plasma (coagulum) and there is but little haemorrhage. New endothelial cells form on the capillaries, form solid buds than canalized buds which grow into the exudate and unite with similar buds to form a new vascular network. Provided there is not irritation or infection healing is complete in five or six days and it has been necessary for only a few leucocytes to migrate to the area. This is called healing by primary union or 'first intention.'

In open wounds or apposed incisions that have failed to unite by primary union, healing is by granulation. Comparatively cellular and highly vascular, granulation tissue is newly formed from the deeper portions of the wound. In the base of the wound, new capillaries form from the nearby blood vessels as described in the last paragraph. They grow upwards at right angles to the surface to form capillary loops. Rapidly formed, this vascular tissue is produced in an attempt to fill the gap. Shortly fibroblasts, plump spindle-shaped cells which may be formed from existing fibrocytes, from mononuclear leucocytes or from reticulo - endothelial cells appear in numbers and at first arrange themselves parallel to the capillary loops but very quickly form at right angles to these new vessels. Collagen fibres appear with them. Probably formed by the fibroblasts, the mode of collagen fibre formation is not fully understood, but it is now known that ascorbic acid (vitamin C) is essential to the process. Adequate ascorbic acid is now an accepted constituent in post-operative diets. In the early stages of granulation, polymorpho-nuclear leucocytes appear to form 'laudable pus'. When the open breach is sufficiently filled in marginal epithelium proliferates and commences to cover the granulation tissue. Only when the leucocytes successfully defend the new vascular tissue against bacteria can the epithelium completely cover the wound. At first consisting of a thin layer of flattened cells, the new epithelium cells then differentiate into the superficial

Chapter III. Cont'd.

Repair of Wounds and Tissue Destruction. Cont'd.

stratum corneum and the deeper malpighian layers. All epithelial cells have excellent powers of regeneration, but they are particularly good in mucous membrane. Now the polymorphs gradually disappear; new blood vessels cease forming and devascularisation commences, collagen fibres increase in number and density. Slowly devascularisation is completed and the tissue becomes cicatrised (scar tissue). The newly formed epithelium is normally thinner than normal epithelium. Specialised tissues such as sweat glands, hair follicles and sebaceous glands do not reappear.

In higher vertebrates including man, most of the specialised tissues cannot regenerate and are usually replaced by connective tissue. However the skin and mucous membrane have satisfactory regenerative capacities. The repair of various body tissues is now to be outlined.

Once fully formed, nerve cells have no power of proliferation. Portions of the cell however, usually the peripheral axon will grow as long as the neuroglia cell remains vital. Thoma tells of the establishment of the 'Peripheral Nerve Registry' established in the United States of America during the second world war. (7)

Provided there is no obstruction of the bony canal (e.g. in inferior dental nerve) regeneration of the axon may take place without surgical interference. Failure to unite is probable where the sectioned nerve ends are widely separated, as in a displaced fracture or where the canal is obstructed by new bone or a fragment of tooth. Neurorrhaphy (suturing the separated nerve ends) may be performed within thirty days after sectioning. A report in 1946 showed about 80% nerve regeneration after nine months. Thoma described tinell's sign of nerve regeneration whereby a tingling sensation in the peripheral section by tapping over the site of nerve division.

When ordinary striated muscle is incised, the sarcolemma proliferate and form multinucleated plasmoedal projections, but the action is slow so that union usually takes place by ordinary connective tissue replacement. Wounds of the heart and nonstriated muscle are repaired by white fibrous tissue.

Chapter III Cont'd.

REPAIR OF WOUNDS AND TISSUE DESTRUCTION. Cont'd.

A haematoma is formed when bleeding takes place into a wound and physiological clotting occurs. Liable to infection a haematoma may become inflammatory, but if it remains sterile, a capillary network forms as it does in granulation tissue and fibroblasts invade the clot forming collagen fibres parallel to the new vessels and finally cicatrization of the haematoma takes place. This is called organisation. In a similar manner a thrombus in a blood vessel may be organised and covered with endothelium. Organisation implies the penetration of avascular material such as a fibrinous exudate, a thrombus, a haematoma foreign or dead by new blood vessels. The degree of fibrosis may vary. In the haematoma, haematoidin, the iron-free and haemosiderin the iron-containing components of haemoglobin molecules are present. Leucocytes (polymorpho nuclear and mononuclear), fibroblasts and macrophages from the histiocytes are usually present in all cases of organisation. To prevent excessive fibrous tissue formation and to reduce the possibility of infection, surgical evacuation of haematomata is often advisable.

In "The Dental Treatment of Maxillo-Facial Injuries," Sir William Kelsey, Fry and Terrence Ward give a brief but clear account of bone repair. (8) Normal bone consists of an organic matrix of collagen fibrils arranged in layers called lamellae, the fibres in each lamella being parallel but in each of the layers the fibrils take a different direction. The fibrils of the organic matrix are embedded in a hard cementing substance. In cortical or compact bone, consisting mainly of hard tissue the lamellae form concentric rings encircling the Haversian Canals. Lying within the lamellae (in cavities called lacunae) are osteocytes (bone cells.)

Radiating from the osteocytes lying in the lacunae are narrow channels (canaliculae) containing the cell processes of the osteocytes which communicate with the vascular soft tissue of the haversian canals. Cancellous, spongy or medullary bone also possesses lamellae enclosing osteocytes, but here the collagen fibrils all run more or less parallel to the surface of the trabeculae. In all bone, where the hard and soft

Chapter III Cont'd.REPAIR OF WOUNDS AND TISSUE DESTRUCTION. Cont'd.

tissues approximate (along the Haversian canals and on the surfaces of the trabeculae) are quiescent osteoblasts. New lamellar bone can be formed only on a pre-existing hard surface. Osteoclasts which absorb bone can work only at hard tissue surfaces. The surface area of cancellous bone is much greater than that of compact bone and consequently resorption and deposition take place much more rapidly in this part of the bone. Some osteoclastic activity may be due to a lowering of the pH, and it is possible that the osteoclasts in part at least act in this way. The blood calcium, phosphorus and phosphatase level and some endocrine glands also affect bone regeneration. Surrounding the entire surface of the compact bone excepting the articular cartilage is a fibrous membrane, the periosteum. It consists of two layers, the inner being osteogenic and the outer containing blood vessels and nerves which supply the bone.

When a bone is fractured, there is haemorrhage from torn blood vessels and a haematoma forms. In all cases, some inflammatory reaction takes place with the normal sequelae of vasodilatation and extravasation. Inflammatory proliferation and granulation tissue is formed. Where the fractured bone contacts the granulation tissue, osteoclasts appear and resorb the damaged bone surface. To some extent this resorptive process penetrates the Haversian canals and cancellous spaces. After fourteen days this initial resorption of hard tissues shows radiographically as a widening of the fracture line. Very plump young osteoblasts, similar to fibroblasts appear in the granulation tissue and form long wavy bands of connective tissue fibres, associated with which is a cementing substance in which the calcium salts will ultimately be deposited.

The organic matrix with its cementing substance, thus laid down, is called osteoid and always precedes ultimate calcification. The calcified areas of bone deposition arranged in 'bars' become united to form a 'continuous scaffolding' and the 'woven bone' thus formed is called callus. Callus is quite similar to initial bone in the developing skeleton. After three weeks, callus forming in the granulation tissue

Chapter III Cont'd.

Repair of Wounds and Tissue Destruction. Cont'd.

has enclosed a number of osteoblasts which assist in the ultimate formation of adult bone. Although this new bone (callus) is not arranged in lamellar form like compact and cancellous bone, it is a form of bone, and appliances cannot now further reduce to fracture although slight changes in position may take place if splints or pins are removed at this stage.

After about forty days the process of complete calcification still lags behind the formation of the organic matrix, but the trabeculae are now much thicker and the soft tissues much reduced. It may take months or years for the woven bone of callus to be removed and replaced by adult bone.

Continued movement of the delicate granulation tissue between fractured bone may tear it necessitating fresh ^ahematoma formation, subsequent inflammatory reaction and osteoclastic reaction. Repeated often enough, this will delay healing and result in fibrous union. If traumatic movement is continued long enough, resorption of the bone ends is so great that the granulation tissue is no longer torn by shearing but merely distorts. Then the granulation tissue matures to fibrous scar tissue and calcification can never take place unless this is surgically removed. By a process of eburneation from osteoclastic activity and covered with dense compact. This process of fibrous healing with eburneation is used when 'flase' joints are deliverately formed at the angle of the mandible in the treatment of ankylosis, and at the temporo-mandibular joint when the condyle is fractured and displaced and surgery is not considered the treatment of choice. When it occurs as an undesired complication in the treatment of a fracture, it is necessary to remove the fibrous tissue, remove the hard eburneated bone and immobilize the parts again.

The healing of bone fractures may also be complicated by infection which may gain entry from the mouth, as fractures are almost always compound in the oral cavity due to the muco-periosteum adhering firmly to the bone. Disturbance of the blood clot increases the chance of infection.

CHAPTER III CONT'D.Repair of Wounds and Tissue Destruction. Cont'd.

Fractures compound to the skin surface are not so common, but the risk of infection is much greater. Foreign particles of clothing, wood and gravel are difficult to locate and likely to cause supuration. Some hold the opinion that there is less natural resistance to bacteria introduced from an external source.

The question of removing teeth lying in or near the line of fracture has caused some discussion. If the cementum of a root has been denuded of its periodontal membrane, an excellent pathway for the access of organisms has been created. Where periapical infection of an involved tooth already exists, the tooth is non-vital or the pulp likely to die from trauma, removal is indicated. Whether the tooth will help in immobilization, and whether its removal later would be an embarrassment are important considerations. The writer of this review has found it safer to err on the side of removal.

Infections, when they do develop, are usually suppurative causing more extensive bone loss. Sequestra may form and osteoclastic activity is resumed at some distance from necrotic bone to facilitate its separation. When separation is complete, sequestra may be removed to facilitate the formation of fresh granulation tissue. Callus cannot form in the presence of suppuration.

In comminuted fractures, all fragments with periosteum attached may remain viable and should be retained. In the absence of infection, necrotic bone will be resorbed by osteoclasts and should remain if excessive instrumentation is required for their removal. After 4 - 8 weeks living bone fragments feel 'coated' when touched with a blunt instrument, but dead bone 'grates'.

Fry and Ward describe how a minimal movement may stimulate bony repair but advise against this treatment because of the narrow safety margin.

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P A R T I.

CHAPTER IV.

PYOGENIC INFECTIONS OF THE MOUTH AND JAWS.

References: In general, facts are derived from "Oral Surgery," Vols I. and II; and "Oral Pathology," (The C.V. Mosby Co., St. Louis, 1954.) by Kurt Thoma, "Oral and Dental Diseases," (E. & S. Livingston Ltd., Edinburgh, 1951.) by Hubert H. Stones, "Oral Surgery," (W.B. Saunders Co., Philadelphia and London, 1956.) by W. Harry Archer and from cases treated by the writer.

Professor Kurt Thoma, who wrote "Oral Surgery" and "Oral Pathology" is obviously an outstanding pathologist, apart from any ability he may have as a surgeon. "Oral Surgery" emphasises clinical rather than the laboratory experience. "Oral Pathology" is a detailed publication to be read in conjunction.

Professor Archer's manual of "Oral Surgery" contains numerous case histories: in fact this is the feature of this text book. Well compiled, this reference book appears to reflect the personality of the author, who evidently has a strong sense of moral responsibility.

Hubert H. Stones, Professor of Dental Surgery at the University of Liverpool has produced a detailed work in "Oral and Dental Diseases." Too much of the work could be placed more aptly in a text-book on conservative dentistry or periodontia.

PYOGENIC INFECTIONS OF THE MOUTH AND JAWS.

In this chapter, note form is used in reviewing those conditions where the related facts are well known or accepted. Longer discussions are devoted to new or contentious material.

Acute dento-alveolar abscess.

Aetiology.

a. Caries- pulpitis - extension through apex, bacteria and toxins - periodontal membrane.

Chapter IV. Cont'd.

Acute dento-alveolar abscess.

Aetiology Cont'd.

- b. Occasionally trauma-necrotic pulp - blood - borne infection.
- c. Root therapy drugs or damage.
- d. Virulent organisms, resistance of individual, drainage through pulp canal determine acuteness.
- e. Exacerbation of chronic abscess.

Histo-pathology:- Leucocytosis (polymorphs) - periodontal membrane destroyed -- serous exudate-fibrin.

Signs and Symptoms.

Severe pain - tooth elongated - extreme pain to percussion at first -- may ease with necrosis of nerve endings. Swollen mucosa - usually heat aggravated, cold often relieves.

Bacteriology. Usually mixed - streptococcus haemolyticus, staphylococcus aureus -- sometimes st. albus and citreus, micrococcus tetragenus and non-haemolytic streptococci.

In anaerobic cultures, often bacillus ramosus - occasionally B. perfringens, and B. bifidus communis.

~~12. Where granulomata have arisen from acute infections, the polymorphs~~
are gradually replaced by small lymphocytes and plasma cells and the fibrin barrier is replaced by fibroblastic proliferation.

Various figures have been given for the percentage of granulomata containing epithelial rests. Derived from epithelial remnants of the sheath of Hertwig, the rests will probably always be found if serial sections are made of the lesion. Hill and other workers would seem to support this view. It seems certain that these epithelial rests provide the lining of cystic cavities, which may form and this seems to the writer to be an important factor in considering the advisability of an apicectomy following root therapy where an apical granuloma exists.

Chronic periapical abscess:- from central suppuration of granuloma due to bacteria or chemicals - Leucocytes and red corpuscles in cavity -- inner wall, inflammatory cells, lymphocytes and plasma cells, few macrophages and very occasionally giant cell-area of attempted organisation -- outer wall, fibrous capsule.

Chapter IV. Cont'd.BACTERIOLOGY.

Most commonly streptococcus veridans (alpha or short-chained group, relatively low virulence.)

Thoma quotes appleton's figures:-

Alpha streptococci	86%
Beta streptococci	5.5%
Gamma Streptococci	3.9%
Delta streptococci	4.4%

Actinomycosis and tubercle bacilli occasionally.

Stones tabulates figures of 206 periapical areas of all types which include:-

Str. veridans	61% pure and mixed cultures.
Staph. aureus	28% pure cultures.
Staph Aureus	32% pure and mixed cultures.
	15% pure cultures.

Other types of streptococi, staphylococci, B. Coli, pseudomonas pyocyanea, ditherooids and micrococci less frequently.

Fistula or sinus formation.

Progressive alveolar bone resorption - surface perforation-- discharge into mouth (chronic sinus) occasionally tracks along mucoperiosteum to discharge externally (submental, submaxillary, even distant sites such as thorax). -- Walls of sinus inflammatory with surrounding fibrous tissue -- sometimes surface epithelium has penetrated.

Cholesteatoma.

Foam cells, -- fatty degeneration - formation cholesterin crystals - cholesteatoma cysts formed with major content cholesterin -- slit like spaces alcohol soluble.

Tooth resorption.

Cementum contacts infections -- cell necrosis -- necrotic cementum is now foreign body -- osteoclasts, resorption -- dentine may also be involved -- secondary-dentine may form -- secondary osteocementum from reformed cementoblasts if periodontal membrane not completely destroyed.

TREATMENT.

- a. Exodontia without curetting.
- b. Pulp canal drainage and root therapy.
- c. Local anaesthesia may not be fully effective.

Comment. Archer classifies these abscesses into classes with or

Chapter IV. Cont'd.Treatment. Cont'd.

without soft tissue oedema and states that medical graduates often oppose immediate removal of the tooth. Provided excessive trauma can be avoided there is no doubt that exodontia may be carried out.

Thoma states that primary acute dentoalveolar abscesses are rare, and are often due to exacerbation of chronic lesions.⁽¹⁾ This point is not made in Stone's "Oral and Dental Diseases," and experience would indicate that rapidly forming acute abscesses occur quite frequently following untreated traumatic injuries to the teeth, and that rampant caries often produce acute symptoms without evidence of any pre-existing chronic phase.

MODE OF SPREAD OF PERIAPICAL ABSCESS.

Lysis of bone-----subperiosteal abscess.

Collateral oedema ----- corresponding lymph nodes tender --
periosteum ruptured may spread as in diagram -- diagrams have been used to describe the modes of spread of suppurative infections and to demonstrate the anatomy of the spaces involved. They are composite sketches derived from:--

Thoma -- Robinson, "Oral and Dental Diagnosis," pp 40 -- 41.

Messler -- Schour, "Atlas of the Mouth."

Brash, J. C., "Cunningham's Manual of Practical Anatomy" Vol III,
11th Edn. 1952.

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(SEE ILLUSTRATIONS OVERLEAF.)

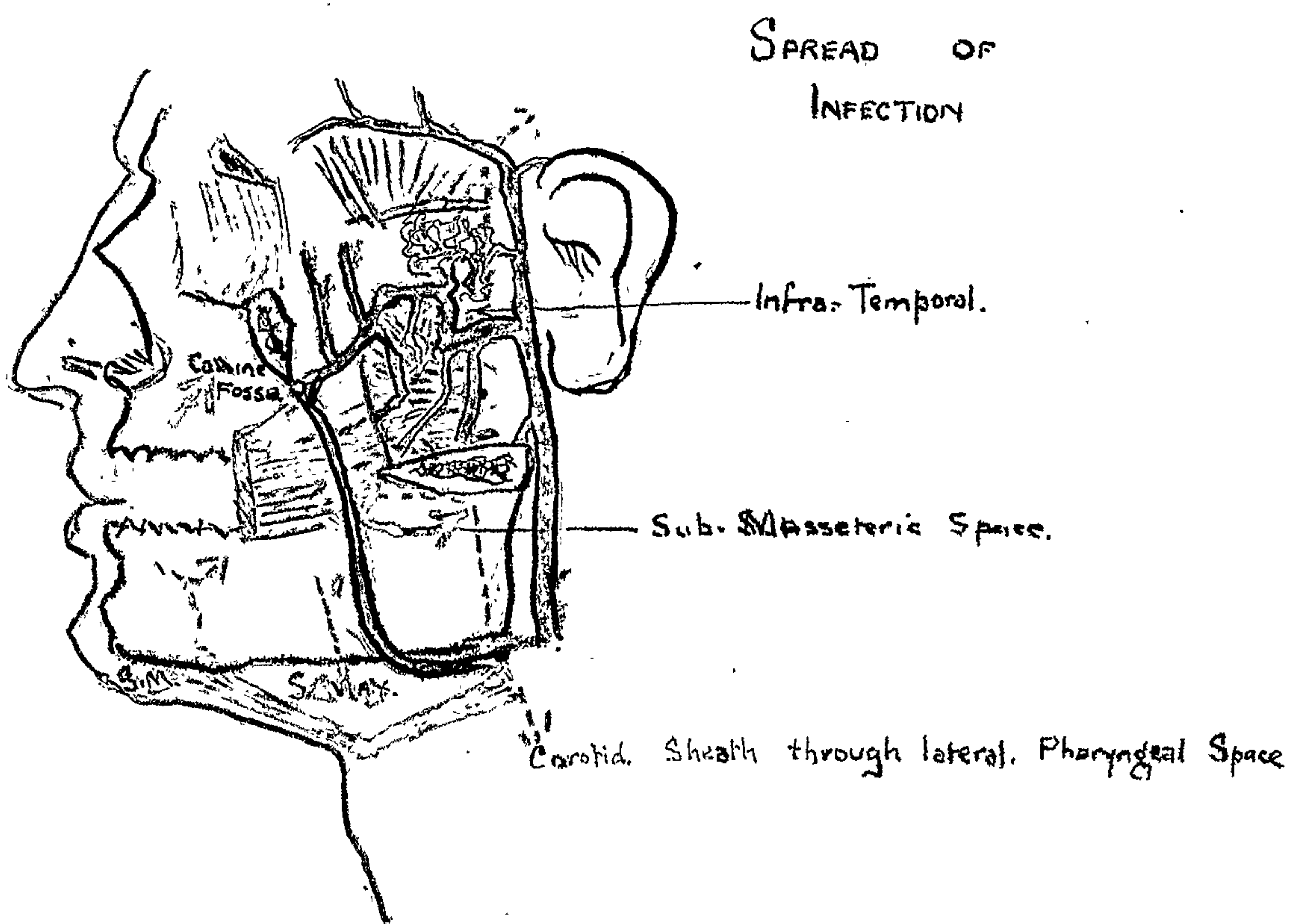
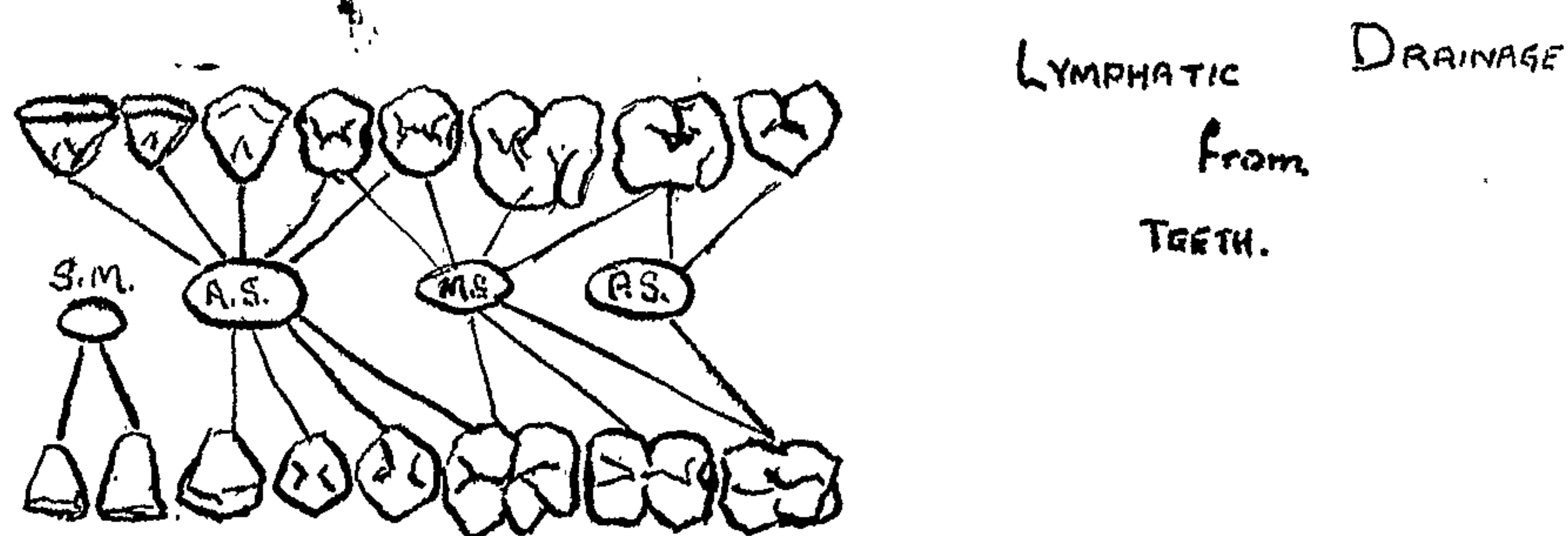
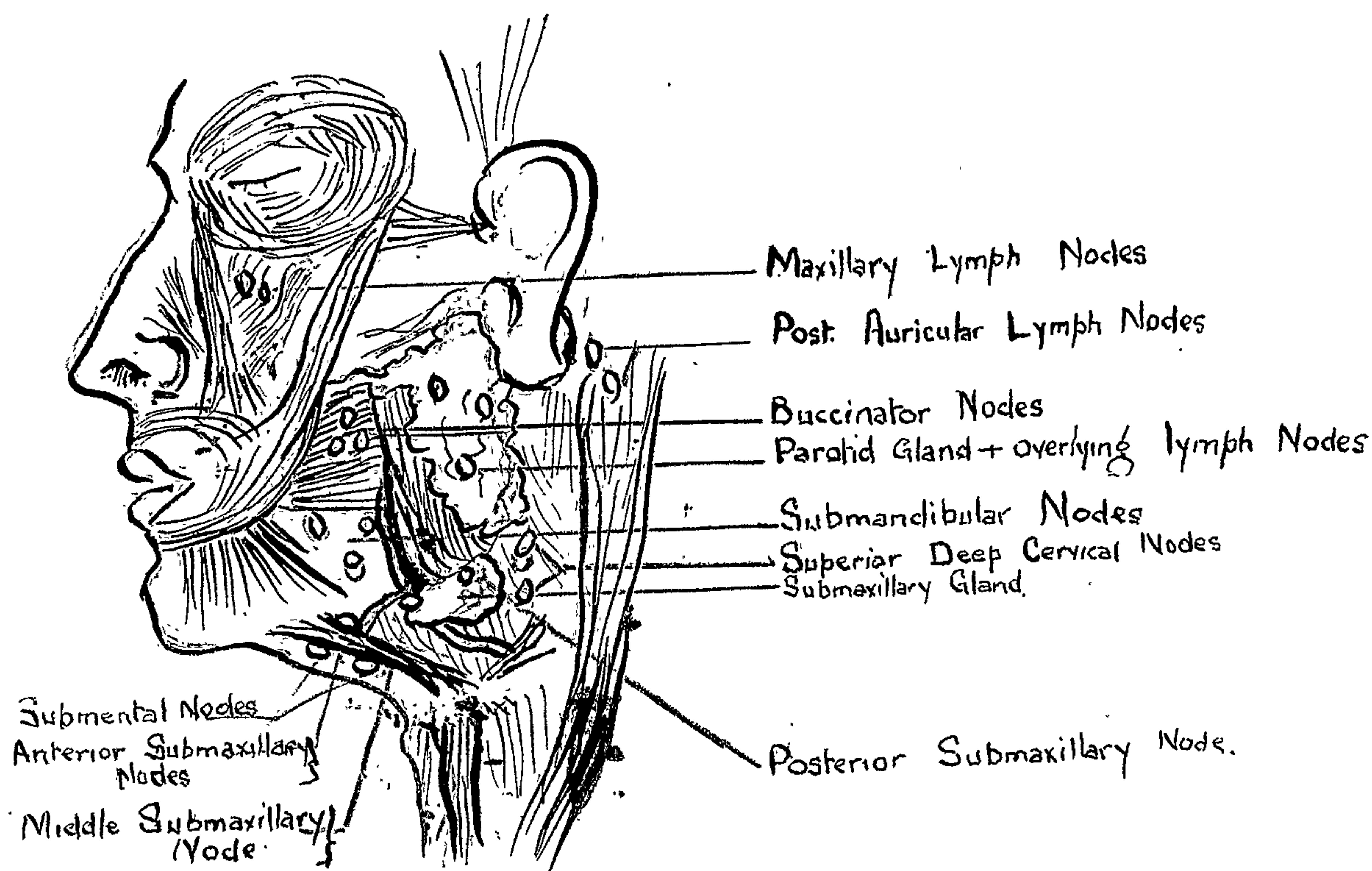
Periapical Granuloma and Chronic Periapical or Dento-alveolar abscess.AETIOLOGY.

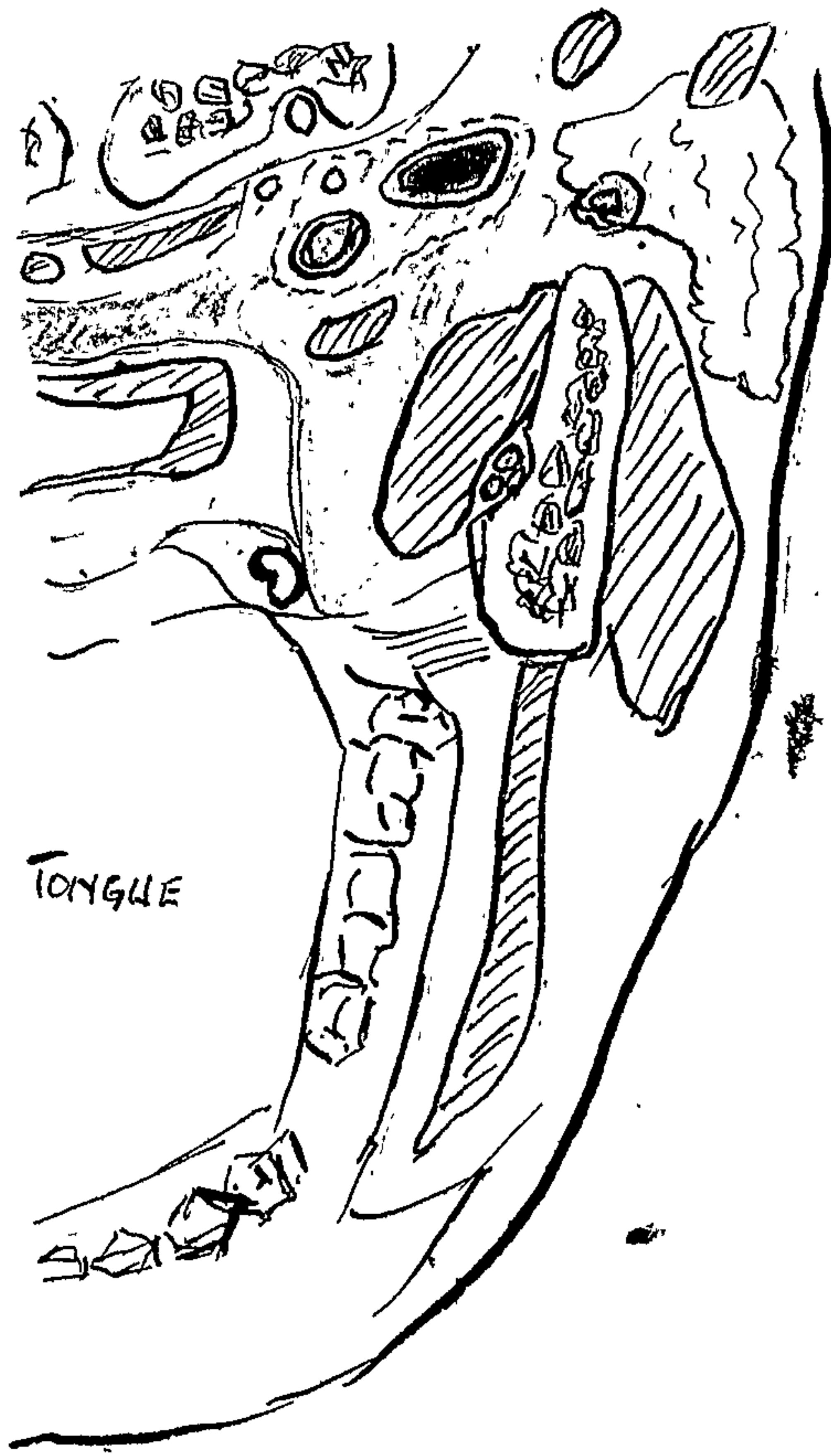
a. Pulpitis -- gangrenous pulp -- periapical spread -- inflammatory reactions with lysis of bone.

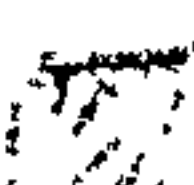
b. Acute abscess ----chronic abscess.

In 1946, Hill suggested that pyogenic bacteria at the apex produced chronic abscesses, and that granuloma had a distinct aetiology from non-pyogenic bacteria. ⁽²⁾

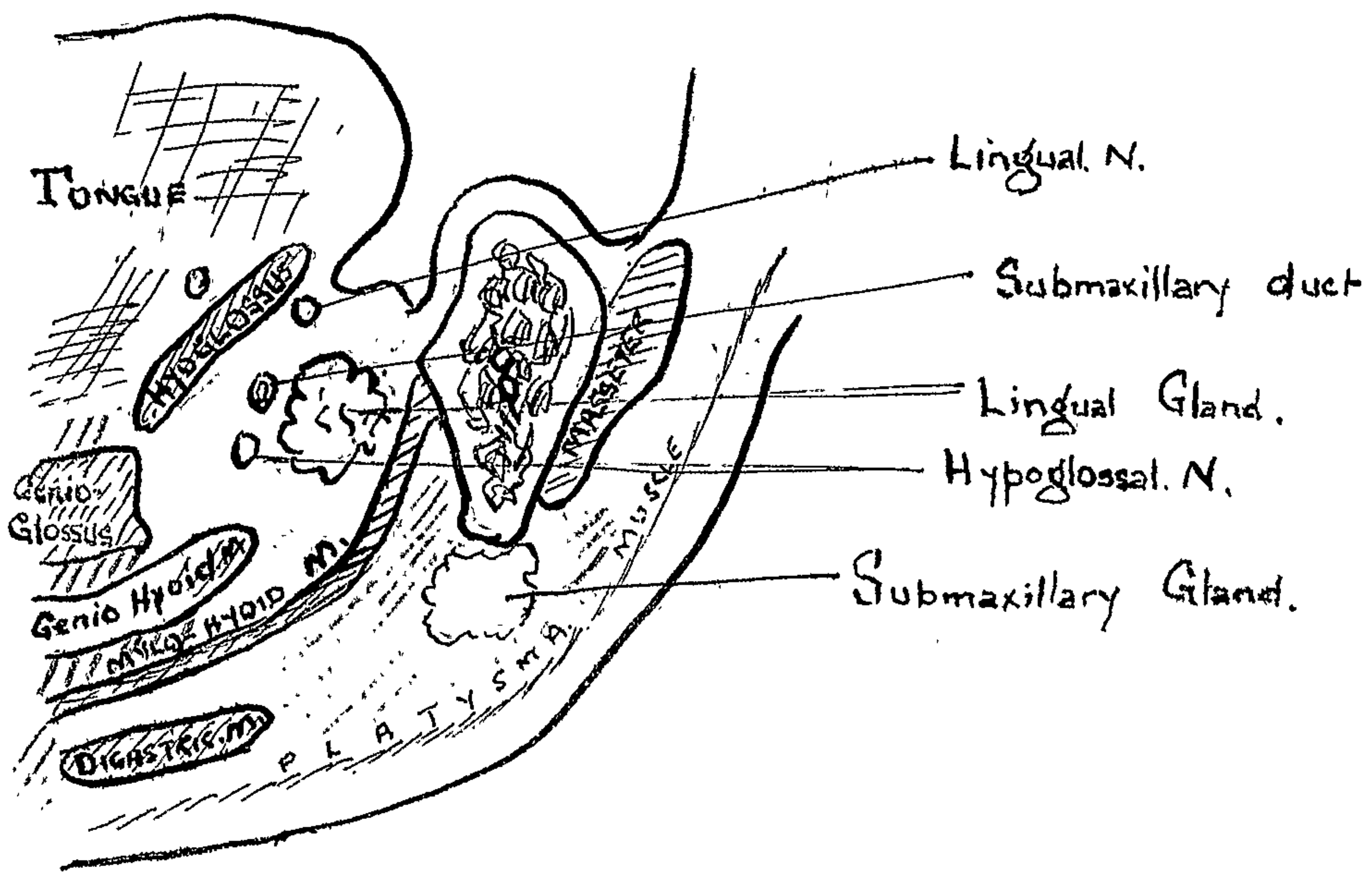
LYMPH NODES OF FACE AND NECK.

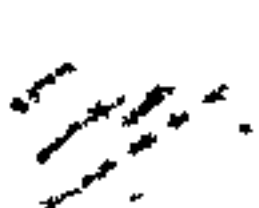




-  Retropharyngeal Space.
-  Parapharyngeal Space
-  Carotid Sheath

- Infections of Parapharyngeal Space. meet resistant barrier before penetrating Carotid Sheath



-  Sublingual Space.
-  Deep Sublingual Space
-  Submaxillary Space.
-  Submental Space.

Chapter IV. Con'd.

HISTOLOGY AND PATHOGENESIS.

Primary granuloma -- low grade infection -- chronic inflammatory cells invade periodontal membrane -- small lymphocytes and plasma cells:- A few polymorphonuclear leucocytes, macrophages and sometimes foam cells and osteoclasts -- fibroblasts and new blood vessels.

Hypercementosis.

If periodontal membrane (not directly contacting infection) remains vital -- secondary cementum on whole of apex from cementoblast -- apical foramen sometimes obliterated -- difficult exodontia (avulsion contraindicated, value of X-rays.)

Sclerosed granuloma.

Infection defeated -- inflammatory cells disappear -- collagen growth-ossification to form sclerosed bone -- if no ossification, fibrous healing.

Condensing osteitis.

Very low grade infection -- stimulates osteoblasts -- bony sclerosis on trabeculae diminishing or obliterating marrow spaces.

Residual infection.

Remains after extraction -- frequently due to small tooth fragment. Persistent inflammatory granulation tissue -- radiolucent.

Lymphangitis.

Is rare, but when it occurs, the vessels are clearly defined as they extend down the neck.

Lymphadenitis.

See sketches for location and drainage paths.---

Acute lymphadenitis from acute infections -- slight enlargement -- elastic soft and sensitive to palpation -- usually some subcutaneous oedema. Chronic lymphadenitis -- enlarged painless and not adherent, nodes may remain permanently enlarged and subject to tuberculous infection.

In differential diagnosis, adenopathy resulting from systemic conditions must be considered. Myelogenous and lymphatic leukaemia, lymphosarcoma, syphilis, tuberculosis and infectious mononucleosis, (glandular fever) must be considered as possibilities. Where there is

Chapter IV. Cont'd.

bilateral adenitis systemic conditions⁽³⁾ or stomatitis should be considered. Specific tests and blood counts will help in diagnosis.

CELLULITIS.

Diffuse spread inflammation of connective tissue -- not localised as abscess -- usually streptococcal (streptokinase and hyaluronidase) often of dental origin -- widespread oedema and exudate containing granular leucocytes. Clinical feature, "hard brawny" swelling with pain over affected area -- febrile (100+) condition with malaise and prostration in severe cases. -- Lymphadenitis.

Rapid feeble irregular pulse -- may progress to diffuse phlegmon or widespread suppuration. -- Streptococcal cellulitis may be inflammatory spread without suppuration.

Chronic cellulitis -- from infections of low virulence or inadequately treated. -- Acute cellulitis -- "woody phlegmon" -- biopsy assists in differential diagnosis.

TREATMENT OF CELLULITIS.

Most surgeons now use massive doses of antibiotics, still often in conjunction with 1 gm. of sulphadiazine every four hours. But the principle of encouraging fluctuation and establishing drainage at the earliest opportunity is, as ever, essential. The cause of infection should be diagnosed and quickly eliminated. Immediately a specimen is obtained, sensitivity tests using "sensitabs" should be made to determine the most effective antibiotic.

It is most unwise to rely on antibiotics alone; they should be regarded as useful adjuncts to thermotherapy and drainage by incision. External hot poultices (flaxseed, antiphlogistine) encourage fluctuation, which is the ideal state for incision, but if after 5 to 7 days there still persists a brawny induration which pits on pressure and the general condition is still febrile, an incision should be made and exploration with a blunt instrument (to avoid damage to vessels) carried out to locate suppuration. Where fluctuation has been established, incision is followed by the use of blunt ended Hilton's forceps to open the connective tissue spaces. A wick of gauze^{or} twisted rubber may be inserted

Chapter IV. Cont'd.

TREATMENT OF CELLULITIS. CONT'D.

to maintain the opening thus formed, but Professor Arnott's technique of using perforated rubber tubing is the most effective means of ensuring continued drainage.

Care should be taken that all infected spaces are discovered. Drainage and antibiotic therapy is continued until all discharge ceases, and the general symptoms subside.

Dysphagia and fever cause dehydration of the patient and adequate fluid and liquid diets should be taken. Therapeutic doses of Vitamin B complex and ascorbic acid are advisable.

Archer does not distinguish between abscesses and cellulitis of the intermuscular spaces. While the treatment is similar, the prognosis of a well defined abscess is better than in cellulitis and a differentiation should be made.

Almost all texts and Steadman's Medical dictionary do not distinguish between the term phlegmon and cellulitis, but Thoma suggests that non-suppurative cellulitis is a phlegmon.

LUDWIG'S ANGINA.

Ludwig in 1826, described a bilateral cellulitis of the floor of the mouth. Frequently arising from dental infection, the condition is often fatal, but present day treatment has improved the prognosis. In "Oral Pathology", Thoma cites eight cases of which six recovered. In non-suppurating types of Ludwig's Angina it is impossible to establish drainage, but where suppuration occurs and drainage can be established the prognosis is more favourable.

Ludwig's original description of the essential features was (4)

1. Insignificant inflammation of the throat, which disappears.
2. Woody swelling which does not pit on pressure.
3. Hard swelling of tongue, forming a reddish or bluish callus ring within the inner border of the mandible.
4. Well defined border of induration of neck, surrounded by healthy connective tissue.
5. Slight or no involvement of the glands.

Elevation of the tongue is also an important sign.

Chapter IV. Cont'd.

LUDWIG'S ANGINA.

The submaxillary and sublingual spaces are always involved and there may be an acute rapid spread to the other areas. Involvement of the mediastinum has been reported.

The temperature may vary from 99° to 105° . A moderate temperature associated with marked clinical signs may signify an unfavourable prognosis.

Bacteriology.

Generally due to streptococcus, of the haemolytic, viridans or non-haemolytic type, staphylococcus aureus and albus, fusiform bacilli and Vincent's spirochaetes are commonly present.

Aetiology: The majority of cases are due to dental or tonsillar infection. Because their roots reach below the mylohyoid ridge, the lower second and third molars are frequently the source of infection. Undernourishment is often an important predisposing factor.

Treatment: Apart from the treatment essential in cellulitis, it must be emphasised that oedema of the glottis or tongue may cause rapid asphyxiation unless tracheotomy is promptly carried out. Winter stresses the importance of not waiting, but acting on the slightest evidence of cyanosis.

Intravenous infusions of dextrose are necessary where deglutition is impaired.

OSTEOMYELITIS.

The great majority of cases of pyogenic infection of the jaws arise from infected teeth. As pointed out by Fleming, there is no clear pathological distinction between osteitis and osteomyelitis.⁽⁵⁾ Quoting Dorland's definition of osteomyelitis as:- "Inflammation of a bone, inflammation of the Haversian spaces, canals and their branches and generally of the medullary cavity," Fleming finds it convenient to distinguish clinical osteomyelitis on the basis of:-

1. The presence of pus.
2. The tendency to spread.
3. The formation of sequestra.

To Thoma, the essential distinction is the absence of a pyogenic membrane, and he classifies the adult lesions as chemical osteomyelitis, suppurative osteomyelitis, ossifying osteomyelitis and irradiation

Chapter IV. Cont'd.OSTEOMYELITIS. Cont'd.

osteomyelitis.

Osteomyelitis of the Jaw in Infants and Children.

All authors describe osteomyelitis in infants as a separate entity. Only about 80 cases have been reported.

Pathogenesis and Aetiology.

Infection, the source of which is the subject of controversy — originally maxillary sinus suggested, but it now seems that crypts of deciduous molars are likely source — infection possibly from mother's nipple through small break in mucosa. — Perhaps from vagina during parturition, haematogenous involvement also occurs. — Staphylococcus aureus most common (Wilensky) — Streptococcus, pneumococcus septicæmia and B. coli may also be isolated.

Clinical features.

Maxilla most common site but mandible also affected. In some cases sudden onset — highly febrile — severe systemic reaction, rapid pulse, delirium, prostration. If maxilla involved, red facial swelling, ecchymosis — swelling of palate and alveolus — fistulae and suppuration often through nose — sometimes ocular cellulitis — difficulty in nursing. In second form child ill but physical signs not so marked. In yet another type, slow onset, moderate pain and slight temperature. Sequestra form and exfoliate often with tooth germs.

May be fatal but many recover. Roentgen examination difficult.

Treatment:— supportive, nutritional — antibiotic — assist sequestration.

OSTEOMYELITIS IN OLDER CHILDREN AND ADULTS.Acute Osteomyelitis.

"Muir's Text-book of Pathology," in describing acute osteomyelitis of all bones states that the disease occurs most commonly in children between 8 and 12 years old, when there is active bone growth and that staphylococcus aureus in the most frequent causative organism. (6)

In the jaws, the presence of teeth and sometimes dental infection, the different nature of the cortical bone plates and a lesser collateral circulation especially in the mandible modifies the occurrence of the disease. (7) Odontogenic infection is usual cause in the jaws, whereas

Chapter IV. Cont'd.

Osteomyelitis in Older Children and Adults. Cont'd.

the maxilla is most frequently the site in infants, the mandible, due to its poorer blood supply is more often affected in children and adults, and while staphylococcus aureus is still the likely predominant organism, streptococcus is often present.

Clinical Features.

Partial or total -- may be localised to such areas as premaxilla and less frequently the tuberosity -- in mandible part or whole of the body may be affected but often does not involve the ascending ramus. -- Linsey reported a case of osteomyelitis of the condyle following extraction of upper molar teeth, presumably through cellulitis of the pterygo-mandibular space.⁽⁸⁾ Thoma also refers to this complication.

Spongy gingivae with suppurative discharge at margins. -- Mobile teeth. Elevated temperature -- often high. Severe persistent pain -- often before other symptoms manifest. Pulse rate increased, but often not high. A uniform swelling extending over a wide area. Trismus where site approximates muscles of mastications.

Aetiology.

Predisposing causes:-- Lowered resistance -- nutritional, especially Vitamin C, -- diabetes, anaemia, leukaemia and lowered resistance after influenza, measles, scarlet fever and pneumonia.

From direct extension of Infection -- non-vital teeth -- residual infections -- infection around foreign bodies. -- Nasal and sinus disease -- pericoronitis -- ulcerative stomatitis.

From traumatic causes -- fractures, especially compound -- curettage of infected sockets -- clumsy traumatic surgery, especially when burrs are used in place of chisels.

From haematogenous source:-- infected thrombi -- metastatic staphylococci⁴ thrombi -- tuberculosis, syphilis and actinomycosis -- often multiple osteomyelitis from haematogenous source.

Pathology.

Essentially involves the spongiosa, Haversian canals and periosteum usually arises in spongiosa and spreads through the communicating blood vessels, often thrombosis -- damaged blood supply -- necrosis --

Chapter IV. Cont'd.

Osteomyelitis in Older Children and Adults. Cont'd.

separation of necrosed portion by line of granulation tissue -- mainly separation by absorption of living bone at margin of necrosis.

Repair process from osteoblastic activity of stripped periosteum -- new bone sometimes poorly developed (involucrum).

Sequestrum may form one unit but often there are several small sequestra. -- Occasional report of entire mandible sequestering.

In maxilla, sequestrum normally replaced by fibrous tissue.

Leucocytosis -- up to 20,000 per c. mm.

Bacteriology.

Usually staphylococcus aureus also streptococcus haemolyticus, pneumoniae, micrococcus tetragenus, E. coli and eberthella typhosa.

Radiology - not conclusive in diagnosis but valuable -- a mottled appearance, -- alternating rarefaction and condensation -- stripped periosteum sometimes detected -- series of Xrays show progress of condition and clear dark band of demarcation indicates time for removal of sequestrum.

Differential Diagnosis.

Malignant neoplasms: history, biopsy: total and differential white cell count.

Actinomycosis: Bacteriology if possible; site of lesion; chronicity.

Osteitis fibrosa cystica: Similar radiogram -- blood serum Ca⁺⁺ and phosphatase clinical symptoms.

Syphilis. Wasserman Test.

Complications.

Maxillary sinusitis. -- Parasthesia -- especially of inferior dental nerve.

Pathological fracture.

Pyæmia and metastatic abscesses from septic thrombi -- especially likely from staphylococcus aureus. Cavernous sinus thrombosis.

Cellulitis and Ludwig's angina.

Treatment.

Supportive: hospitalisation in all but minor cases. -- Therapeutic Vitamin D and C, 250 mg. per diem high protein and caloric diet; high calcium and phosphorus content -- attention to oral hygiene.

Chapter IV. Cont'd.

There is considerable divergence of opinion on the use of heat. Winter favours the use of hot internal saline washes with external cold compresses. Stones considers that the use of heat may spread infection while Thoma believes that many cases of the disease are due to the injudicious use of heat on suppurative abscesses. It is probable that the use of heat is justified where collateral cellulitis exists. Drainage of soft tissues and sockets must be maintained throughout by the use of fenestrated tubing.

The jaws should be immobilised where pathological fracture may occur.

Chemotherapy and Antibiotics.

Their use has greatly improved the prognosis -- massive and continued dosage (see section on chemotherapy and antibiotics for precautions.) Repeated sensitivity tests are important.

Surgical.

Most authors advise against early surgical intervention and Professor Arnott is adamant on this point. Barton quotes Blum on conservative treatment: "There is only one treatment for osteomyelitis and that is conservative; watchful waiting, evacuation of pus, whenever and wherever it collects, and finally removal of sequestra when they are fully separated." (9)

It is however, sound practice to establish drainage of soft tissues as soon as fluctuation occurs. Except where involved teeth are extremely mobile, exodontia should be delayed in the acute phases.

When sequestra are completely separated, their removal can be safely carried out. An intraoral approach is usually satisfactory, but an external incision may be necessary where the inferior border of the mandible is involved. The post or pre-auricular approach is indicated for the condyle, but the coronoid process may be approached through an incision of the pterygomandibular raphe. Roentgenograms should be used to determine the timing for sequestrectomy.

Should sequestrum removal leave undercut margins, Thoma advises 'saucerization' whereby tissue is removed to form a saucer-like cavity.

Chapter IV. Cont'd.Acute Osteomyelitis. Cont'd.

Drainage tubes should be used if any discharge is expected.

Stones describes Mowlem's treatment of osteomyelitis by decorticectomy, carried out by removing the dense cortical bone at the inferior border of the mandible and the outer cortical plate, excising spongiosa until only fresh healthy bleeding bone is exposed and re-suturing the muco-periosteum. During his visit to Australia in 1956, McGregor also advocated this operation. In 1949, Wass advocated that this operation be carried out early. It would seem that such an early interference would easily produce a severe acute exacerbation.

CHRONIC OSTEOMYELITIS.

Less severe symptoms -- prolonged course -- lower leucocyte count, 8,000 -- 10,000 per c.mm. -- protracted occasionally sub-acute phases -- intermittent expulsion of necrotic bone. -- Search for less frequent causal organisms and suitable antibiotic -- X-ray therapy, 60 -- 100 R units bi weekly, helpful. (10)

OSSIFYING OSTEOMYELITIS.

Chronic osteomyelitis with sclerosis of spongiosa -- seen in tertiary syphilis, from weak toxins and perhaps from thrombi in intraosseous vessels. -- Treatment is by radical excision.

CHEMICAL OSTEOMYELITIS.

May be caused by caustic agents, phenol paraformaldehyde, -- mercurial poisoning -- inflammation of oral mucosa -- chemical necrosis of bone -- secondarily infected to produce osteomyelitis -- this condition usually confined to alveolar bone -- sequestrum of large portion of alveolar process with teeth.

Phosphorus necrosis -- chronic periostitis from irritation of phosphorus vapours -- deposit of new bone and old bone become necrotic -- secondarily infected from teeth or stomatitis causing severe osteomyelitis. Large sequestra or entire bone gradually surrounded by involucrum.

PERIOSTITIS.

More common in maxilla and mandible than in other bones.

Types:-- traumatic, chemical, suppurative, chronic and ossifying.

CHAPTER IV. Cont'd.

PERIOSTITIS.

Traumatic periostitis -- tender -- ecchymosis -- pain -- slight swelling -- suppurative -- fever and general symptoms -- collateral swelling -- subperiosteal abscess -- drainage.

Periostitis ossificans -- chronic inflammation -- bone deposited -- hyperostosis -- involucrum (syphilis.)

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Thus far, a series of pyogenic infections have been described, starting from the simple dento alveolar abscess. In some cases the opportunity has been taken to discuss the non-suppurative forms of these conditions. Apart from the apical abscess the following conditions may also lead to a spread of infection:-

PERICORONITIS.

Partially erupted teeth with overlying gingival flap (operculum) surrounded by remnants of the follicle present ideal site for infection - damage in occlusion and food impaction. -- Most common in third molars, especially mandibular, but also erupting first molars and other teeth which are partially impacted. -- Pericoronitis, acute, sub-acute and chronic -- mixed infections but especially watch for Vincent's -- pericoronal abscess where enclosed in follicular crypt -- partially erupted tooth susceptible to caries -- bone resorption -- neuralgic pain -- spread of infection likely from lower third molar, parapharyngeal, peritonsillar, submaxillary and sublingual abscess.

Treatment:- Reduce inflammation of acute condition (glycerin and tannic acid; glycerin and iodine -- antibiotics) remove operculum -- if impacted, surgical removal.

PERIODONTAL ABSCESS (Parodontal Abscess).

Although of significance to the oral surgeon, those periodontal diseases usually treated by the periodontist are not here discussed. However, there is no doubt that the parodontal abscess should be mentioned in this chapter. A complication arising from periodontal disease or gingivitis, these abscesses form in the pockets or between the roots of multicrooted teeth.

Chapter IV. Cont'd.PERIODONTAL ABSCESS Cont'd.

Aetiology: General resistance -- diabetes mellitus important -- scurvy of deficient vitamin C. -- blood dyscrasias; local -- failure to drain back through gingival or periodontal pocket -- trauma (tooth brush bristle, fish bone, food impaction.)

Signs and Symptoms: sometimes masked -- percussion not so pathognomic -- slight to severe swelling -- occasionally a fistula.

Diagnosis: Sometimes difficult -- Xray assists but various angles must be used to locate -- pulp nearly always vital.

Histopathology in acute and chronic conditions similar to periapical abscess. Thin alveolar bone often completely destroyed.

Vigorous chewing may produce transient bacteraemia due to tooth movement in 75% of cases (Round Kirkpatrick and Hails 1936) and thus the condition could have more significance in focal infection than apical conditions.

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THE FURTHER SPREAD OF PYOGENIC INFECTION.Infection of the Maxillary sinus (empyema.)

From a number of causes -- colds, influenza, scarlet fever, measles, diphtheria, from the nasal cavities and other paranasal sinuses.

Stones states that 8 -- 20% of infections of the antrum of Highmore are of dental origin. This is probably a very conservative figure. In 1915, Brophy thought the percentage would be 75, but the practice of dentistry was then in a different era. But in 1943, Bauer made histological examinations of the Schneiderian membrane (lining the sinus) and found a remarkable correlation between its inflammatory changes and periapical, periodontal and pulpal infections of the maxillary teeth. These experiments were carried out on autopsy material. More recently, after taking biopsy specimens of the antral lining of thirty two patients with infection of the maxilla, Fleming found an inflammatory reaction in every case. ⁽¹¹⁾ He considered that the ready spread to dental infection to the maxillary sinus was due to the inseparable blood supply of the antrum and teeth and that an intact lining with wide bony separation was insufficient protection.

CHAPTER IV.. Cont'd.The further Spread of Pyogenic Infections. Cont'd.

There is considerable variation in the relation of the maxillary sinus to the apices of the upper teeth and where the upper first permanent molar tooth has been extracted early, there may be very little alveolar bone separating the sinus from the oral cavity. It may be mentioned here that this state presents a hazard in exodontia, for the whole of the tuberosity may be fractured easily. Should this occur, it is best not to break the mucosa, but repair the fracture and later remove the tooth by careful surgical methods. In any case, this would have been the most desirable course.

ACUTE MAXILLARY SINUSITIS.

Often from acute dental infections. Also from extractions and fractures involving the maxillary wall.

In some cases localised inflammatory without exudate — common cold. When from dental focus — purulent discharge — hyperaemia of membrane, oedema in submucosa and membrane may fill cavity — leucocyte infiltration — localised abscesses — purulent discharge in unoccupied antral cavity. Signs and symptoms — typical of acute inflammation with exquisite severe neuralgic pain and strong sensation of pressure — throbbing odontalgia (confuses diagnosis) often purulent discharge from nose — foetid breath — pus in middle meatus — usually swelling of cheek and lower eyelid and soreness to pressure especially in infraorbital region and canine fossa.

Complications.

Septicaemia — pyaemia, — retrobulbar cellulitis — meningitis — cavernous sinus thrombosis.

CHRONIC MAXILLARY SINUSITIS.

Either follows acute disease, primary — vague neuralgic pain, unpleasant taste and odour especially in mornings — middle meatus may contain pus or extruding polyp. — Pain may be absent.

General Symptoms: frequent colds — pharyngitis — gastro-intestinal symptoms — fatigue often from secondary anaemia and from toxæmia — sallow complexion.

Chapter IV. Cont'd.

Chronic Maxillary Sinusitis.

Histopathology: Usually osteitis -- oedema, chronic inflammatory cells, fibrosis, cystic degeneration -- granulation tissue with mucosal proliferation to form polyps -- which may completely obliterate the sinus. Some eosinophils are associated with lymphocytes and plasma cells, pavement type squamous epithelium in polyps.

Radiology: -- Water's position -- suppuration, even foggy appearance -- polypoids, spotty radiopacity.

Treatment:

It is Winter's opinion that all sinus treatment should be carried out by the rhinologist and that the operations should not be performed through the oral cavity. Most authorities now agree that sinus conditions of dental origin may be properly performed by the oral surgeon and that the Caldwell -- Luc operation through the canine fossa provides excellent and safe access in removing polypoid tissue and roots. Frequent normal saline lavages using the Higginson syringe may be carried out in cases of acute empyema following accidental exposure of the sinus in dental extraction.

It is convenient to mention here the closing of antro-oral fistulae, which may persist after exodontia involving the antral floor. With the proper use of Xrays and the surgical removal of teeth, this would be a less frequent complication. For many years, the use of a Copper Sulphate pencil applied to the opening of the fistula has brought some success. If this has failed, many surgical methods have been tried, but in recent years the use of buccal or palatal pedicle flap embodying the excellent blood supply of the greater palatine artery is preferable. The mucosa around the fistula is "freshened," a broad based palatal flap containing adequate blood supply folded and sutured over the opening. Although at first bulky, there is a rapid reshaping of the palatal mucosa and the prognosis is excellent.

SEPTICAEMIA.

Organisms enter and multiply in blood stream -- rarely sufficiently numerous to be detected by microscopic examination of blood but are easily cultured from it.

Chapter IV. Cont'd.

SEPTICAEMIA.

Prognosis grave -- massive antibiotics -- most commonly from virulent streptococci and meningococci.

Bacteraemia.

Bacterial invasion of blood stream without successful multiplication -- found to be common from periodontal lesions.

In sub-acute bacterial endocarditis there is a continual bacteraemia, and bacteraemia would appear to be the original cause of the disease.

"It will be readily be understood, that when bacteria gain entrance to the blood in any way, there is always the risk that they may settle in some part of the body and produce serious lesions..."⁽¹²⁾

Metastatic lesions -- suppurative meningitis, arthritis.

Multiple abscesses (pyaemia) especially in lungs, brain, kidney and heart wall. Infected thrombi also cause pyaemia.

CAVERNOUS SINUS THROMBOSIS AND THROMBOPHLEBITIS.

These are rare and grave complications which may result from trauma and infection.

^{Thrombosis}
Thrombophlebitis is an inflammation of a vein from an infected thrombus and Cavernous Thrombophlebitis is the condition which may result from infection in:--

1. The lip, angle of the mouth, nose and eyelids, via the superior labial, anterior facial, supra-orbital, inferior and superior opthalmic veins.

2. The intra-nasal septum, conchae posterior ethmoidal, sphenoidal and rarely the maxillary sinuses through the ethmoidal veins and wall of the sphenoidal sinus.

3. The tonsils, maxilla, parapharyngeal space (from lower molars) through the pterygoid plexus of veins, through emissary veins to the cavernous sinus.

Signs and symptoms.

Headache, pain of the orbit on the affected side, conjunctival oedema forming a swelling around the cornea (chemosis) opthalmoplegia and ocular proptosis.

Nausea, and vomiting. High temperature -- up to 104° F. Meningeal

Chapter IV. Cont'd.Cavernous Sinus Thrombosis and Thrombophlebitis.

involvement in later stages, when mentality is impaired.

Where infection ascends through the sphenoidal sinus or petrous temporal bone, cranial symptoms may develop without the ocular signs.

Bacteriology: Usually staphylococcal or streptococcal.

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Brain abscesses, meningitis and lateral sinus thrombosis have been reported following oral infection. Crowe and Kelley report the development of Carotid-Cavernous Sinus fistula following facial injury⁽¹³⁾ The symptoms of diplopia, bruit of the eye, buzzing noises from intracranial pressure resulted from damage to the internal carotid artery wall leading to rupture and discharge of arterial blood into the cavernous sinus. (not necessarily infection)

Finally, in this section on the spread of infection, the pathway provided by the carotid sheath must be mentioned. Lying dorsally in the parapharyngeal space, the common ^{carotid Artery} and internal jugular vein are enclosed in processes from the cervical fascia, which usually shuts off infection of the space but on the rare occasions when infection enters the sheath, pus may find its way as far as the mediastinal cavity. The prognosis then, of course, is very grave.

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PART I.

Chapter V.

THE QUESTION OF DENTAL FOCUS OF INFECTION.

It is felt that a discussion of this contentious subject must be included in a Review of Literature entitled "Pathology and Medicine in Oral Disease." Generally Medical and Dental Science has calmly and carefully examined new ideas and finally accepted or rejected them with dignity. This cannot be said of the theory of the focus of infection. The answer is still not known, -- the question is unsolved and therefore discussion is necessary.

DEFINITION:

In the last chapter the direct spread of infection to nearby and distant parts was described. That this spread takes place is indisputable and the reasons for its occurrence are readily explained by a study of anatomy. "By focal infection is meant the setting up of secondary infection at a distance from the oral lesion." (1) The spread is assumed to be via the lymphatics or blood stream as opposed to that of direct anatomical continuity.

HISTORY:

The possibility of 'oral sepsis' has been suggested at intervals since the time of Hippocrates, but the somewhat emotional story begins with William Hunter's denunciation of 'septic dentistry' in 1910. When one considers the effect of the era of great bacteriologists in the mid-nineteenth century and the almost purely mechanical nature of Dentistry in the early twentieth century, the indictment was probably inevitable. Impetus to the theory of focal infection came from the writings of Billings (1912) and Rosenow (1914). There followed an era of mass extractions, -- the reaction was extreme, and certainly both physicians and dentists advised extractions on the flimsiest clinical signs and often without radiological evidence of lesions. Non-vital teeth were often condemned out of hand.

By the mid-thirties many eminent bacteriologists were sceptical and realised that scientific proof of the theory was lacking.

Chapter V. Cont'd.

THE QUESTION OF DENTAL FOCUS OF INFECTION. Cont'd.

By the mid-thirties many eminent bacteriologists were sceptical and realised that scientific proof of the theory was lacking.

In September, 1948, the proceedings of the Discussion Group of the Institute of Dental Research of the United Dental Hospital of Sydney were reported in the "Dental Journal of Aust." (2) (3) In June 1951, Easlick submitted a report to the Council of Dental Health of the American Dental Association which was an evaluation of the literature on the role of dental foci of infection in systemic disease and the references included the Australian's opinions. In general, the theme was that proof was lacking, but there was no outright condemnation of the whole theory. Of the Australian lecturers, Professor Ward was the most condemnatory and his main objections were the lack of scientific proof. Most of his discussion centred around foci in relation arthritis and it now seems likely that scepticism towards the focal theory for this disease will be justified.

Under such headings as "Focal Infection Debunked" and "Don't pull those teeth" Easlick's work was reported to the public in the lay press of the United States. This produced a violent reaction from Mead and Belding in the aggressively independent journal "Dental Items of Interest." In June, 1952, Mead presented an article entitled "A Discussion of the American Dental Association's Attitude on Focal Infection." In January the following year his next article on the subject was more balanced and was really an excellent evaluation of the unsolved problems involved. (4)

Since then, there have been few references to the subject in dental literature. Thoma deals with the subject in "Oral Pathology" briefly and sensibly, using a heading, "The latest Concepts of Focal Infection." (5) Stones in "Oral and Dental Diseases" is more thorough and his careful treatment of the subject indicates a desire to an ultimate solution to the problem. (6)

Chapter V. Cont'd.

THE QUESTION OF DENTAL FOCUS OF INFECTION. Cont'd.

In "Oral and Dental Diagnosis," Thoma and Robinson devote a well written chapter to the subject, but deals with focal infection in conjunction with direct extension of dental disease, (6) Clearly, the time has come when the more obscure concept of focal infection should be separated from discussions on the well accepted process of direct extension.

Perhaps the only point in relating this history is to emphasise that dental science must progress along the lines of careful analysis, clinical investigation with the use of controls and sound laboratory procedures in co-ordination with the other sciences.

TRANSMISSION OF INFECTION.

a. Via the Blood Stream.

The haematogenous mode of spread immediately suggests itself as an explanation of the focal theory. In the last chapter, septicaemia bacteraemia and infected thrombi were described. It can be fairly stated that cavernous sinus thrombo-phlebitis is a proven example of bacterial transmission via the blood stream. Almost as well accepted is Fleming's theory of maxillary sinusitis from a dental source (7) where there is a bony separation, through the interconnecting blood vessels. Okell and Elliott reported a significant incidence of bacteraemia (usually streptococcal) in associated with periodontal lesions. Stones describes the work of Lazansky, Robinson and Rodofsky recording bacteraemia in 2% of cases following a single extraction.

It is possible that bacterial toxins may produce distant lesions even where the organisms themselves are not transmitted. Ward (op. cit.) pleads that the word 'toxins' be used only where poisonous substances have definitely been isolated from a given strain of organism. Comroe suggests that bacterial proteins acting as antigens may sensitise tissues to later bacterial invasion. Rosenow's work demonstrated that certain bacteria have a predilection for specific organs. This is called "elective localisation."

Chapter V. Cont'd.

TRANSMISSION OF INFECTION. Cont'd.

Infection may spread through the lymph vessels. Regional infection of lymph nodes is common, especially in children. This positive evidence of lymphogenous infection is sufficient to show that there is at least some justification for the concepts of focal infection. The multiple lesions that occur in advanced syphilis and tuberculosis are further demonstration that haematogenous and lymphogenous transmission is not a myth. In these instances, it is evident that the anti-bacterial properties of the blood are not effective as they usually are for pyogenic organisms, and the regular occurrence lesions leaves no room for doubt in these cases.

There now follows a brief discussion of the diseases which have at times been attributed to dental foci of infection:

Acute suppurative myocarditis: Cappell⁽⁸⁾ mentions that in acute suppurative osteomyelitis especially where the causal organisms are staphylococci, the myocardium is often affected with blood borne suppurative lesions.

Subacute bacterial endocarditis is still commonly ascribed to dental foci. Muir's Text-book (ibid) states "Infection probably takes place chiefly from the mouth, more rarely from the naso-pharynx, especially after minor operations. The work of Okell and Elliott has shown the importance of dental sepsis and teeth extractions in leading to entrance of such low grade micro-organisms into the blood stream and tonsillectomy is also effective --- even firm biting on the teeth affected by apical abscesses can lead to the escape of organisms."

Referring to the last statement in this quotation it is well to state that bacteraemia from peridental pockets is likely to be more common. (Vide supra Ch. IV).

Streptocci viridans generally the causal organisms of sub-acute bacterial endocarditis, are usual in pyogenic periapical lesions, cellulitis, and coccal gingivitis.

Bacterial diseases of the heart valves should be distinguished from rheumatic endocarditis which is probably non-bacterial. Comroe and his.

Chapter V. Cont'd.

Transmission of Infection. Cont'd.

colleagues⁽⁹⁾ remind their readers that subacute bacterial endocarditis occurs only where there already exists some previous valvular or endocardial lesion. The writer has been called to examine a case where bacterial endocarditis had developed after the removal of an apparently uninfected tooth. There was a fatal termination. The practitioners concerned concluded that a condition of sub-acute bacterial endocarditis had already existed, and that a transient bacteraemia from a normal extraction had caused an exacerbation of the condition. Examination of the mouth revealed the normal appearance after exodontia and there was no local inflammation.

At present, it seems wise to use sulphonilamide or antibiotic cover⁽¹¹⁾⁽¹²⁾ when performing exodontia for patients known to have suffered from sub-acute bacterial endocarditis or rheumatic fever.

Nephritis.

It is probable that the underlying cause of glomerulonephritis may sometimes be due to dental infection.⁽¹⁰⁾ A perusal of case histories would seem to indicate clearly that this condition usually results from an infective focus (usually tonsillitis).

The following is a case history⁽¹³⁾ illustrating this point:-

"J.H. Six weeks before admission, a 37 year old man had an abscessed tooth extracted. Six days later, oedema was noted and protein and red blood cells were found in the urine....."

Comroe, Collins and Crane (loc. cit.) state that dental infection may be an aetiological factor in pyelitis, pyonephrosis and perinephric abscesses.

In glomerulonephritis and pyonephrosis, removal of infected teeth must be delayed until the patient's general condition has improved; excepting where there is a steady decline which justifies more immediate intervention.

An exacerbation of chronic nephritis may occur following exodontia and as streptococcus is usually the causal organism triple sulphonilamides should be used pre-operatively and post-operatively.

Chapter V. Cont'd.

Diseases of the Joints.

In the past decades, dental focus was usually bracketed with diseases of the joints and related structures. Probably the ready acceptance of the theory in relation to these diseases has produced the present scepticism.

Arthritis may be ^{of} traumatic, degenerative, neoplastic, ^{or} infective origin or may be due to chemical irritation and endocrine disturbances. Some of the infective types are due to specific organisms, e.g. tubercle bacilli, gonococci, spirochaetes. These are of known aetiology. Acute pyogenic arthritis (septic joints) often follows otitis media and tonsillitis and is possibly of focal origin.

Rheumatoid arthritis (synonyms: atrophic, proliferative, non specific infectious, infective, spondylitis ankylo-poietica) is listed by Gomroe and his colleagues (op. cit.) as an intra articular arthritis of unknown aetiology probably related to focal streptococcal (?) infection.

The same authors (ibid) classify the various forms of fibrositis, myositis ossifera and myositis fibrosa as being possibly due to a non-specific infection. (?) They recommend the removal of focal infection in rheumatic fever (especially infected tonsils) and rheumatoid arthritis as early as possible allowing for the patients' condition. Whilst stating that dental extractions will not cure rheumatoid arthritis, the claim is that generally improved health will benefit the sufferer. Extractions should be carried out one at a time.

Other diseases.

Stones (op. cit, vide supra) quotes various authors who have suggested dental foci of infection as causes of ocular lesions and diseases of the nervous system and skin.

Case History.

In 1943, W.B. a male aged 45 years was referred to the writer by his physician for examination of the oral cavity for possible infected foci. The patient was suffering from a corneal ulcer (purulent Keratitis). Routine full mouth roentgen-rays revealed the presence of a radicular cyst at the apex of the upper right lateral incisor tooth. The cyst on

Chapter V, Cont'd.

Other Diseases. Cont'd.

removal, proved to be infected. The lesion had been symptomless and the tooth was not carious. It had become non-vital as a result of a blow received in the boxing ring and no root therapy had ever been carried out. The lesion in the eye healed spontaneously within eight weeks of operation.

Case histories are reported by Heggett⁽¹⁴⁾, and Stumpf.⁽¹⁵⁾

Heggett suggests that over-stimulation of the sympathetic fibres of inflamed pulps may cause gastro intestinal disturbances and his work is mentioned not because the case histories are true examples of focal infection, but to illustrate the variety of modes by which secondary conditions may be found to develop when the problems are ultimately solved. Stumpf's work is important because of his genuine effort to approach the problem on sound bacteriological grounds. Reasoning that, if the focal theory were sound, vaccines prepared from the primary focus should relieve the condition caused, he prepared such autogenous vaccines and claimed favourable results from their use.

It seems likely that more work of a statistical nature such as that of Grossman⁽¹⁶⁾ in addition to careful laboratory experiments will be necessary in the ultimate solution of the problem of oral foci. The main value of isolated case histories is to demonstrate that proof for or against focal infection in any given disease is needed.

The Practitioner's Present Duty.

The practising dentist is still required to examine patients referred to him and determine whether likely dental foci of infection exist. In view of the present state of knowledge, each case must be considered on its merits. It must be remembered that chronic infections may ^{ac}exacerbate in the debilitated patient and that in this event direct spread of infection will be more likely. If focal infection is suspected as an aetiological factor examination of the mouth alone is insufficient, - all likely sources should be investigated. The importance of considering the gingival condition as well as the periapical areas has already been emphasised. Residual areas, pericoronitis and infected impactions must be added to the list. Gomes, Collins and Crane (op. citi) warn against multiple extractions in rheumatic fever. Full medico-dental

Chapter V. Cont'd.

The Practitioner's present Duty. Cont'd.

co-operation is essential in deciding the use of antibiotics.

In addition to antibiotic treatment the use of antiseptic mouth-wash immediately prior to exodontia can be considered. Kaosian and his colleagues reported some diminution in occurrence of bacteraemia following the use of aqueous iodine mouthwashes. (17)

Finally, may it be said that the oral surgeon best understands the nature of any oral lesions he discovers, and should give the physician the benefit of his knowledge rather than leave decisions on radical dental treatment to him.

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PART 1.

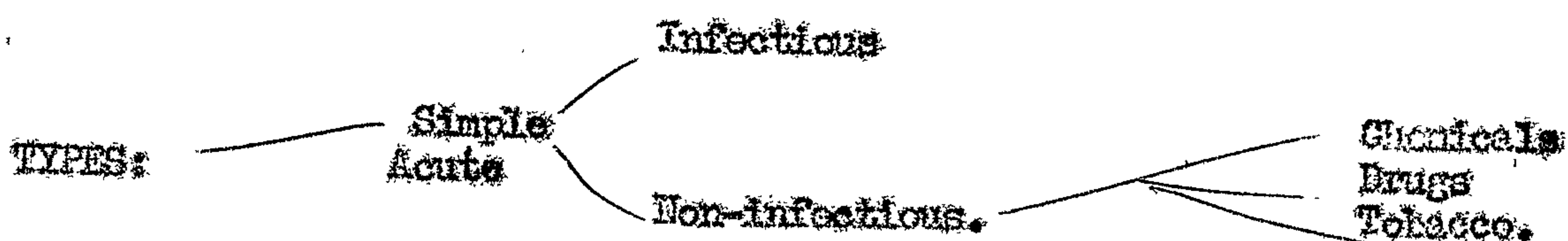
CHAPTER V 1.

INFECTIOUS DISEASES OF THE MOUTH.

With such detailed reference text-books as Thoma's "Oral Pathology" and Stones "Oral and Dental Diseases" available, it has been found convenient to alter the form of the bibliography for this chapter. Authors will be listed under alphabetical order as in "The". The reviewer has used a reference numeral for each author and information cited located by a small letter (1a, 2b etc.) It is not claimed that this is a better method than accepted procedures used in compiling most articles but that it is less clumsy in this case where facts are repeatedly drawn from relatively few comprehensive sources.

STOMATITIS.

Thoma and Robinson (13) give the best definition: "Stomatitis is inflammation of the oral mucosa, whether due to local or systemic factors." In contrast to gingivitis and periodontitis which involve the periodontal membrane and alveolar bone, stomatitis defines inflammation at any site on the oral mucosa.



Catarrhal — accompanied by extra oral or systemic manifestations.

This classification is suggested by Thoma (11a) but has been modified by dividing simple stomatitis with infectious and non-infectious types.

Stones (9a) gives a broader classification, separating those conditions associated with systemic disturbances into separate classes. Thoma's simpler divisions seem to be preferable. It is to be hoped that time and further knowledge will bring a standardisation of nomenclature in these and other disease. A world conference could achieve desirable results.

Chapter VI. Cont'd.Stomatitis Cont'd.Simple Non-infectious Stomatitis.

Traumatic...tooth brush and fish bone ulcer.

Denture irritations -- ulcer.

Hot foods -- sometimes protein coagulation.

Sensitivity to drugs and foods.

Galvanic injuries, -- dissimilar metals with a high potential difference.

Many of the lesions so caused are more correctly defined as ulcers and all do not correctly belong to this chapter. They are included because non-infectious stomatitis must be considered in making a differential diagnosis.

INFECTIOUS STOMATITIS.Aetiology of infectious Stomatitis.

Predisposing factors -- fatigue, mental strain -- dietary deficiencies especially avitaminosis -- faulty hygiene and previous trauma.

Bacteriology. -- most commonly haemolytic streptococci ("U.R.T.I") in simple stomatitis.

In catarrhal stomatitis -- micrococcus catarrhalis, pneumococcus and specific organisms.

CLINICAL SIGNS.

Often at first itching; -- fever 102 -- 103o -- lymphadenitis -- inflammation bleeding and desquamation -- often cheilitis and glossitis foetororis and may be mucus exudate.

Additionally in catarrhal stomatitis, bronchial and gastric catarrhal inflammation -- muco - serous or muco-purulent discharge -- commonly occurs with pharyngitis, colds, tonsillitis and gastro-intestinal disturbances.

Pathology: -- desqu^{ma}ated phagocytic epithelial cells containing streptococci intracellular oedema with destruction of stratum corneum -- penetration of micro organisms -- inflammatory reaction in (Over)

Chapter VI. Cont'd.Infectious Stomatitis. Cont'd.

corium — often leucocytosis.

Treatment: Local; methylene blue. Mandel's paint.

Diet: Ascorbic Acid.

Antibiotics: Penicillin, aureomycin.^e

Non-Specific Membranous Stomatitis:

Distinguished from latter condition by a membrane composed of fibrinous network containing swollen epithelial cells and leucocytes — membrane greyish white surrounded by red halo. (11b)

Bacteriology: Streptococcus viridans or haemolyticus — sometimes staphylococcus albus or diplococcus.

Differential Diagnosis: — Diphtheria — Bacteriological and site of lesion.

Treatment as with infectious stomatitis.

STOMATITIS SCARLATINA.

Scarlet fever — an acute throat infection with fever, nausea vomiting and a fine granular rash — flushed face with pale oral mucosa (3a) — headache and sore throat. Incubation period 1-7, but usually 2-4 days.

Endemic and due to certain strains of streptococci haemolyticus. (9b)
Acute nephritis is a common complication; other significant complications are purpura, abscesses in the neck (ibid), otitis media, arthritis and cardiac lesions. In diagnosis, the Dick test is used — an injection of dilute solution of specific scarlatinal streptococcus toxin — red patch positive. (4b) A characteristic of the rash is desquamation which seldom occurs before the seventh day while the erythema may last 2-3 or 4 weeks.

Oral Signs Throat, fauces and uvula affected first — greyish white furring of tongue (variable) in early stages — later typical strawberry (raspberry) tongue — thickened desquamated epithelium.

In severe case secondary infection by Vincent's organism may cause severe necroses. (9c)

Treatment: Scarlatinal anti-toxins, penicillin, sulphathiazole.

Chapter VI. Cont'd.

STOMATITIS DIPHThERICA.

Diphtheria is an acute inflammation usually affecting the fauces, soft palate tonsils. Less frequently nose larynx and trachea^(2a)
 incubation 2-5 days → sore throat not marked → most common 3-8 years. Causal organism → *Corynebacterium diphtheriae*—mitis, intermedius, gravis (Klebs-Löffler bacilli). Systemic effects from exotoxins → organisms strictly localised.

A foul-smelling, grey, yellow-white or black false membrane composed of fibrin and leucocytes in naso-pharynx and tonsil sometimes extend to palate. ^(3b) Manifestations in the oral cavity proper are rare ^(11c) Membrane may be lifted to expose bleeding surface.

Diagnosis: essentially by smears and cultures, prophylaxis by anti-toxin → Schick test → intradermal injections of small quantity of toxin.

Prognosis: may be fatal.

Treatment Diphtheria toxoid. → Due to immunisation severe attacks are now uncommon.

ULCERATIVE STOMATITIS.

Thoma (11d) rightly pleads that the term aphthous stomatitis be used no longer in describing this condition. The term, aphthae is loosely used and should be reserved for vesicular eruptions. However the term 'ulcerative stomatitis' is frequently used to describe 'Vincent's' infection. Many cases formerly described as 'aphthous stomatitis' are now recognised as 'herpetic gingivò-stomatitis (Q.V. 'Virus Infections of the Oral Cavity.)

Aetiology → predisposing factors → local trauma and neurotrophic influences → sickly children and debilitated adults.

Bacteriology usually mixed but mainly staphylococci and streptococci pyogenes.

Clinical signs: General mucosal inflammation → numerous irregular necrotic ulcerations.

Symptoms: fever, malaise, lymphadenitis.

Treatment: Systemic and nutritional → aniline dyes → local and parenteral penicillin and aureomycin.

Chapter VI. Cont'd.

ULCERATIVE STOMATITIS AND GINGIVITIS.

Synonyms: Necrotising Ulcerative Stomatitis, Trench Mouth, Vincent's Infection, ^UPlant-Vincent's Infection, Fusospirochaetal, Fusospirochaetal Stomatitis, Ulcerative Gingivo-Stomatitis, Necrotic gingivitis, ulceromembranous gingivitis.

Signs and Symptoms:

Eroded crater-like grey or greyish-yellow ulcerations, particularly on the gingival margins and interproximal tissues. (6) Gingivitis describes the condition when the ulcers are confined to the gingival margins, ulcerative stomatitis, when other parts of the mucosa are affected and the term, Vincent's angina (1%) (9) used when the throat is involved. The condition may be acute or subacute.

Acute ulcerative stomatitis -- grey ulcers with loose membranous surfaces characteristic odour and metallic taste -- excessive salivation.

Temperature 99 - 102°F, toxaemia, malaise, pain and dysphagia in Angina.

Sub-acute fusospirochaetal gingivitis -- is usually confined to the gingivae -- less acute symptoms -- usually no ulcerations, hypertrophied sensitive gingival margins.

Hutchinson (op. cit.) states that sub-acute and chronic Vincent's infection is really indistinguishable from sub-acute or chronic marginal gingivitis. Certainly, Vincent's organisms can be usually isolated in the latter conditions, but where acute ulcerative gingivitis has progressed to the sub-acute stage the term is useful, as reversion to the acute form is likely. Thoma (11c) points out that the so called membrane of the ulcers is, in fact, a slough.

Aetiology, Bacteriology and Pathogenesis.

Of recent years, the exact aetiology of Vincent's infection has caused some discussion. Thoma (loc. cit.) states that the exciting cause of the disease is the bacillus fusiformis (fusobacterium Planti-Vincenti) and the spirillum Vincenti. Stream (10) reported that the disease may be initiated by a bacterial complex:- Bacillus fusiformis,

Chapter VI. Cont'd.Ulcerative stomatitis and gingivitis. Cont'd.

Borrelia (spirillum) *Vincenti*, a vibrio and gram positive coccus. Thoma considers that the secondary invasion of streptococci or diplococci consumes oxygen and creates an ideal anaerobic state for the growth of fusiform bacilli. Experiments quoted by Stones^(9c) indicate that inoculation of the organisms alone may not cause a clinical Vincent's infection. It would seem that the resistance of the host tissue resistance the virulence of the organisms are important. (Hutchinson op. cit.)

Bacillus Vincenti — a large cigar shaped gram negative non-mobile fusiform bacillus 5 — 15u long and 1 u thick — more deeply staining in polar region — anaerobic cultures, small white discs.

Another type (Stones):— 14 u long; 0 . 3 u wide — actively motile anaerobic spirochaetes.

Transmission:— contagious — but lowered tissue resistance necessary— diet and hygiene important.

Importance of virulence in transmission (Hutchinson op. cit.)

TREATMENT.

Essentially relief of acute symptoms followed by elimination of pockets. Acute stage — attention to nutrition especially ascorbic acid. Most authorities favour the use of antibiotics — penicillin and aureomycin — Hutchinson rightly condemns the procedure of (unnecessary, danger, allergy and moniliasis) — advocates immediate conservative prophylaxis which was formerly opposed, (5) prophylaxis creates aerobic condition. Exodontia and general anaesthesia strongly contraindicated.

Host of topical medicaments have been used. — Churchill's Iodine and 10% Silver Nitrate (very caustic and possibly cancerogenic); 6 — 10% Chromic Acid (increases tissue destruction and decalcifies tooth); Aniline dyes, Hydrogen peroxide (rapid disintegration from organic matter).

Suspect blood dyscrasias where acute phase is persistent.

Chapter VI. Cont'd.

Ulcerative Stomatitis and Gingivitis Cont'd.

Thoroughly remove all likely foci after acute phase has subsided -- overhanging margins, carious cavities, pericoronitis, gingival pockets, infected tonsils and fistulae.

Comments.

As stated by Gomroe and his co-authors, ^{(239) et} the recent tendency to underestimate the seriousness and possible epidemic form of fusospirochaetal stomatitis is to be deplored. They and Stones quote the significant increase in the disease in war years. Certainly the healthy mouth is rarely affected in civil life.

Most writers now emphasise the importance of predisposing factors. Deficiency vitamins A, B or C; existing gingivitis or specific infections, diabetes and debilitating diseases. Blood dyscrasias, agranulocytic angina, leukaemias, aplastic and mononucleosis may be complicated by Vincent's infection.

Large numbers of cases are still treated with antibiotics only by the medical profession, with no attempt to eliminate likely anaerobic areas after the acute phase has subsided.

GANGRENOUS STOMATITIS.

Synonyms: Noma, cancrum oris.

A progressive gangrenous involvement of the mucous membranes or mucocutaneous orifices occurring most frequently in the mouth but also in the nose, eyelids, auditory canal vulva, prepuce and anus. (8) At any age but most common in first decade.

Exciting Cause: Usually appears to be Vincent's organism (often after extractions in acute phase) -- sometimes not present, but other organisms, micrococcus tetragenus staphylococcus, streptococci or bacillus coli may be present.

Predisposing Factors -- are really the essential cause -- lowered resistance in poorly nourished children especially after measles and scarlet fever -- deficient vitamin B complex and other nutritional elements -- increased susceptibility after typhoid fever, with blood dyscrasias, cardiovascular disease and diabetes.

Faulty oral hygiene, infected operculum (test for Vincent's

Chapter VI. Cont'd.

GANGRENOUS STOMATITIS.

organisms important.)

Muir's Text-book (2b) emphasises the importance of anaerobic wound infection in this condition and gas gangrene (*Clostridium Welchii* causal) -- hence avoid traumatic surgery. -- Diphtherial inflammation predisposing in some cases.

Clinical Course.

Often first manifestation -- unbearable foul dusky red or nearly black inflammatory patch frequently near third molar teeth, erupting first molars, angle of mouth or buccogingival fold -- develops to small ulcer -- rapidly spreading gangrenous decomposition -- necrosis of surrounding tissue with painful collateral oedema and purulent line of demarcation -- perforation of cheek as necrotic tissue falls away -- necrotic bone and attached teeth may come away -- Thoma states jaws, eyes and neck may be involved -- septicaemia, prostration lung abscesses -- prognosis grave 70--80% fatal -- shocking deformities with survival.

Most authors fail to comment on the temperature. Archer^(1a) was unable to ascertain the temperature at onset of disease in a case report. Histopathology -- necrotic tissue with inflammatory reaction -- thrombo-vasculitis.

Blood: Stark (op. cit.) reports a case with leucocytosis and reduced red cell count. -- The literature is deficient in this respect.

Treatment: Early surgical excision or electrocautery -- mild irrigation with Dakin's solution (Archer et al.) -- sulphonilamides or antibiotics -- heavy dosage -- institute broad spectrum antibiotics therapy immediately and then carry out sensitivity tests -- multivitamin, high-calorie diet -- blood transfusions (Archer and Stones).

SYPHILIS.General description. (2c)

A specific disease caused by *Treponema pallidum* (*Spirochaeta Pallida*) -- essentially chronic course -- may be acquired or congenital.

Acquired: -- Primary, secondary and tertiary stage.

Chapter VI. Cont'd.

SYPHILIS.

Primary stage — 3-4 weeks (or longer) incubation — primary sore or hard chancre (Hunterian chancre) — small painless dull red papular thickening — induration — ulcerates — scanty exudate in which spirachætes may be examined by dark ground illumination — confusion with other spirochaetes possible — Wasserman test usually negative at this stage [histopathology of primary lesion:— Cellular granulation tissue beneath epithelium — lymphocytes, plasma cells and mononuclear leucocytes — epithelium irregularly thickened and stretched — granulation tissue vascular, endarteritis and periarteritis induration due mainly to packing of round cells — no focal arrangement of cells and giant cells uncommon (c.f. tubercular nodules) — spontaneous disappearance of primary lesion in 6-8 weeks — most common on external genitalia but also on fingers, lips and in mouth.

Secondary stage:— haematogenous spread of organisms — multiple secondary lesions of skin and membranes after 3-3 months — generalised rash with headache, anaemia and intermittent fever — often alopecia — buccal and pharyngeal mucosa, snow white shiny catarrhal patches which may break down to form grey, shallow "snail-track" ulcers — may also occur on tongue, lips and soft palate.

Muco-cutaneous surfaces of anus, vulva and perineum develop 'condyloma latum', — flat raised papules — slight lymphadenitis — Wasserman now positive.

The lesions of this stage are highly infective.

Histopathology of secondary lesions:— Vascular engorgement with round cell infiltrations (plasma cells predominate) of sub-epithelial connective tissue — similar reaction around hair follicles. — Lesions regress and disappear after a few weeks, but may recur.

A moderate microcytic or ²microcytic hypochromic anaemia.

Tertiary stage:— follows immediately or may become manifest years later — the essential feature is gumma formation — at first pale pink, slightly translucent — central necrosis to form yellow necrotic material — later undergo absorption and cicatrization — may produce extensive destruction of nasal bones, palate (perforation probable) and

Chapter VI, Cont'd.

SYPHILIS.

larynx. — Concomitant cardiovascular lesions are serious, nervous diseases, locomotor ataxia and general paralysis.

Histopathology of third stage:— Necrosis surrounded by fibrous tissue— interstitial inflammation and fibrosis — lesions similar to those of primary lesion with necrosis superimposed and more frequent appearance of giant cells (which are smaller than those of tuberculosis and not surrounded by concentric endothelioid cells.)

Blood Picture:— In tertiary stage, there is frequently severe anaemia usually hypochromic when the cardio-vascular system, liver or spleen are affected. Mercurial treatment may increase the anaemia until there is an improvement in the condition, when the blood count approached normal. Eosinophilia sometimes in syphilitics.

Congenital Syphilis. (9f) Transmission of *treponema pallidum* through the placenta, especially later in gestation — foetus may be aborted (especially when mother recently infected) — may be borne alive with manifestations of syphilis, 'macular-roseolar' eruptions of mouth and nose, "snuffles" shortly after birth — maybe at first normal but later manifestations, bridge nose, rhagades (ulcerating fissures at angles of lip which leave scars), Hutchinson's incisors with notched incisal edge. (Possibly this malformation may be caused by other infections.) — Moon's molars (dome-shaped first molars). Typical tertiary gumata may later appear.

Significance in Dentistry.

Lesions of all three stages may present in the oral cavity — most commonly those of second stage, less frequently the third stage and more rarely the primary.

The dentist may be the first to have an opportunity of making a diagnosis.

In oral surgery, it should be remembered that the patient's resistance is lowered ^(1b) and post-operative infection is more likely.

Trifacial neuralgia and pulpitis may result from syphilitic^s. ⁽¹³⁾

It may be mentioned in passing that the conservative dentist is

Chapter VI. Cont'd.SYPHILIS. Cont'd.

able to remove the stigma of Hutchinson's teeth by the use of fused porcelain jacket crowns.

Physicians and dentists can and have been infected in examining patients, the primary chancre appearing on the fingers. Rubber gloves should be worn.

Care should be taken to avoid cross-infection of patients by care in sterilisation of instruments, brackets, operating tables and even the dental chair. Lucas and Kramer (7a) state that even weak antiseptics are effective and that the organism is susceptible to drying. Hand-pieces used should be placed in hot oil sterilizer immediately and surgical instruments washed in soap and water and autoclaved for 30 minutes. Boiling for twenty minutes is effective but autoclaving is preferable.

Differential diagnosis.

Treponema pallidum, a thin spiral organism, 5-12 μ long with 6-12 coils is a motile organism difficult to stain. However, it can often be seen in syphilitic exudates in dark-ground illumination.

Serological tests, (Wassermann, Kahn and Hinton.)

Occurring at any age and presenting in variable forms, the disease can confuse differential diagnosis. Tubercular lesions and actinomycosis can usually be differentiated by bacteriological and serological methods. A history, if given greatly assists. In suspicious cases a repetition of Wassermann's complement fixation test is often required.

Treatment.

Intramuscular arsphenamine, bismuth and mercurial preparations.

Very high doses of penicillin have been found effective.

Mercurial preparations may produce mercurial stomatitis or a "blue mercury line" in the gingivae. Therapeutic bismuth will produce similar signs as well as headache, albuminuria and jaundice. (36)

TUBERCULOSIS.

A specific infection due to *mycobacterium tuberculosis* (bacillus tuberculosis; tubercle bacillus).

Chapter VI. Cont'd.

TUBERCULOSIS. Cont'd.

Bacteriology: Small rod shaped organisms difficult to stain.---

Stains red with Ziehl - Neelson method. Two common forms bovine and human. Gram positive (if it takes the stain), non-motile, non-sporing and non-encapsulated -- resistant to drying but readily destroyed by moist heat -- strong resistance to antiseptic -- protoplasm contains wax-like substances.

Clinically, produce acute and chronic lesions of diverse form in any tissue of the body.

World wide distribution, but particularly in temperate climates -- overcrowded communities -- hygiene, nutrition and sunshine important.

Infection by inhalation or swallowing (milk; pasteurisation important.)

Two main age groups -- infancy and early childhood, and middle age.

Generally but not invariably pulmonary tuberculosis due to human strain of bacillus -- initial lesions of bovine-type commonly in alimentary canal and lymph nodes -- latter highly infective to young children.

Typical Tissue Reaction of Mycobacterium Tuberculosis.

Small inoculation -- focus of reaction -- swollen epithelioid or endothelioid cells with a zone of round cells chiefly lymphocytes. -- Thus forms a tubercle follicle -- bacilli damage tissue -- nuclei disappear, cells degenerate and die to form a structureless homogenous necrotic centre (Weigert's coagulative necrosis) -- assumes caseous or cheese like consistency -- typical picture; necrotic centre surrounded by endothelioid cells, which in turn are surrounded by small round cells:-- Amongst endothelioid cells are tuberculous giant cells large and irregular cells with oval or round nuclei resembling those of endothelioid cells and arranged at the periphery. Centre of cell may be hyaline in appearance due to necrosis.

Tuberculous nodules non-vascular -- if the patient's resistance is high or the organisms destroyed by medical treatment, fibrous tissue is deposited around the follicle and walls it off.

This is a typical chronic tuberculous lesion -- but the picture may vary in different parts of the body and acute and sub-acute forms of the disease frequently occur:--

Chapter VI. Cont'd.

TUBERCULOSIS. CONT'D.

Acute miliary tuberculosis— multiple small tuberculous nodules throughout an organ due to extensive dissemination of the bacilli at the one time — most common in children — not necessarily due to special virulence but rather to widespread inoculation.

Caseous lesions — from the lesion of several tubercles with much necrosis and caseation in centre. In bones, caseous material softens, attracts polymorphonuclear leucocytes to form caseous pus which may then track along muscle surfaces — cold abscesses.

Tuberculous granulation tissue.

Abundant granulation tissue when typical giant cells may form.

Fibrotic lesions:- Slow localised growth with much fibrous tissue reaction due to toxic products. — Fibroid tubercles — in lungs, extension of fibrous tissue may cause interstitial pneumonia.

Tuberculous ulcers typically forming on mucous membrane surfaces from direct inoculation — small at first, — spread — intractable.

Sub-acute lesions — more acute reactions in supersensitive individuals, especially when infection is on serous surfaces — fibrinous or serous exudates — lymphocytic reaction.

Blood Picture: Whitby and Britton (op. cit.)

Acute miliary tuberculosis:- A moderate progressive hypochromic anaemia with intense leucopenia, the majority of cells being polymorphs; Reduction in blood platelets: sedimentation rate greatly increased.

Acute pulmonary tuberculosis:- Often a slight microcytic or macrocytic hypochromic anaemia; Where lesions are septic, a leucocytosis with (65% neutrophils, 25% lymphocytes and 5 — 8 % monocytes:- Where hyperplastic lesions exist, total white cell count normal or nearly so, but increase in monocytes 10%.

In Oral Lesions: The latter count is significant — An increase of monocytes indicates activity of the tuberculous lesion: an increase of lymphocytes may mean healing: Secondary pyogenic infections cause an increase of neutrophils.

Chapter VI. Cont'd.

TUBERCULOUS. Cont'd.

Allergy. An individual who has overcome a primary infection will then be sensitive to the organism. This is the basis of Mantoux test whereby endotoxin prepared by heating and killing bacilli and concentrating the filtrate (tuberculin). If a patient has ever been infected with tubercle bacilli, an injection of tuberculin, given intradermally, will produce a positive red reaction. As most adults react positively, the test is not of great value in diagnosing oral lesions.

Active Immunity. Small doses of B.C.G. (Bacille — Calmette — Guérin) vaccine, given intracutaneously in early infancy or to older Mantoux negative reactors likely to contact sufferers.

Diagnosis — history and environment important — if organisms can be found — Microscopical appearance alone is diagnostic — negative results do not exclude tuberculosis.

Histological examination of biopsy material may reveal typical tubercles or the organism. Examination of sputum.

Pulmonary Tuberculosis.

The lungs are the most common site of infection and are important to the oral surgeon who frequently requests X-rays of the thoracic cavity to assist in diagnosis of an oral lesion.

In child: often no acquired immunity — primary caseating localised lesion.

(Ghon lesion) — extension by lymphatics to glands at the hill of the lungs — enlargement and softening from caseation — haematogenous spread may produce military tuberculosis and tuberculous meningitis — sometimes fatal. — The younger the child, the worse the prognosis.

In Adults: Chronic tubercle.
Excavation of chronic tubercle.
— "Chronic phthisis."

Tuberculous broncho-pneumonia.

Caseating pneumonia with excavation — acute phthisis.

Acute military tuberculosis (galloping consumption.)

Secondary localised metastatic tubercles.

Tuberculosis of the Mouth and Surrounding Tissues.

A recent comprehensive review of the literature has been published

Character VI. Cont'd.Tuberculosis. Cont'd.

by Thilander and Wamstrom. (12)

A summary is given:-

Two types -- primary and secondary.

Primary:- due to infected instruments, food and objects. -- Some doubt its existence but most authorities recognise its ^{occurrence} ~~existence~~.

Secondary infection:- certainly the most common form, -- widely divergent estimates of its incidence in relation to its occurrence in other parts of the body. -- Usually occurs between 20-50 years of age but reported cases in children -- is probably more common than generally estimated, but relatively small percentage of oral lesions may be due to:-

1. Resistance of oral tissues.
2. Cleansing action of saliva.
3. Presence of saprophytes and an antagonism between normal and pathogenic oral flora.

Predisposing factors:- poor oral hygiene existing mucosal lesions, trauma (extractions), pyogenic foci and leucoplakia.

Pathology of tubercular infection:-

1. Through expectoration in open tuberculosis.
2. By lymphogenous and haematogenous spread.
3. Infected food (especially milk.)
4. Air-borne infection.
5. Spread by continuity. (facial lupus and tuberculosis of pharynx and larynx.)

Teeth as portal of entry (Seharschmidt,) thence may spread by:-

1. direct lymphatic routes to tonsils and lymph nodes of bronchi and lungs.
2. supraclavicular lymph nodes to pleura.
3. Lymph and venous stream to the lungs (most likely.)

Sites of infection (Brodsky):-

	<u>No. of cases.</u>
Pharynx	22.
Tonsils	19.

Chapter VI. Cont'd.

TUBERCULOSIS.

	<u>No. of cases.</u>
Tongue	16.
Cheeks, Gingivae, Floor of Mouth.	9.
Lips	6.

Classification:-

Lupus of the oral mucosa — granulating form of tuberculosis through spread from lupus of face and occurring simultaneously with it. Soft small, red or grey — white nodules which do not caseate and rarely ulcerate — detected by pressing glass against mucosa.

Tubercle form — Small firm grey nodules the "size of a pinhead" — marked tendency to caseous necrosis and formation of micro-abscesses — if near mucosal surface, small tuberculous ulcers.

Miliary tuberculosis — occasionally in oral cavity — extensive small grey tubercles which ulcerate — grave prognosis.

Tuberculous ulcers — most common manifestation — granular nodules decomposition — opalescent blisters — ulceration — coalescence to form extensive irregular ulcers red and inflamed undermined edges, but with little or no induration (c.f. cancer) — yellow or grey, surface — often [^]'sentinel tubercles' nearby — 'mouse eaten appearance' — usually sensitive and painful on palpation.

Tuberculous ulcerations of Tongue.

Tuberculous ulcerations forming deep fissures — usually situated at margins develop fingerlike process from primary lesions — no induration unless secondary infection.

Tuberculosis of bone (Jaws). Slow chronic course — a rarefying osteitis — infected by:-

1. Direct extension from mucous membrane.
2. Tubercle bacilli traversing carious cavity and root canal.
3. Most commonly via blood and lymph vessels.

The authors quote Pichler and Trauner who found 60% of tuberculosis in jaws in children under 16 years.

Chapter VI. Cont'd.

TUBERCULOSIS. CONT'D.

Spontaneous drainage of caseous pus through a fistula. Mandible most common site and may be considerably swollen — sometimes whole bone involved with caseous necrosis and suppuration — rarely temporo-mandibular joint involved.

Complications: Spontaneous fracture, loosening or cariation of teeth — dermatitis at fistular orifice — Tuberculosis bacilli are seen in pus — chronic course — grave prognosis.

Tuberculous Granuloma central bone infection usually via carious teeth with positive sputum — similar to other granulomata.

Tuberculous periodontitis — rare as pure infection — little more common as mixed — in pure infection, bony involvement.

Signs and symptoms: variable — usually signs and symptoms from tuberculosis in other parts of body — most reports are that oral tuberculous lesions are painful — in tuberculous bone infection pain not marked.

Diagnosis: In addition to measures already outlined, the writers suggest inoculation of a test guinea pig with some of the infected material — Biopsy invaluable.

Treatment — Radical surgery previously main treatment — difficulty of complete eradication and reinfection was common — Antibiotics and chemotherapy now supplements or replaces surgery — Streptomycin, P.A.S. (para-aminosalicylic acid) and I.N.H. (iso-nicotinic acid hydrazide) have been found beneficial; Thio-semicarbaz (Contaban, T.E.K.) closely related to sulphonamide has been useful — these agents have largely replaced the caustics, Zinc Chloride, Silver Nitrate and Acetic acid.

X-rays, radium and electrocoagulation often used now. Tuberculous osteitis by surgical and chemical therapy — if curettage or surgery is carried ^{out} cover should be provided with streptomycin and P.A.S.

LUPUS VULGARIS. — a skin manifestation of tuberculosis — original lesion is a raised red-yellow intradermal node. — The glass test (vide supra) may be used to assist diagnosis — nodules spread through lymphatic channels of corium — may break down, ulcerate and undergo cicatrization — may extend into oral cavity (vide supra).

Chapter VI. Cont'd.

TETANUS.

(a) Causal organism tetanus bacillus (*Clostridium tetani*) — a gram positive, sporing, motile, non-capsulated bacillus $4 \times 0.4\mu$ — when spores are formed — 'drum-stick appearance' — other clostridia very similar — anaerobic (7b). Earliest sign — trismus with spasms of masseter muscle — painful paroxysms — muscles of neck and face then affected ('trismus sardonius') — symptoms spread to trunk and limbs with severe bodily contractions from the slightest stimulus bringing severe exhaustion. — Death from heart failure or asphyxia. — Has been known to follow exodontia or fractures.

Differential Diagnosis (4c 12b) from trismus in infected impacted third molars, where spasms of contraction are not characteristic, from muscular rheumatism — no trismus of cellulitis (external swelling always present and earlier onset of trismus in tetanus).

Spasms of hysteria — history.

Bacteriological diagnosis should be supplemented by culturing organism, injecting mice or guinea pig and observe for characteristic spasms.

Treatment: Tetanus antitoxin a short but rapid high immunity. Inject immediately when necrotic wounds are received.

Formal toxoid gives immunity of longer duration.

TULARAEMIA. (9c & 11g)

Aetiology *Pasteurella tularensis* gram positive rod-shaped organism 0.7 μ in length. Contracted from tick-bite contact with rabbits.

Clinical features.

Acute and Chronic.

Organisms enter by way of eyes, tonsils, tongue finger and toes — severe pain and fever, swelling of lymph nodes — ulcers may form on floor of mouth and tonsils — swollen glands may form so called 'cold abscesses' may be severe stomatitis and so-called glossitis.

Thus there are oculoglandular, pharyngotonsillar typhoidal and glandular forms.

Treatment: Incision and curetting of abscesses with streptomycin therapy.

Chapter VI. Cont'd.

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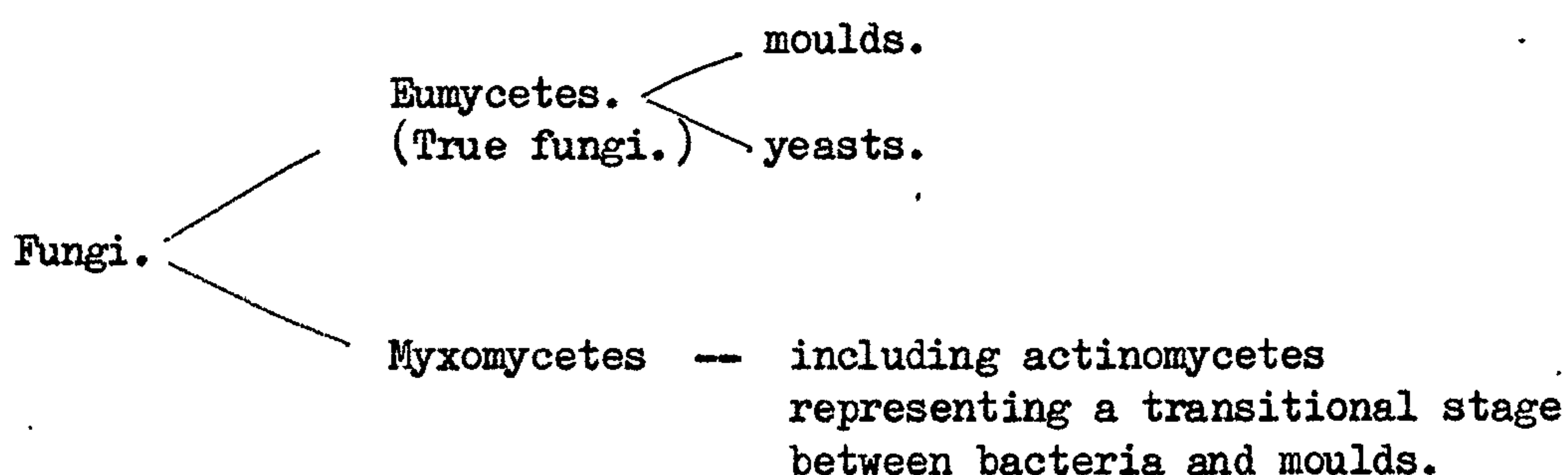
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P A R T. 1.CHAPTER VII.FUNGUS INFECTION OF THE MOUTH.

(Bibliography as in Chapter VI.)

Classification:- Skinner, Emmons and Tsuchiya (4a) state that moulds, yeasts and actinomycetes are Fungi which are Thallophytes devoid of chlorophyll.



Many fungi parasitic for man and animal present one form in the body and another when artificially cultured.

True yeasts are unicellular although irregular clusters may form during active growth.

Moulds are multicellular, and long filaments (hyphae) are formed by the end to end arrangement of these cells. The term mycelium is used to describe the intertwining filaments.

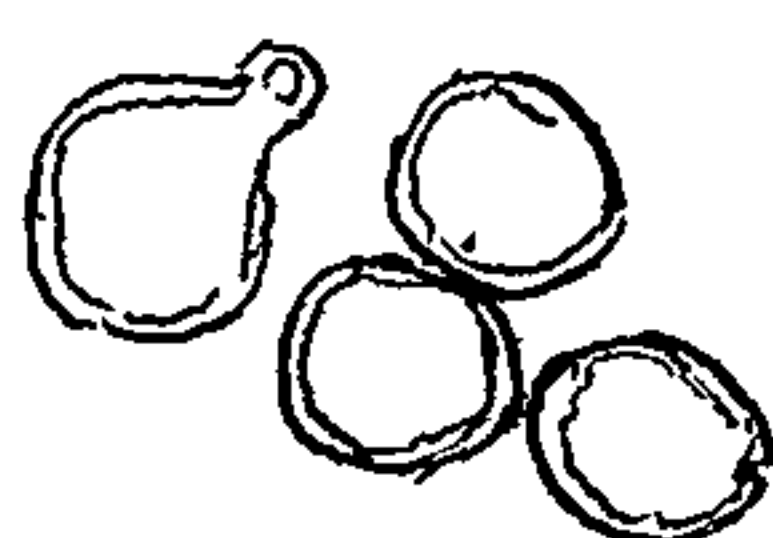
Normally, fungi are reproduced by specialised cells called spores but yeasts reproduce by budding.

Fungus cells resemble those of higher organisms, possessing a definite cell wall composed probably of chitin and cellulose.

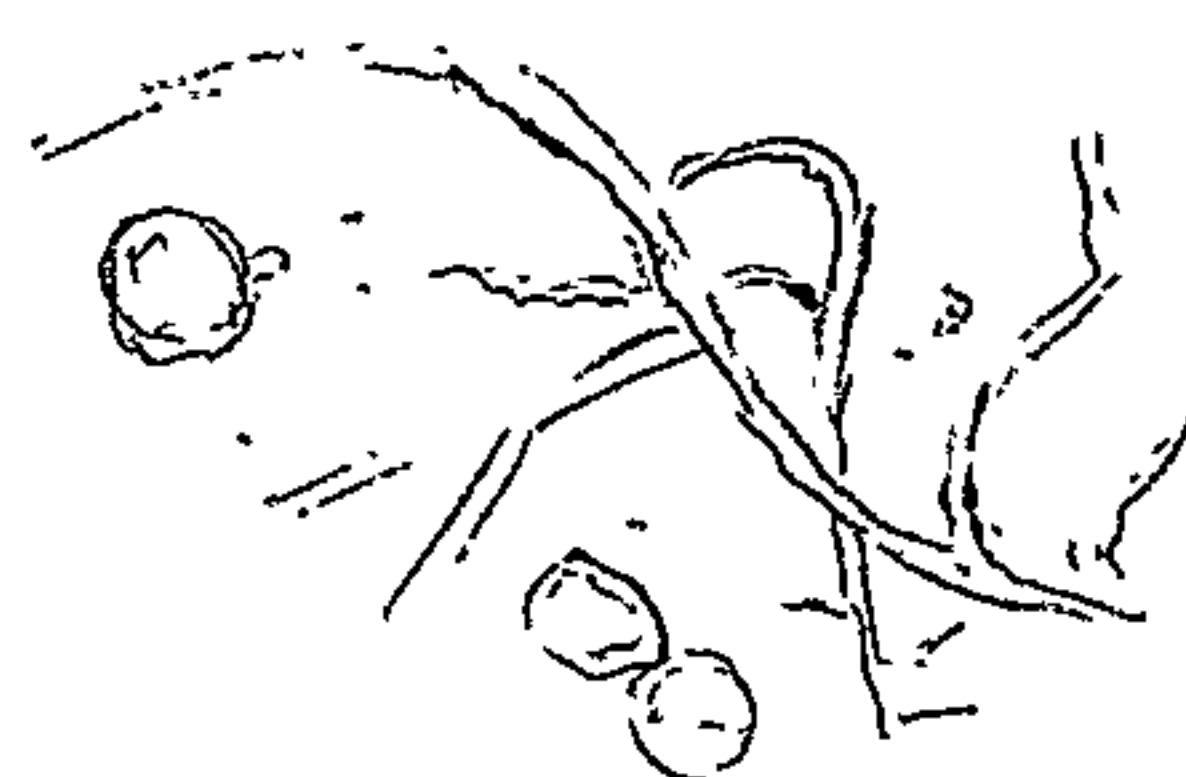
Depending for their nutrition upon the organic matter synthesised by other organisms (no chlorophyll) the cells have the power to accumulate reserve material in their cytoplasm.

MONILIASIS

Moniliasis is the commonest of the oral mycoses. The causal yeast-like fungus *Candida Albicans* is a parasite of the mucous membranes, occurring most frequently in the mouth and occasionally in the vagina. (5b) Significant in clinical diagnosis is the presence of pseudohyphae on the cells. Those (4) without pseudohypae are not considered pathologic. The mere presence of some forms of *candida albicans* must not be taken to indicate that the condition is candidiosis.



Appearance in
Culture



Appearance from. direct
Smear.

Chapter VII.

MONILIASIS. Cont'd.

Lilienthal (2) in a report on yeasts and yeast-like fungi in the mouth, stated that *Candida Albicans* is the only pathogenic specie of the "yeast" group.

The former term "Monilia" is incorrect and is becoming obsolete although the word "Moniliasis" used to describe the disease may survive. In addition to the mouth and vagina the fungus may extend through the gastro-intestinal tract, be isolated from the sputum, possibly cause lesions of the bronchi lungs and produce an eczema-like skin lesion. Thrush. Both Stones (6) and Thoma (7a) describe thrush (*Monilia* or *Candida Stomatitis*) as occurring mainly in infants but also, less commonly, in adults with debilitating diseases.

The condition produces a soft painless white patch resembling 'coagulated milk' (Thoma). The lesions vary in size and appearance but the patches are always firmly adherent, ^{so} that when it is raised, a moist red haemorrhagic base is exposed (c.f. leukoplakia, where surgery must be used to remove the white area). The lesion is usually whiter and more extensive than that of diphtheria.

Formerly, epidemics of thrush, especially in institutions were not uncommon, but of recent years the disease is not so often seen. Personal experience would lead the writer to believe the condition is not so rare in adults as Thoma and Stones relate.

Scales, Van Huysen and Summers (op. cit.) describe a granulomatous form of moniliasis. The lesion described presented as a reddened lobulated swelling containing the more typical white flecks in the crevices.

Symptoms: Excepting for local irritation, no general symptoms develop. It must be remembered however that the condition, when seen in adults usually follows debilitation from cancer, typhoid fever, tuberculosis or malnutrition. The lesions, already described, usually remain localised, coalescence and spread to other mucous membranes and the skin occurs.

The disease may be fatal when the skin and scalp are infected and the organism is isolated from the faeces.

Monilial Glossitis.

In this condition the red smooth tongue may contain furry patches similar to those on monilial stomatitis and is sensitive to condiments, hot fluids and tobacco.

Denture Sore. Mouths.

Stones (op. cit.) reminds the reader that it is wise to test for *candida albicans* in a denture sore mouth. The same author names Chronic latent oral moniliasis as being possibly predisposing to leukoplakia and epithelioma.

Histopathology:- There is marked surface degeneration of the mucous membrane with the superficial layers destroyed, oedema and fungus infection of the stratum granulosum and some round cells infiltration of the corium.

Chapter VII. Cont'd.

MONILIASIS. Cont'd.

Treatment.

1. Alkaline mouthwashes.
2. Antibiotics, with possible exception of streptomycin, useless. —
Many authors now suggest that moniliasis will frequently result from antibiotic therapy through destruction of the cohabitant flora. Archer ⁽¹⁾ recommends that oral undecylenic acid be used in conjunction with any of the broad spectrum antibiotics to prevent moniliasis.
- 3.. Removal of patches by electrodissection (Stones).
4. 2% solution of asterolcitrate as a mouthwash (Scales and co-workers, op. cit.)
5. 10 -- 20% solution of sodium caprylate, propionic acid (vide infra) auartenary ammonium compounds.
6. The condition is difficult to treat. General health and nutrition, especially Vitamin B complex therapy are very important. The diet should be low in carbohydrates, as they can be used as a source for the growth of the "yeasts."

PERLECHE

Stones (op. cit.) includes this condition with other mycoses, and states that *Candida albicans* or other saccharomycetes are isolated from the lesions. However, care must be exercised in ascribing a condition to *Candida Albicans* merely because it is obtained from the affected area. Certainly nutritional standards and faulty oral hygiene have a role in the setiology of perleche.

Clinical features: Ulcerations or erosions at the angles of the mouth with an extension of the lesions over the skin -- usually bilateral.

Treatment: Attention to diet, oral hygiene and mild antiseptics.

Comment: Probably ('perleche' could be used in describing angular lesions which appear to be predominantly infectious and the term 'cheilosis' reserved for those lesions where the main aetiological factor appears to be a deficiency of Vitamin "B" complex or a deficient vertical dimension in natural or artificial denture.

PHARMACOLOGY OF SOME ANTIMYCOTICS (3)

Acidum Caprylicum -- a yellow to light oily liquid with an offensive odour -- very soluble in alcohol and almost insoluble in water -- a fatty acid usually used as a salt.

Sodium Caprylate -- cream granules freely soluble in water.

Use: 10---20% solution applied to the area after cleaning --
No irritation of sensitisation.

Acidum Propionicum (Syn Propanoic Acid, Methyalacetic Acid.)

Colourless fatty acid very soluble in water -- used as the calcium or sodium salt -- sometimes in combination with caprylates in mixtures and compound jellies.

Chapter VII. Cont'd.

PERLECHE. Cont'd.

Acidum Undecylenicum. Yellow liquid with characteristic odour.

Dose: 112 Gr. a day in divided dose -- may be increased to 150 -- 225 Gr.

Given internally may cause nausea, vomiting and diarrhea.

Uses: mainly as local application, 2.5 or 5% may be used in conjunction with zinc undecylenate.

ACTINOMYCOSIS

Both Thoma (7b) and the authors of "Moulds, Yeasts and Fungi" (5c) state that actinomycosis in animals is a disease possessing a predilection for the jaws which may be caused by different fungi.

In 1991, Wolff and Israel isolated a pure culture of actinomycosis bovis from an active lesion and since then the fungus has also been known by the name Actinomycosis Israeli, also known as A. bovis and A. hominis. Unfortunately, in the same year, Bostroem, in attempting to isolate A. Bovis cultured aerobic streptomyces and thereby created confusion. The Boestrom fungus is common in soil and vegetation;--hence the misconception that Actinomycosis may be contracted by chewing straws. Skinner and his co-workers state that A. Bovis probably never occurs on vegetation while Thoma asserts that the fungus is commonly found in the soil and on vegetation.

In man the causal organism is A. Bovis.

Actinomycosis of the Jaws.-- occurs in city as well as country dwellers.

As a central lesion -- or the soft tissues around the mandible.

Central Actinomycosis.

Often symptomless central bone destruction -- discovered by Xray and diagnosed on removal.

Sometimes no soft tissue involvement -- other times swelling and fistula.

Ultimately bone expansion 'neoplastic type.'

Acute or sub acute inflammation when associated with pyogenic organisms -- tissue necrosis -- discharge (sulphur granules) -- reverts to chronic form with recurring fistulae and multiple abscess.

Chronic form -- granulating osteitis often symptomless -- swelling of lymph nodes only if sub-pyogenic organisms present. Almost always in mandible, especially at angle but occasionally in maxilla, orbit, nose or cranium when prognosis is graver.

Cervico-facial Actinomycosis.

Involving cervico-facial tissues or submaxillary space -- slow suppuration with fibroblastic reaction -- common in third molar region -- painless hard swellings -- purplish discolouration -- lumpy face and sometimes trismus -- small points of fluctuation which release discharge containing sulphur granules.

Chapter VII. Cont'd.Actinomycosis. Cont'd.Histopathology.

Vascular granulation tissues polymorphonuclear leucocytes in acute form.

In chronic form, lymphocytes, plasma cells, histiocytes, foam cells and mononuclearcytes. Sometimes difficult to locate the fungus. Polymorphonuclear neutrophils may congregate around the fungi.

'Sulphur granules' are characteristic.

Blood picture: Leucocytosis 20,000--30,000; progressive anaemia later.

Mycology. Anaerobic or micro-aerophilic. Difficult to isolate -- remove tissue from granule by rolling between glass -- mix in melted agar and incubate at 37° C.

Crooked branching filaments with hyphae 0.5 -- 1 u in diameter.

Gram positive.

Diagnosis:

1. Suspect any suppurative inflammatory lesion resistant to treatment.
2. Site -- mostly of cervicofacial type -- multiple granulating fistulae -- but site and appearance varies -- may resemble carcinoma on tongue.
3. Diagnosis mainly by laboratory methods (vide supra) -- foam cells helpful.
4. Hand lens examination of sulphur granules.
5. Xrays helpful but not pathognomic -- osteitis or rarefaction in smaller bone lesions.
6. Microscopic examination of granules (low power) -- clubs at periphery.

Treatment.

1. Oral dosage of Potassium Iodide 40-60 grams up to 250 gm. daily.
2. Penicillin and sulphonilamide often useful.
3. Local treatment with Iodine.
4. Irradiation.
5. Surgical excision usually necessary.
6. Some use caustics -- Carnoy's solution, 50% KOH.

BLASTOMYCOSIS (5d)

The term Blastomycosis has been misused. In Europe, blastomycosis is used to describe any disease caused by budding yeast-like fungi. Again the writer deplores the lack of standardisation in terminology and spelling.

With the recent influx of people from all parts of the world, Australian oral surgeons must be alert for evidence of diseases which they were unlikely to encounter in previous years.

American Form:

Causal fungus: Blastomycosis dermatitidis -- When isolated from lesions similar appearance to candida albicans but larger with thicker walls -- do not have the capsule of some fungi -- no endospores or ascospores when grown in culture at 37°C on blood agar the colonies are prolific, yellowish white

Chapter VII. Cont'd.

BLASTOMYCOSIS. (5d)

to tan and waxy -- worm-cast type of colony.

When grown in colonies, resembles *Histoplasma capsulatum* (q.v.) -- there is an immunological cross reaction between the two in skin tests.

Inoculation of laboratory animals is difficult but may assist in diagnosis.

The disease has been most common in America especially around the Mississippi Valley and has apparently appeared in England. Stone (op. cit.) describes the disease.

The occurrence of Blastomycosis dermatitidis outside the animal body has not been demonstrated.

Clinical features:

Primary lesions pulmonary or subcutaneous papillomatous ulcerative lesions which may concern the dentist when appearing on the lip, tip of nose, buccal mucosa, palate, tongue, gingivae or mandible.

Primary blastomycosis of lungs may resemble pulmonary tuberculosis. May become generalised -- systemic blastomycosis -- haematogenous spread -- Multiple abscesses especially in subcutaneous tissues -- abscesses are soft, fluctuant, painless without heat or redness -- considerable suppuration - systemic blastomycosis usually fatal.

Primary cutaneous blastomycosis papillomatous lesions which ulcerate and do not heal (c.f. carcinoma) -- secondary nodules enlargement coalescence -- to produce elevated mass of granulation tissue which releases pus on slight pressure and may be covered with a yellow crust.

Differential diagnosis between malignant neoplasms and tuberculous ulcer -- isolation of fungus important.

Histopathology:

Inflammatory granulomatous reaction, -- giant cells, numerous monocytes, epithelial proliferation with finger like processes -- minute miliary abscesses.

Treatment:

Often unsuccessful but localised conditions may respond to Sodium Iodide, tincture of Iodine, Xradiation or curettage.

SOUTH AMERICAN BLASTOMYCOSIS.

Synonym: Paracoccidioidal granuloma.

Casual fungus: *Zymonema brasiliense* (*Paracoccidioides Brasiliensis*) -- When isolated from pus, spherical cells 10-60r in diameter -- some cells are budding and resemble Blastomycosis dermatitidis.

Grows slowly in culture at 37°C most common in Brazil, but known in other South American countries.

Chapter VII. Cont'd.SOUTH AMERICAN BLASTOMYCOSIS

Clinical: usually affects the mouth, nose and gastro-intestinal tract. Ulcers -- peripheral spread -- coalescence -- rapid extensive tissue destruction -- granulating lesions enlargement and ultimate breakdown of regional lymph nodes -- then haematogenous spread to involve lungs spleen liver and other organs -- usually fatal. Not treatment has proved successful.

HISTOPLASMOSIS (6b & 8)

Synonym; Reticulo-endothelial Cytomycosis.

Casual fungus: Histoplasma Capsulatum.

--from tissue; -- oval budding cells, 3-5u -- usually seen in cells of reticulo-endothelial system -- in heavy infection may be extracellular fungi.

Cultured on blood agar at 37°C appearance is similar.

Clinical Features.

A mycosis with irregular fever leucopænia, anaemia, splenomegaly emaciation -- frequently negetative endocarditis or ulcerative enteritis.

May be papular or ulcerative lesions of skin and mucous membranes.

In mouth ulcerations are often painless, but Stones describes them as painful, -- commonly involves tongue, but may appear elsewhere -- ulcers may become deep seated -- covered with grey or pink membrane.

The organism may be found in tissue of bone marrow biopsy, in the lymph glands which are enlarged, in the monocytes and the polymorpho-nuclears, or it may be isolated from the oral or skin lesions.

The mycosis offer a challenge to the dentist's ability. Isolating the causal fungus is sometimes difficult and until successes achieved in doing so skill in recognising clinical signs and eliminating other possible causes in differential diagnosis is important. In the cases where candida albicans is isolated from a lesion, some thought and perception are required to decide whether the fungus is present merely as a secondary invader.

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[OVER]

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P A R T. 1.CHAPTER VIII.VIRUS INFECTIONS OF THE ORAL CAVITY.

The story of viruses is still unfolding. By the beginning of the twentieth century, the effect of Pasteur's investigations was being truly felt. One by one the causal organisms of the various infectious diseases were being isolated and their guilt in the aetiology of many diseases was proven beyond all doubt. Yet, in many characteristically infective disease no causal bacteria could be found. It was Pasteur himself who suggested that living agents were indeed responsible in these cases but that they were invisible, even to microscopic examination.

Shortly it was found that these 'ultramicroscopic' viruses could be passed through earthenware filters and still remain infective. Later, using collodion membranes, with pores of varying dimensions it was found possible to assess the sizes of different viruses. For example the virus of Variola tr. smallpox was found to be 0.2u in diameter, whereas the smallest viruses may be only 0.01u.⁽¹⁾

Now, with the advent of the electron microscope, there is hope that viruses will be classified and named as the bacteria have been.

Under ideal conditions, the largest viruses can be discerned by ordinary microscopic methods and in some virus infections, 'inclusion bodies,' which appear to be aggregates of viruses, may measure up to 20u in diameter.

It is still not certain that viruses are in fact, living bodies. Some of the smaller types are not much larger than some molecules, but the fact that they are apparently capable of multiplication and can be destroyed by many antiseptics would suggest 'life.' Antibodies are developed against many virus infections. Viruses are completely parasitic, and cannot exist for long outside the living cell. Outside the body of their hosts, they can be cultivated only in the presence of living cells and fertile hen's eggs are often used for this purpose.

Virus diseases are found throughout nature in the animal and vegetable kingdoms. Many are highly selective, being parasitic not only to a particular host but choosing certain cells in which to multiply.⁽²⁾

Other viruses have far greater adaptability (e.g. influenza virus.)

Intercellular virus infection may lead to secondary inflammation with ultimate necrosis or alternatively cellular proliferation. The latter response has led to the 'virus theory' in the aetiology of malignant neoplasms. Cameron⁽³⁾ relates that electron micrographs of milk of nursing mothers with a family history of cancer had revived consideration of virology as a possible cause of cancer.

Chapter VIII. Cont'd.

Virus infections of the oral cavity. Cont'd.

A virus may live in cells for years without producing disease to suddenly increase in virulence and become pathogenic. In other instances, viruses may be generally quiescent and produce disease at intervals.

Many virus infections cause the host to develop a strong lasting immunity, but in Herpes simplex, frequent recurrent attacks are not uncommon.

Of the texts reviewed, Thoma, in "Oral Pathology" (op. cit.) gives the most detailed account of the virus infections seen in and about the oral cavity. His work is used largely in the following summary. Where information is culled from other articles references are cited.

Herpes Simplex (The Cold Sore).

Manifested as the similar conditions herpes facialis, herpes labialis and herpes mentalis which may occur at the one time from the same causal virus; herpes genitalis and herpes cornealis.

Acute herp^{et}ic stomatitis is now generally considered to be the effect of the virus of herpes simplex upon children who have not yet developed any specific antibodies.

Herpes labialis and mentalis:-

Groups of vesicular eruptions up to one third inch in diameter -- contains clear fluid which when transferred to a rabbits cornea causes lesions containing inclusion bodies. -- Thin yellow adherent crusts form and desquamation of the mucosa occurs before the lesions disappear in about ten days.

French⁽⁴⁾ describes four stages: -- the appearance of slightly red spots, effusion under epidermis with formation of clear vesicles, -- opaque, sometimes purulent change and finally shrivelling to form yellow-brown crusts -- detachment to leave temporary brown skin. (congestive, vesicating, dessicating and macular stages.)

Crusted stage of multiple facial herpes distinguished from impetago by the former's rapid course, localisation and frequent occurrence on the lips.

The lesions frequently occur in association with other virus infections, such as the common cold. (coryza) Danger of secondary invasion by other organisms. (5)

Herpetic Gingivo-stomatitis:- Usually from 1-6 years, -- severe febrile condition -- early congested areas and groups of vesicles are pathognomic but condition not usually seen at this stage -- ulceration and coalescence of vesicles -- may affect inner surface of lips, margins of tongue, gingivae buccal and sublingual mucous membranes.

Chapter VIII. Cont'd.

Virus infections of the oral cavity. Cont'd.

Malaise, poor appetite, excess salivation -- may be cervical adenitis and diarrhoea.

Tends to occur in poorly nourished children with faulty hygiene -- has been described in epidemic form -- can be diagnosed by inoculation of rabbit's cornea. -- Intercellular inclusion bodies.

Other virus infections may follow in those afflicted with herpetic stomatitis.

Antibodies develop in serum during convalescence.

Histopathology:- intraepithelial vesicles developing the stratum granulosum-- oedema and inflammatory infiltration of corium, -- mostly lymphocytes. -- 'ballooning' degeneration of cells (often multinuclear.)

Treatment:- Thoma reports use of small-pox vaccine. -- The same author relates of success with aureomycin but the reviewer has found that the antibiotics and local medication have no apparent value. -- However hospitalisation with strict attention to hygiene and diet supplemented with Vitamin B complex entirely successful. -- Warm saline irrigations were used.

HERPES ZOSTER. ('Shingles.') ('Zona.')

Groups of vesicles on an erythematous base following the course of a nerve (usually intracostal) -- due to a neurotropic virus distinct from that of herpes simplex.

Often affects overworked, tired or debilitated people, and may occur in cold damp weather -- pyrexia with pain where lesions are to develop -- of diagnostic significance; almost always unilateral (more often right than left.)

Disease is not usually recurrent and the history may suggest an association with varicella. -- All authors suggest a close relationship between the virus of zoster chicken-pox.

Sometimes occurs on the forehead, conjunctiva and mouth. Fifth, seventh and ninth cranial nerves may be involved. Complete paralysis of the facial nerve, vestibular and cochlear branches of the eighth nerve is Ramsey Hunt Syndrome -- with vertigo, nausea, pain in tongue, throat and ear.

Zoster lingualis occurring on tongue.

Histopathology:-

Epithelial degeneration with formation of vesicles -- eosinophilic bodies as in herpes simplex -- intercellular inclusions (Zoster or Lipschutz bodies.)

Treatment:-

Injections of Vitamin B1 - two to three 5 mg. doses.

INFECTIOUS MONONUCLEOSIS ('Glandular Fever').

An acute or sub-acute infectious virus disease characterised by enlarged lymph glands and an increase in the monocytes and lymphocytes of the circulating blood. (6)

Acute ---- usually in children.

Sub-acute ---- usually in young adults.

Chapter VIII. Cont'd.Infectious Mononucleosis ('Glandular Fever'.) Cont'd.Clinical features:-

In adults:-

- (a). Glandular type.
- (b). Anginose type.
- (c). Febrile type.

Glandular Type:- invasive stage with headache, malaise and fever $102-3^{\circ}$ with torticollis may simulate symptoms of meningitis -- relatively slow pulse, 4th to 10th day pink maculo-papular rash -- eruptions disappear and in 1-3 weeks, generalised enlargement of lymphatic glands which are moderately tender and uncomfortable -- sometimes enlargement of spleen-lymph glands may remain enlarged for 12 months -- sore throat not common in this form.

Anginose type:- Sore throat the distinguishing feature with formation of membrane resembling that of diphtheria -- may be secondary invasion of Vincent's organisms or herpes simplex.

Febrile Type:- Resembling typhoid fever.

In children:- Acute -- very early glandular enlargement -- often epistaxis -- no rash -- cervical group of glands on left side most commonly affected. -- High fever for about fourteen days. -- In young children leucocyte count up to 40,000 per c.mm.

Blood Changes:

In invasive stage of adult form, up to 30,000 white cells per omm, 80% of which may be granulocytes. -- With enlargement of glands the typical blood picture of glandular fever appears:-

Total leucocyte count about 20,000 per cmm, 40-80% of which are 'Mononuclear cells;' lymphocytes, monocytes and abnormal mononuclear cells, probably primitive monocytes.

Erythrocytes and platelets usually normal.

Diagnosis When the disease concerns the oral surgeon (anginose type) and enlargement of cervical lymph glands) examination of the blood will differentiate the condition from diphtheria (c.f. anginose mononucleosis) or other forms of lymphadenitis.

The Paul-Bunnell test (based on the fact that the blood in this disease contains heterophil antibodies) may be used.

Treatment Symptomatic -- appropriate therapy should Vincent's infection develop -- Thoma suggests Kayo syrup or bland mouthwash.

NO surgical interference with glands, which are NOT likely to suppurate.

FOOT AND MOUTH DISEASE. (Epidemic Stomatitis).

Common in cattle, hogs, sheep and goats in some countries in Equope -- may be transferred to humans by milk and become epidemic -- probably due to a filterable virus and infection takes place through a break in the skin or mucosa.

Chapter VIII. Cont'd.

Foot and mouth disease. (Epidemic Stomatitis).

Incubation period 2 - 10 days. Multiple tiny vesicles in lip, tongue and pharynx which ulcerate to cause pain and salivation.

Pain of short duration and lesions heal in 2 - 3 weeks.

Diagnosis:- By inoculation from the lesion of guinea pig's foot -- typical disease development.

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THE EXANTHEMATA.

Diseases characterised by skin eruptions -- includes scarlet fever, but those due to the filterable viruses are described here. -- The oral manifestations in Varicella, Rubella and Rubella are often of diagnostic importance in oral surgery.

RUBEOLA.

A very infectious disease of childhood, spread by droplet infection.

An acute virus disease -- sometimes fatal.

Constitutional symptoms, fever, headache, catarrhal inflammation of throat and nose for three days before maculo-papular rash develops.

(French, op. cit.) -- persists five days.

Koplik's Spots; irregularly shaped bright red spots containing small blue-white flecks (Thoma, op. cit.) may be seen in the mouth 1 to 4 days before the rash. Koplik's spots are usually on the internal surface of the cheek -- may also develop on hard or soft palate.

Incubation period prior to manifestation of Koplik's spots, -- 8 to 10 days.

Possible Complications: Nephritis, otitis media, bronch-pneumonia and meningitis.

RUBELLA ('German Measles')

An acute virus infection usually of milder form in which the rash may resemble that of scarlet fever. On close examination, however, it may be distinguished, by localising areas where macular characteristics are evident and it occurs behind the ears and on the forehead, which is not the case in scarlet fever (French, op. cit.)

Incubation period, 5 days to three weeks.

Rash appears first on the face and may spread extensively over the body -- enlargement of lymph glands.

Oral mucosa may show red macules (Not Koplik spots).

Complications are not serious except when the disease occurs during pregnancy when the child may be born with congenital defects; defective vision, cleft palate.

Infection in early life may be responsible for hypoplasia of the enamel formed during the course of the disease.

Chapter VIII. Cont'd.VARICELLA. ('Chicken Pox.')

A highly infectious disease usually affecting children.

Incubation period, 7 days -- vesicular eruptions on skin and in mouth especially the palate.

The papules rapidly become raised, form fluid and dessicate to form scabs.

Successive crops of macules at three to four days intervals. (Thoma, op. cit.)

The viruses of herpes, Zoster and Chicken Pox appear to be closely related.

VARIOLA. ('Small Pox!')

An infectious virus disease with an incubation period of 8 - 10 days - A rash, characterised by pustules, covering the whole body especially the hand, feet and legs -- often effects the oral mucosa:- the macules are small and elevated, -- are cast off to expose eroded areas and ultimately, scars.

Inclusion bodies are present in the epithelial cells.

Often severe, sometimes fatal -- always general symptoms of toxæmia.

MOLLUSCUM CONTAGIOSUM.

This disease in addition to the typhoid-like psittacosis, may be contracted from parrots.

Flattened small growths, resembling 'mother of pearl' buttons (French, op. cit.) with a central depression -- overlying skin smooth and shiny -- occurs commonly in the face, but also on the tongue and buccal mucosa. Histopathology:- large inclusion bodies in cells of squamous epithelium.

ERUPTIVE FEVER WITH STOMATITIS.

Possibly due to virus infection -- described by Thoma (op. cit.) predominal respiratory symptoms with lesions developing at the mucocutaneous junctions -- 18-31 years, -- oral and genital lesions run rapid course, rupturing in 24 hours.

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EPIDEMIC PAROTITIS ('Mumps')

A specific contagious virus disease with a predilection for the parotid gland but occasionally involving the other salivary glands, the uro-genital and endocrine systems.

Usually in childhood but adults may be affected.

Incubation period; -- about 18 days. Headache, sore throat, dysphagia, malaise, chill and sometime convulsions.

Usually confined to salivary glands first appearing on one side and spreading to other. (French op. cit.)

Inflammation at orifice of Stenson's Duct -- oedema of the pharynx. considerable pain.

Chapter Vlll Cont'd.Epidemic Parotitis ('Mumps')/

Complications. -- possibly meningitis, mastitis and deafness -- rarely suppuration of gland.

Differential Diagnosis.

Mumps is usually bilateral after 24-36 hours, -- non-specific infective parotitis is commonly unilateral. Epidemic parotitis is more common in the paroted glands, while occlusion of the salivary duct by calculus is more frequent in the submaxillary glands. In the latter condition the swelling is usually accentuated at meal times. Xrays are helpful.

Chronic unilateral enlargement may be due to a paroted tumour and chronic bilateral enlargement to tuberculosis. Where there is chronic painless swelling of all salvary glands and the lacrymals, suspect Mikulicz's syndrome.

GRANULOMA INGUINALE. (Granuloma Venereum.)

Almost identical descriptions by Thoma (op. cit.) and Stones.⁽⁷⁾

Chronic infective venereal disease probably virus origin -- usually occuring about the genitalia but oral lesions are not uncommon.

Lesions characterized by granulation tissues heavily infiltrated with large mononuclear cells (25-90u).

Types -- (a) Ulcerative.
(b) Exuberant.
(c) Cicatrical -- long standing.

Treatment with 0.04 gms. of ammonium Potassium Tartrate in 100 parts of normal saline.

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P A R T 1.CHAPTER 1X.THE ROLE OF CHEMOTHERAPEUTICS AND ANTIBIOTICS IN DENTISTRY IN1 9 5 7

Excepting the use of chemotherapy in Syphilis, the history of the treatment of infections with chemicals of known composition and with antibiotics goes back only a few years. In that short period, concepts have been adjusted constantly, as facts on sensitivity, selective action, development of resistant organisms and side effects have emerged. Consequently rather exact wording has been used in naming this chapter.

Thompson⁽¹⁾ relates the story well, describing how the work on penicillin may have been delayed by the development of the sulphonamides. In that this chapter must define the present approach to the use of sulphonamides and antibiotics, a few significant dates only are given:-

- 1929: Sir Alexander Fleming accidentally discovered penicillin.
- 1933: Introduction of sulphonamides.
- 1938: Florey continued work on penicillin.
- 1942: Beginning of penicillin era.
- 1942: Walksman announced new antibiotic -- Streptomycin produced from *Streptomyces griseus*.
- 1945: Bacitracin isolated from *B. subtilis* by Meleney and Johnson.
- 1946 Duggar produced chlortetracycline (aureomycin) from *streptomycis aureofaciens*.
- 1947: Chloromycetin (chloramphenicol) isolated by Burkholder from *Streptomyces venezuelae*.
- 1950: Finley produced a broad spectrum antibiotic, ocytetracycline (terramycin) from *Streptomyces rimosus*.
- 1952: Erythromycin produced from *Streptomyces erythreus* by McGuire and Tanner and his co-workers isolated Carbomycin (magnanycin) from *Streptomyces holstedii*.

The Research continues.

As stated by Lane ⁽²⁾ the use of antibiotic therapy has constituted a notable advance in the control of infections. However he asserted that since the first report in 1944 of the use of penicillin in dental operations, the general enthusiasm^a for the merits of antibiotics has been tempered by the development of antibiotic resistant organisms.

Chapter 1X. Cont'd.The Role of Chemotherapeutics and Antibiotics in Dentistry in 1957.THE SULPHONAMIDES.

1. The readily absorbed and more soluble sulphonamides:-

Sulphonilamide.	
Sulphacetamide	(Allucid.)
Sulphapyridine	(M & B 693.)
Sulphathiazole	
Sulphadiazine	)
Sulphamerazine	) The Sulpha-pyrimidine
Sulphamezathine	) Group.
Elkosine	
Sulphafurazole	(Gantrisin)
Sulphatriad	(Sulphadiazine, sulphamerazine, Sulphathiazole).
Sulphadital	(Sulphadiazine, sulphamerazine and Sulphacetamide.)

2. The poorly absorbed sulphonamides:-

Sulphaguanadine.
 Succinyl sulphathiazole (sulphasuccidine)
 Phthalyl Sulphathiazole (Sulphathalidine.)

3. Sulphamar -- of different chemical structure and not inactivated by para-amino-benzoic Acid. (P.A.B.A.)

Those likely to be most useful to the oral surgeon are sulphadiazine, sulphamerazine and sulphafurazol (gantrisin). Thoma (4) advocates their use because of a greater solubility in urine.

Toxic effects of Sulphonamides:-

General malaise, headaches, mental depression, nausea and vomiting are common side effects in sulphonamide therapy, but rarely, occur when drugs of the sulphadiazine group are used.

Sulphanilamide may produce cyanosis.

The surgeon must be alert for signs of drug rash, fever, haematuria and renal pain, and should they occur immediately discontinue treatment.

Rarer but extremely serious complications are:-

Anuria, agranulocytosis, haemolytic anaemia, aplastic anaemia, purpura, exfoliative dermatitis, peripheral neuritis and hepatitis. The allergic cutaneous lesions may be of the morbilliform scarlatiniform types.

Sulphonamides are mainly bacteriostatic and are very effective for coccal infections but their use has been reduced because many of the antibiotics have fewer side effects.

The soluble sulphonamides are inactivated by pus and are thus unsatisfactory in treating closed infections unless supplemented by intelligent surgical procedures to remove necrotic tissue and establish drainage. Thoma (op. cit.) reminds his readers of the chemical similarity between para-amino benzoic acid and these drugs which may account for their ineffectiveness in the presence of pus.

Chapter IX. Cont'd.The Sulphonamides.Resistant Organisms:-

The development of resistant strains occurred quite early. For example Micks (5) in 1949 stated that from 'time to time' a strain of a normally sensitive organism was found to be resistant. Therefore sensitivity tests are invaluable.

Range of Activity:-

Sulphanilamide: some strains of B. coli, streptococcus pyogenes but not pneumococci or staphylococci.

Sulphacetamide:- (Very soluble) -- Wider range including pneumococci.

Sulphapyridine:- Also wide range and effective against pneumococci but very toxic.

Sulphathiazole: Greatest in vitro effect but rapid secretion and frequent allergic reactions contraindicate its use.

Sulphadiazine: Very potent in vivo because of high concentrations maintained in the blood and tissues as a result of ready absorption and slow excretion. It possesses a wide bacterial spectrum. Excepting for haematuria and anuria due to its sparing solubility, side effects are minimal. Adequate fluids and alkalinising diuretics are indicated.

Sulphamerazine: similar potency to sulphadiazine but more toxic.

Sulphamezathine (sulphadiphidine) also resembles sulphadiazine and is one of the least toxic of the sulphonamide. It does not penetrate the cerebro-spinal fluid as well, but for oral lesions is probably one of the drugs of choice.

Sulphafurazole: is rapidly absorbed and secreted and has been recommended for infections of the urinary tract. Provided the urine is rendered alkine, solubility is good.

Sulphatriad: is valuable because the concentration of each component is insufficient to cause crystalluria, but the additive concentration is effective against infections.

Sulphamar: where local treatment is indicated this is the drug of choice -- not affected by pus.

Administration:-

The sulphonamides are usually administered orally. The average adult dose is four grammes statim and 1gm. every four hours for four days. Duration of therapy may be extended to seven days, but excepting for extremely serious conditions should not be continued beyond that period.

Where a greater concentration than 2.5 mgs per centum is required to produce sensitivity in laboratory tests larger initial doses may be used. Organisms resistant to sulphadiazine will probably prove to be resistant to all sulphonamides.

Chapter IX. Cont'd.The Sulphonamides.

Ample fluids, about one pint for each gram of sulphonamide ⁴ should be taken. 1. 3 grams of Sodium or potassium citrate should be administered with each dose to maintain alkalinity of the urine. Daily testing with litmus paper is advised. Sodium carbonate 2 gms. for one of the drug may be used in place of Potassium Citrate.

As destruction of intestinal flora may inhibit vitamin B absorption the complex should supplement the diet.

THE ANTIBIOTICS.

'Antibiosis' is the term used to describe the antagonism which may occur when two or more organisms are growing together. The antibiotics are the antibacterial substances produced by bacteria, moulds and fungi which may account for antibiosis. It appears that their bacteriocidal or bacteriostatic action results from an interference with the normal biochemical activities of the invading organisms.

PENICILLIN:

Of the five main varieties, Penicillin F.G. 12, X and O, Penicillin K is inactive in Vivo and the type G. Is the usual basis of the various forms in clinical use. Probably Penicillin O will be valuable in the future in treating patients who have become sensitive to the type G.

The Oxford unit of penicillin is that amount of amorphous penicillin producing a 24mm. zone of inhibition on an agar plate inoculated with *Staphylococcus aureus*. International units are similar, being based on crystalline preparations.

Because of its low toxicity, the fact that high concentrations can be attained in the tissues, and its rapid absorption crystalline penicillin is used in serious infections endangering life. The usual dosage given intramuscularly is 100,000 units every six hours. In very severe infections the intervals may be three hourly and the dosage has been increased as high as 500,000 units.

Gastric acidity and the alkalinity of the upper part of the small bowel have a destructive effect on penicillin but oral penicillin buffered with aluminium preparations or magnesium hydroxide is used to maintain the blood level in children who have had rheumatic fever. Seldom is intravenous penicillin used. Hyaluronidase may be used to assist the spread of large intramuscular doses.

Other forms of penicillin are used to avoid six-hourly injections:

Procaine Penicillin:- absorption for 24 hours.

Distaquaine and other aqueous penicillin:-

300,000 -- 600,000 units 24 hourly,

Fortified aqueous penicillin:-

Crystalline penicillin G. added.

Daily injections 500,000 units or more.

Chapter 1X. Cont'd.Penicillin Cont'd.

Oily suspensions:- containing procaine penicillin and 2% monostearate may be given twice weekly -- slower absorption -- 500,00 units daily, preferable.

Di-benzyl-ethylene -- diamine penicillin (D.B.E.D. penicillin):- relatively insoluble -- intramuscular injection of 600,00 units gives slow absorption for some weeks.

'Bicillin,' -- containing crystalline penicillin, procaine penicillin and D.B.E.D. penicillin combines all properties.

The regular injections of crystalline penicillin is probably most effective in attaining desirable blood levels and obtaining penetration. Repository penicillin is satisfactory only if the organisms are highly sensitive.

Spectrum for penicillin: gram-positive bacilli, including anaerobic organisms, gram-positive cocci; gram negative diplococci; spirochaetes and actinomycoses.

STREPTOMYCIN.

Major importance in the treatment of tuberculosis.

Adjunct to penicillin in subacute bacterial endocarditis.

In treating penicillin resistant staphylococci.

Administration and Dose:- Usually intramuscular -- from 0.5 grams to 10 grams twice daily.

In tuberculosis: 1 gram twice weekly with para-amino - salicylic acid.

Toxicity: slight in moderate doses -- in heavier doses; vestibular dysfunction, giddiness and deafness due to damage to auditory nerve - damage may be irreversible.

Anorexia, headache, nausea and vomiting.

Thoma (op. cit.) states that dehydrostreptomycin possesses much less neurotoxicity, but Thomson (op. cit.) asserts that it is most likely to cause auditory nerve damage and should not be used.

CHLORAMPHENICOL.

Its use in oral surgery should be avoided as the antibiotic depresses bone marrow function and cases of aplastic anaemia and agranulocytosis have resulted.

THE TETRACYCLINE COMPOUNDS.

Often termed the 'broad ^e spectrum' antibiotics and are effective against gram positive cocci, gram negative bacilli, gram positive bacilli the spirochaetes, actinomycosis, granuloma inguinale, pseudomonas pyocyanea and proteus vulgaris.

The group consists of aureomycin, terramycin and tetracycline.

Chapter. 1X. Cont'd.The Tetracycline Compounds.

Administration is by oral, intravenous or intramuscular routes.

Dose: Oral: 250 mg. four times a day.

Intravenous; 500mg. twice daily.

Children: 100 mg. 4 times a day.

Children one quarter to one half adult dose.

Toxicity: not uncommon -- nausea, vomiting and diarr^hœa -- seldom fatal.

Occasionally staphylococcal enteritis due to secondary infection by resistant organisms.

Candidiasis may develop in the oral cavity or lungs, where abscess formation may result in death.

Tetracycline is the least toxic of these compounds.

ERYTHROMYCIN.

A newer antibiotic and its use should be reserved for those who are sensitive to other suitable antibiotics.

Good clinical results have so far been obtained.

Wide range, but ineffective gram-negative bacilli.

Administration: usually per oris -- tablets with acid-resistant coating.

25 to 50 mgms. per kilogram of body weight every six hours depending on sensitivity tests. Organisms reacting to 1 ug per millilitre are sensitive and the lower dose is sufficient. Nausea, vomiting and occasionally diarrhoea are the only toxic effects so far reported and these are not common.

BACITRACIN.

Bacitracin in topical application is strongly synergistic with penicillin and this constitutes its main appeal in dentistry. It is a component of "P.B.S.C." paste used by some in endodontics.

It is highly toxic when used intramuscularly.

For topical use: 500 -- 10,000 units per cc.

Synergistic Action:-

Streptomycin and penicillin; topical bacitracin and penicillin and suphapyridine. Usually it is safe to use any of the bactericidal antibiotics together:- Penicillin, streptomycin, bacitracin and neomycin.

Antagonism:-

The bacteriostatic antibiotics, (aureomycin, Terramycin, Chloromycetin, Tetracyclin, Erythromycin and Sulphonamides) often interfere with the bactericidal action of the former group.

.....

Chapter 1X.

Present Concepts.

Tolhurst and Williams (op. cit.) state, "The enormous sale of antibiotics bears witness to the general observation that these drugs are often used unnecessarily." There is little doubt that the spectacular results achieved at first caused practitioners to institute penicillin and chemo-therapy for all minor ailments. To the discerning, it soon became evident that all was not well. Acute pyogenic infections merely became subacute and then failed to fluctuate when heat treatment was applied. Reports of toxic urticaria and apparently resistant diseases soon appeared. There was the occasional death from anaphylactic shock.

Lane (op. cit.) lists the following untoward effects.

1. Direct toxic or allergic effects related to the type and for amount of antibiotic used.
2. Sensitivity and anaphylactic reactions due to patient idiosyncracies or sensitization.
3. Secondary inflammations or ulcerations caused by superimposed infections from antibiotic resistant organisms.

In addition .. secondary disturbances of the gastro - intestinal tract and the vitamin deficiencies caused by the change in the intestinal flor."

Further dangers have proved to be the masking of important signs and symptoms with a resultant difficulty in diagnosis. Mere suppression of the infection may make treatment more difficult. Finally, now that most antibiotics are "free medicines," their unnecessary use is nationally extravagant.

Failure in chemotherapy has been due to:-

1. Failure to institute early treatment.
2. The development of 'resistant' strains of organism.
3. Incorrect dosage or insufficient period of treatment.
4. Incorrect diagnosis, either of the disease or the causal organism.
5. Selection of ineffective sulphonamide or antibiotic for the particular organism and failure to carry out sensitivity tests wherever possible.
6. Failure to supplement therapy with correct surgical procedures.
7. Secondary infection such as with *Candida Albicans* or resistant Cocci.
8. Combining antagonistic antibiotics.
9. Failure of the drug to penetrate the lesions -- lack of surgery often contributory.
10. The presence of a previously unsuspected lesion (Tuberculosis or fungus.)

Chapter 1X.

Present Concepts.

In selecting an appropriate antibiotic, Thoma suggests the following method:- examination of direct smears to identify the organism by its morphology and staining, utilization skin tests to test for allergy and sensitivity tests to determine the most effective agent to use. Correct dosage can be gauged from the tests by placing a known amount of each antibiotic on the agar plate.

As late, as 1956, Zubrow (6) states "...an ⁿitelligent guess as to the type of organism involved in the condition to be treated. Laboratory studies may be helpful, but treatment of acute cases must often be instituted immediately." Even now, this is not an incorrect assertion, but if it is at all possible, it is best to delay until laboratory tests have been carried out. The same author favours antibiotic prophylaxis for the prevention of bacterial endo-carditis, bacteraemia, infection in diabetes mellitus, blood dyscrasias, for multiple exodontia and alveolectomy. Therapeutic dosages are also advocated for acute Vincent's infection and pericoronitis. Thomson (op. cit.) exorted medical and dental practitioners ^{to recall} the 'pre-antibiotic' era when patients still recovered from infection and suggested that prophylaxis with antibiotics should be used with caution. Deichmann (7) is probably correct in maintaining that a 'cover' should be provided in treating patients with valvular heart disease, rheumatic fever, renal disease and diabetes. In diabetes mellitus, correction of the blood sugar level with insulin is even more important.

The writer considers the following questions must be answered before prescribing sulphonamides or antibiotics.

1. Has the patient had antibiotics or chemotherapy before?
If so how often? -- Intradermal test for allergy.
2. Is the patient likely to require antibiotic therapy again in the near future for any systemic condition?
3. Can this condition be treated successfully and safely without antibiotics? Some, such as Vincent's infection, pericoronitis and acute localised dento-alveolar abscesses in healthy people, can.

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P A R T 11.

SYSTEMIC FACTORS WHICH CONCERN THE ORAL SURGEON

P A R T 11.Chapter 1.B L O O D.

Basic facts on normal blood and definitions of variations of the normal are given in note form:

Formation:- intravascular or extravascular?

Bone marrow. - 4,000 c.cm. in adult; normally about half of it actively haemopoietic (red in colour); half inactive (fatty.) All bones haemopoietic for first 3 or 4 years of life. At seven years long bones less active - pale red marrow with fat droplets. At ten to fourteen years, patches of yellow marrow, ^{At 20 yrs, long bones yellow,} except upper end of femur and humerus.

In adult; red marrow in skull (maxilla and mandible) bones of thorax, vertebrae and os innominatum; little in upper end of femur and humerus. In old age half of sternum and ribs fatty marrow.

CELLS; See colour drawing.

ERYTHROPOIESIS:

Haemocytoblast. (syn. Lymphoidocyte, haemohistioblast, hamatogone.

Said to be non-differentiated reticulo-endothelial cell precursor to red and white cells.

Proerythroblast (syn. pronormoblast, macroblast, erythrogone, megaloblast, lymphoid haemoblast. 14-19 u.

Early Normoblast (syn. Basophilic normoblast, early erythroblast, normoblast type A.) 11 - 17 u.

Intermediate Normoblast: (syn. Poly Chromic normoblast, late erythroblast; normoblast type B. 10 - 14 u: small quantity haemoglobin.

Late Normoblast orthochromic normoblast, normoblast type C. 7 - 10 u increasingly haemoglobinised.

Reticulocyte young erythrocyte polychromatic staining.

Erythrocyte: normal red cell ^{7-2 M.} 7 - 2 u. biconcave disc: no reticular material - normally 4,200,000 to 6,400,000 per c. mm. - not a living cell, lives 14 - 200 days, but probably averages 120 days.

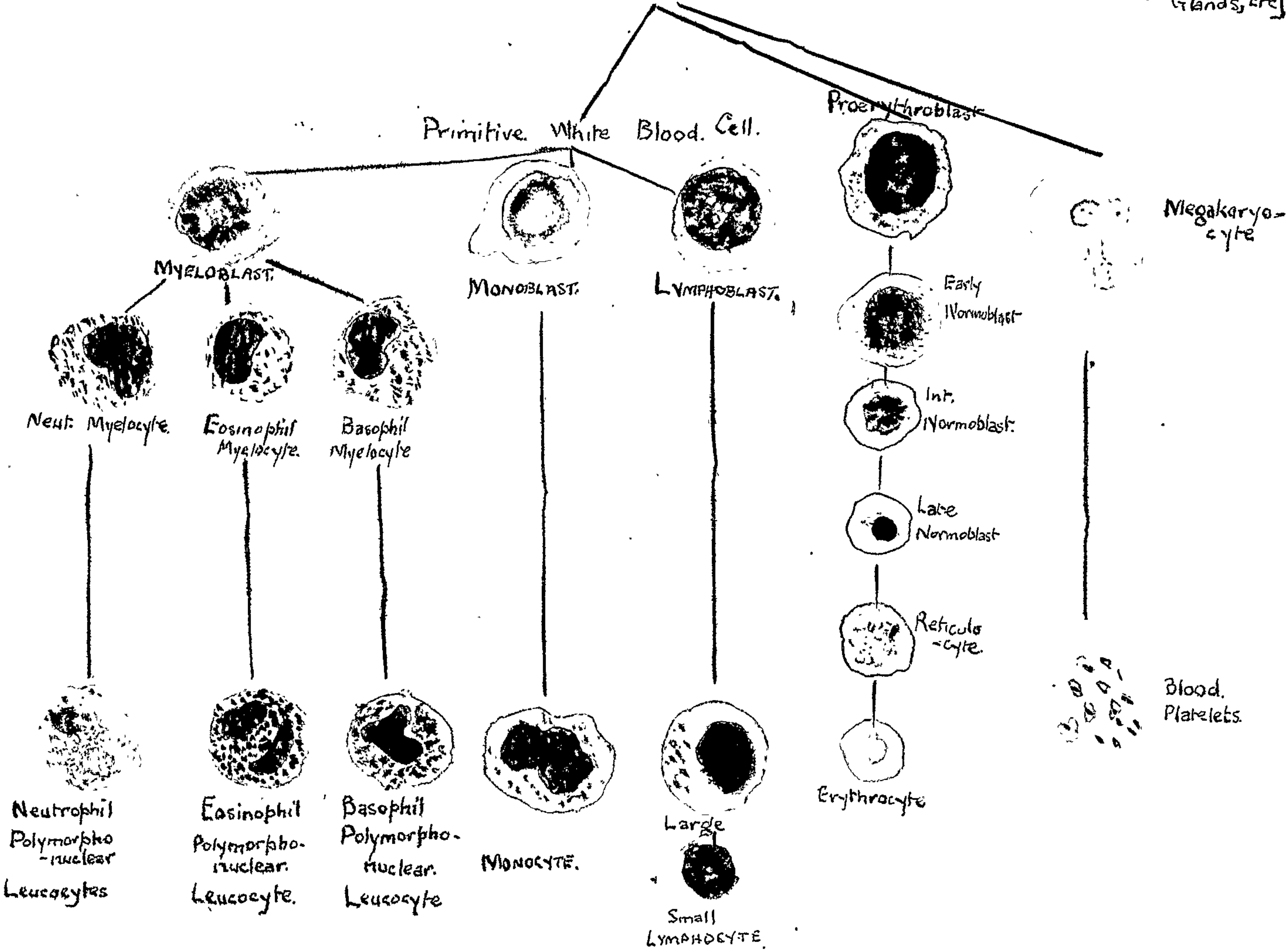
THE ORIGIN OF BLOOD CELLS

FROM 'DISEASES OF THE BLOOD'

by WHITBY, STRLONEL, E.H., AND BRITTON C.J.C.

5, 5, 1947

THE RETICULO-ENDOTHELIAL SYSTEM [Bone Marrow, Spleen, Lymph. Glands, Etc]



1

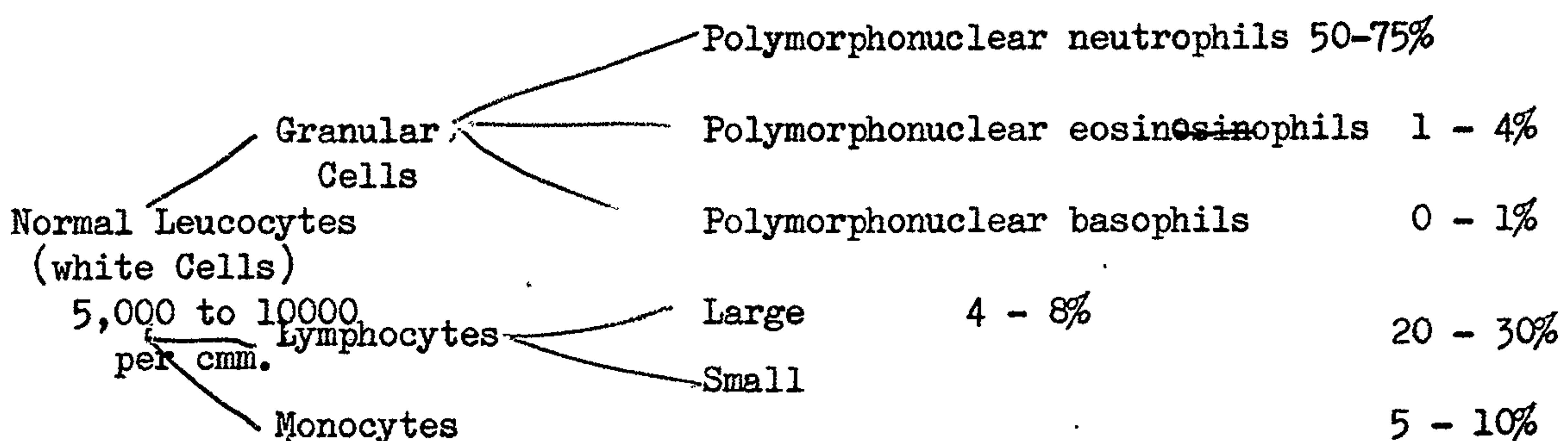
Chapter. 111. Cont'd.

Erythrocytes. Cont'd.

Are eventually fragmented by friction in peripheral circulation --
poikilocyte, partly fragmented red cell -- further fragmentation to
form microcyte -- ingested by phagocytes of reticulo endothelial
system.

.....

Leucocytes



Leucocytes -- living cells with nuclei rich in nucleo- protein. -
contain lipoids, glycogen, cholesterol, ascorbic acid and enzymes.

Note: (proteolytic enzyme in polymorphonuclear granulocytes.)

Granular cells contain histamine. Fluctuation in count between 4,000 -
11,000 / cmm. of no significances, rhythmic fluctuations every hour.

Granulocytes live three to five days, most are finally destroyed in
reticulo-endothelial system -- some in blood stream -- nuclei 1-4 lobes
(more in older cells.) Stimulus for production of leucocytes varies with
type of cell -- largely chemistactic. Artificial stimulation of
production of polymorphonuclears by injection of nucleic acid, --
pyogenic cocci release nuclear products by tissue destruction.

Granulocytes are actively amoeboid and phagocytic.

Monocytes actively phagocytic for foreign particles. Appear to be destroyed
in reticulo-endothelial system.

Lymphocytes average life less than one day. Slight phagocytic powers. --
Defensive cells which form anti-bodies.

Granulocytes leave the body by passing through bowel. Always present
in growing connective tissue -- disappear when growth ceases. Also
present around tuberculous lesions.

Chapter 1 Cont'd.

Granulocytes. formed in myeloid tissue - confined to red bone marrow.

Monocytes, origin doubtful - but probably from reticulo-endothelial system - may, however, be in lymphocyte class.

Lymphocytes - non - granular cells - products of lymphoid tissue entering blood stream through lymph stream and thoracic duct.

Cells of myeloid series contain oxydase (also in myelocytes.)

Neutrophils and possibly other granulocytes contain proteolytic enzymes leading to lysis and softening of tissues.

Neither of these enzymes in lymphocytes.

Haemoglobin.

Carried by the red cells, haemoglobin is a chromoprotein, the molecules of which are extremely large, each containing one atom of iron. Readily combining with oxygen to form oxyhaemoglobin, each atom of iron unites with two oxygen atoms. Normally there are 14-17 grams of haemoglobin in 100 cc of blood, and each gram carries 1.34 ccm of oxygen.

Probably formed in red cells in the red marrow, haemoglobin conveys oxygen to the tissues and removes carbon dioxide to the lungs. When red cells finally breakdown, the contained haemoglobin spits into iron free bilirulin (haematoidin) which is transported to the liver to form one of the bile pigments and haemosiderin containing iron which is used by the marrow to elaborate fresh haemoglobin.

Blood Platelets - essential to proper coagulation - coagulation does not occur without platelet disintegration - agents which hasten disintegration accelerate clotting and vice versa - will not disintegrate without Ca.⁺⁺
In coagulation, flow over wound - attach to surface - disintegrate - release enzyme, thrombokinas (syn: thromboplastin, cephaline) activates prothrombin of blood to form thrombin.

250,000 - 5000,000 per cmm - normal number varies -- also associated with clot retraction and adhesion to blood vessel walls in repair, in transfusions, platelet survival time 3 to 5 days -- destroyed in spleen

Chapter 1. Cont'd.Blood Platelets. Cont'd.

and rest of reticulo-endothelial system. Tissue injury stimulates platelet production.

ABNORMAL HAEMOPOIESISHyperplasia.

Following haemorrhage, the red marrow proliferates to replace some yellow marrow, when there may be tenderness over bones. Here the reaction is confined mainly to erythroblastic tissue, although there is some response from the myeloid cells.

Acute coccal infections provoke a bone marrow response that is mainly leucoblastic and the marrow is pink in contrast to the deep red erythroblastic marrow.

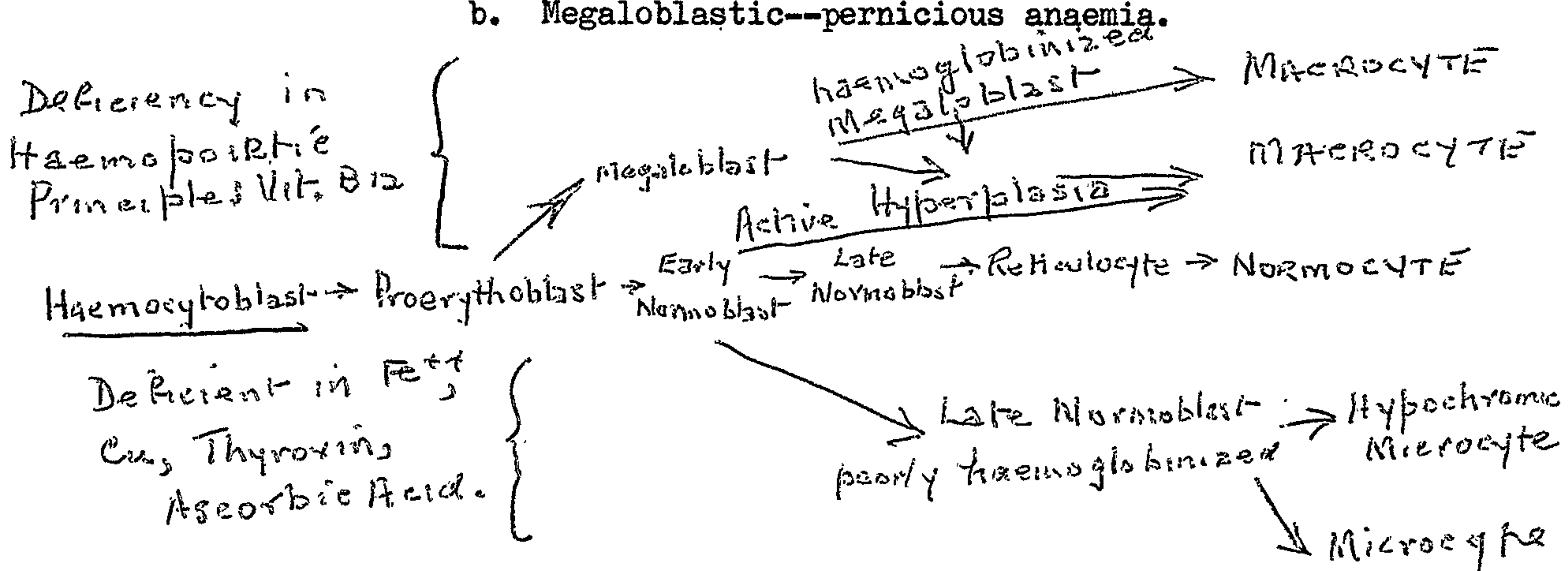
In leukaemia, the marrow may be grey - yellow usually with a slight red tinge.

When marrow becomes aplastic, the red marrow is largely replaced by pale, fatty watery tissue.

At first, all blood cells increase in marrow hyperplasia, whether the reaction is finally leucoblastic or erythroblastic.

Summary of reactions.

1. Leucoblastic --
 - a. Neutrophilic -- Acute coccal infections.
 - b. Eosinophilic
 - Basophilic -- Leukaemias.
 - Myelocitic
2. Erythroblastic
 - a. Normoblastic -- haemorrhagic anaemia, haemorrhagic and Fe deficient anaemias.
 - b. Megaloblastic -- pernicious anaemia.



Adapted from
WHITBY AND BRITTON

Chapter 1. Cont'd.

Hyperplasia. Cont'd.

In simple hyperplasia, there is a speeding of cell division in the earlier stages and of haemoglobinization. The process in normoblastic and the re-opening of a greater number of primitive cells with haemoglobin is known as a "shift to the left." The extent of this shift indicates the strength of the stimulation or reaction and many of the early cells are polychromatic (irregularly stained) and the cytoplasm of many of the intermediate normoblasts are eosinophilic. In moderate simple marrow hyperplasia the finally formed erythrocyte will probably be of normal size (normocyte), but in severe iron deficiency they are small (microcytes). If the proliferation is very active the final erythrocytes are larger than normal and are known as macrocytes and the marrow is macronormoblastic.

Where erythropoiesis is disturbed by a deficiency of the haemopoietic principle (liver), the usual formation of normoblasts is replaced by a series of megaloblasts (early, intermediate and late) which ultimately form large erythrocytes called megalocytes or macrocytes (14-19 u.)

Abnormal Cells in Peripheral Circulation.

a. Nucleated red cells -- Any of the nucleated red cells of the marrow may be seen in the blood stream when the bone marrow is active. In dishaemopoiesis, megaloblasts in varying stages of formation may be seen.

b. Nuclear Remnants

Cabot rings -- staining red-purple with Romanowsky stains and probably denaturated protein from cell degeneration -- often associated with stippling and polychromasia showing immaturity -- seen in pernicious anaemia, lead poisoning and leukaemias, but not diagnostic.

Howell - Jolly bodies - true red blue staining nuclear fragments - evidence of immaturity in secondary and pernicious anaemias, leukaemia, alcoholic jaundice and following splenectomy.

Chapter 1. Cont'd.Abnormal Cells in Peripheral Circulation.

- c. Polychromatic Cells diffuse purple or purple-red and cells showing punctate basophilisin or stippling (dots of blue material) are both forms of reticulocytes, and indicate immaturity.
- d. Reticulocytes -- normally 2% of red cells, may rise to 50% in severe anaemias.
- e. Hypochromic cells are deficient in haemoglobin and stain lightly.
- f. Spherocytes are darkly staining red cells which have lost their bi-concave shape.
- g. Leptocytes are the very thin red cells of Mediterranean fever and regenerating blood. The haemoglobin appears at the margin and the cells stain as target cells.
- h. Anicytosis -- great variation in size of red cells.

Diagnostic Tests for Red Cells.

Haemoglobin may be estimated as the percentage of normal by Haldane's carboxyhaemoglobin or Sahli's haematin method.

Normal results are:-

<u>HAEMOGLOBIN</u>	<u>MAN</u>	<u>WOMAN</u>	<u>AVERAGE</u>
grams per cent	15.6	13.7	14.5
Haldane per cent	113	98	105
Sahli per cent	90	80	85

The percentage of haemoglobin usually varies with blood cell count is higher in polycythaemia (increased red cell count in erythrocytosis, Erythremia.) If the reduction of haemoglobin is not as great as the reduction in blood cell count the anaemia is hyperchromic, in the reverse, hypochromic.

Red Cell Count

5,500,000 for average normal male.

4,800,000 for average normal female.

5,000,000 convenient normal count for both sexes.

Variations of $\pm 5\%$ insignificant diagnostically,

Colour Index.

This is a method of expressing the mean haemoglobin content of a single erythrocyte.

The normal is:-

$$\frac{\text{Haemoglobin (\% of normal)}}{\text{Red Cell count (\% of Normal)}} = \frac{100}{100} = 1.$$

Chapter 1. Cont'd.Colour Index. (cont.)

An 0.15 variation not necessarily significant and different figures are obtained from Sahli's and Haldane's method of estimation.

Anaemias may be divided into three classes by the colour index.

- a. Where greater than 1, pernicious types.
- b. Where about 1, post-haemorrhagic^{gic} anaemia.
- c. Where less than 1, chlorotic anaemias.

The following is a useful classification:

		<u>Colour index.</u>
<u>Normal cell count</u> (Normocythaemic)	Normocytic and hypochromic	Less than one
	Microcytic and hypochromic.	Less than one.
Increased cell count (Polycythaemic or hypercythaemic)	Normocytic and hypochromic.	Less than one.
	Microcytic and Hypochromic.	Less than one.
Decreased Cell Count. (hypocythaemic)	Macrocytic and hyperchromic	Greater than 1.
	Macrocytic and normochromic	Greater than 1.
	Macrocytic and hypochromic	Greater, equal to or less than 1.
	Normocytic and Normochromic.	Equal to 1.
	Normocytic and hypochromic.	Less than 1.
	Microcytic and hypochromic.	Less than 1.

The term hyperchromic should be used only when the colour index is greater than one, and not for describing the colour of a stained cell.

Because it depends partly on cell size and partly on haemoglobin concentration, the value of the colour index is somewhat limited.

The Mean Corpuscular Volume (M.C.V.) gives the average volume of a single red cell in cubic microns.

Normal average: 86 cu.

The Mean Corpuscular Haemoglobin Concentration (M.C.H. C.)

and Mean corpuscular Average Thickness (M.C.A.T.)

Gives valuable comparisons with the normal when making a diagnosis.

These values are a clear guide in indicating changes of cell size and haemoglobin content of each cell.

Chapter 1. Cont'd.

In the circulating blood the presence of numbers of nucleated red cells signifies excessive bone marrow production; early and late normoblasts, active but normal haemopoiesis; megaloblasts indicate that abnormal haemopoiesis exists (pernicious anaemias). A reticulocyte count (supra-vital preparations), helps to assess the efficacy of treatment and is a guide in indicating whether transfusions are necessary.

The tourniquet test is carried by counting the number of petechial in a 2 X 2 cm. square on the inner forearm five minutes after the release of the rubber cuff of a sphygmomanometer. A count of more than ten petechiae is abnormal.

Leucocytosis.

Leucocytosis is an increase above 10,000 per cmm. of leucocytes in the circulating blood. Where the number decreases below 4,000 per cmm., the proportion of each type of white cell present and the presence of abnormal or primitive leucocytes is revealed by a differential leucocyte count. Variations in the number of leucocytes have the greatest clinical and diagnostic significance. According to the predominant cell present the condition may be termed, neutrophil leucocytosis, lymphocytosis, eosinophilic or basophilic leucocytosis. Similarly deficiencies of particular cells are described as neutropenia, lymphopenia, monocytopenia and eosinopenia.

The numbers and relative proportions of the different white cells are given at the beginning of this chapter, and the diseases associated with abnormal white cell counts have been enumerated in Part One. In addition to those conditions mentioned, there may exist physiological leucocytosis where variations of the white cell count occurs in normal health. With exercise, ingestion and digestion of food, and exposure to the sun, minor variations occur in the leucocyte count. With severe pain, violent exercise and major emotional crises, there may be a more marked leucocytosis.

Primitive leucocytes, myeloblasts, myelocytes, lymphoblasts and

Chapter 1. Cont'd.

Leucocytosis Cont'd.

and monoblasts occur in the leukaemias and in excessive leucocytosis.

Adventitious blood cells may appear on occasions. Plasma cells possibly derived from lymphocytes, though normally found in chronic lesions are rarely seen in the circulating blood, but they may appear with jaundice, multiple myelomata, in measles and in leukaemia.

Turk's irritation cells may be identical with plasma cells but the cytoplasm stains a darker blue and the cytoplasm has not the cartwheel appearance of those cells. Of no diagnostic value, they may appear in the circulation in severe anaemia, leukaemias, measles, German measles, malaria and in any condition where leucocytosis is marked. Basket and smear cells are degenerating leucocytes.

In either leucocytosis or leucopenia, there is always a "shift to the left" when the condition is a response to infections, toxæmias or haemorrhage. As with erythropoiesis, the expression, "shift to the left" is used to describe the appearance of more primitive cells. Cooke in 1930, simplifying Arneeth's work classified granulocytes into five main types or group:-

Group, 1. With a curved unlobed nucleus.

Group, 2. With a filament joining two lobes.

Group, 3. Two filaments.

Group, 4. Three filaments.

Group, 5. Four or more filaments.

The greater the number of filaments and lobes, the older is the cell.

A "shift to the right," showing more of these multilobed mature cells is seen in vitamin deficiency diseases, pregnancy anaemia, sprue and pernicious anaemia.

Schilling in 1929 outlined a simpler method of interpreting the leucocyte count. He divided granulocytes into four classes:-

1. Myelocytes (mostly metamyelocytes).
2. Juvenile polymorphonuclears (C - shaped or bean-like nucleus)
3. Stab Cells with a wavy nucleus.
4. Segmented or multi-lobed polymorphs.

In normal maturation the juvenile polymorph progresses to the multi

Chapter 1. Cont'd.Leucocytosis. Cont'd.

lobed form, but in deleterious conditions such as toxæmia it forms the "Stab" cell with a pyknotic, immature nucleus. Schilling^{states} that Stab cells were common in the degenerative reactions of typhoid fever, tuberculosis, kala azar, protozoal diseases and malaria. Regenerative reaction on the other hand produced numerous juvenile but no Stab cells.

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Whitby, Sir Lionel E.H., and Britton, C.J.C., "Disorders of the Blood," J. and A. Churchill, Ltd., London, 5th Ed., 1947.

An excellent comprehensive publication; well illustrated and dealing in some detail with the oral manifestations of blood dyscrasias. In naming cells and diseases synonyms are given, this assisting in a review of literature.

French, Herbert and Douthwaite Arthur H., "Index of Differential Diagnosis of Main Symptoms," John Wright & Sons, Ltd., Bristol, 6th Ed. 1945. A valuable reference book for the general practitioner; diseases and symptoms are listed alphabetically, so that it is easy to refresh one's memory in making a differential diagnosis. The author's treatment of the "anaemias" though somewhat condensed is remarkably clear.

P A R T. 11.CHAPTER 11.COAGULATION AND HAEMORRHAGE.

It is first proposed to discuss coagulation and certain blood tests which assist in the diagnosis or control of spontaneous and post-operative haemorrhages.

Coagulation.

Coagulation is essentially due to fibrin formation. Thrombokinase (syn: thromboplastin, cephaline) from the blood platelets, free calcium ions in the presence of vitamin K. act on the prothrombin of the circulating blood to form an enzyme-like substance, thrombin. The thrombin thus formed, reacts with the soluble fibrinogen of the plasma to form fibrin.

Actually there is some doubt as to the exact function of the platelets. Howell (1935) considered that calcium ions, alone will cause the prothrombin to change to thrombin. It was his opinion that the function of thrombokinase was to neutralize the blood anti-thrombin (heparin), to enable coagulation to take place. Morawitz claimed that platelet disintegration took place when these bodies contacted damaged tissue surface to liberate thrombokinase, which then reacted with the prothrombin.

It is certain that platelets play a role in clot retraction and strengthen the fibrin network already formed. Certain also is it, that the platelets adhere to the ruptured surface of a blood vessel and are important in thrombus formation to seal the breach.

Clotting or coagulation time is determined as an important diagnostic aid. Greatly prolonged in haemophilia, there is also an increase in obstructive jaundice (lack of calcium, fibrinogen or prothrombin.) A determination of the prothrombin time may reveal prothrombin deficiency. Excess carbon dioxide prolongs clotting and coagulation is sometimes prolonged in leukaemia, X-ray and radium disease and benzol poisoning. Normal clotting time is 2-6 minutes.

As stated above, numerous platelets assist satisfactory clot retraction. Even where platelets are plentiful, inefficient retraction

Chapter 11. Cont'd.Coagulation. Cont'd.

may be due to fibrinogen deficiency, hypoprothrombinaemia and lobar pneumonia. Determination of clot retraction assists in diagnosing essential thrombocytopenia. The normal bleeding time is 2 - 5 minutes.

Red cell fragility tests are carried out by observing haemolysis of those cells in saline solutions of varying concentrations. The normal is 0.3 to 0.45 saline per cent and there is excessive fragility in congenital haemolytic icterus.

The sedimentation rate is observed by taking the time of precipitation of red cells in a tube containing an anti-coagulant. The rate increases where there is tissue degeneration; in inflammation and toxæmia. The rate is naturally higher in women and further increased in pregnancy. The determination of sedimentation rate is a valuable guide in prognosis.

Bleeding time is determined by making a single puncture in the ear lobe, absorbing the blood without touching the skin every thirty seconds until bleeding stops. An improved method is to incise the small piece of skin that protrudes through a hole with a sharp razor. By this method, averages normal bleeding time is 3 mins. 25 secs., and abnormal figures provide valuable information in differential diagnosis.

Bile pigments formed from the disintegration of erythrocytes may be present in the blood stream as iron-free bilirubin and its derivatives urobilin and urobilogen. Van den Bergh's reaction determines the amount of bilirubinaemia from haemolysis as apposed to that caused by bile obstruction.

Haemoglobin compounds are detected by the spectroscope.

Haemorrhage. (1)

Post-operative primary haemorrhage is always a likely complication of oral surgical procedures. It is important to appreciate the different causes of primary haemorrhage.

Chapter II Cont'd.Haemorrhage Cont'd.

Arterial haemorrhage is recognised by a spurting of bright red blood, venous bleeding by a strong even flow of darker blood, and capillary ooze is continuous and slow.

Accepted methods of control are by suturing to approximate the edges of the wound. Gelatin foam, oxidised cellulose gauze, adrenalin gauze (not absorbable); spider web, phenacetin, tannic acid powder, Ferri perchloride, 1-2% human fibrinogen, human fibrin foam, human thrombin and hydrogen peroxide are now tried and proved in arresting bleeding. Coagulation is assisted by having the patient close on a sterile gauze pad, preventing movement of the blood and enabling fibrin to be formed. Irrigation of the mouth with normal saline is inadvisable until shrinkage of the clot has been effected.

The use of a haemostatic starch-terramycin sponge and powder is reported by Peter J. Diconza to give favourable results. ⁽²⁾ Tyler, stating that a heparin-like substance in the blood may cause haemorrhages where blood counts are normal used toluidine blue with success in seventeen cases. ⁽³⁾ The therapy is indicated where protamine-titration shows the presence of heparin type substances in blood with a normal microscope picture.

A preliminary investigation reveals that a useful new haemostatic may have been found in adrenosen salicylate, which is administered by injecting 5 mg. intra-muscularly every two hours, or taken orally, 1-5 mg. every three hours. ⁽⁴⁾ Prepared from a derivative of adrenochrome, menosemicarbazone combined sodium salicylate, it does not effect the blood pressure or pulse rate as adrenalin does. It appears that the haemostatic will be most useful in prophylaxis and treatment of bleeding due to increased capillary permeability.

Vitamin K is naturally synthesised by the intestinal flora and absorbed with fat. Essential to the formation of prothrombin in the liver, it may be deficient in obstructive jaundice, other liver damage, haemorrhagic diathesis, sprue, idiopathic steatorrhea and melaena neonatorum; its use is indicated where the prothrombin time is increased. ⁽⁵⁾⁽⁶⁾⁽⁷⁾ Vitamin K, available as methyl-naphthaquinone ('Prokayvit,' 1-5mg. intra-venously)

Chapter 11 Cont'd.Haemorrhage Cont'd.

muscular injections), and as acetoethylnaphthaquinone ('Kapilon,' orally 2 - 10 mg., 24-48 hours pre-operatively) is useful only in those cases where prothrombin deficiency is due to faulty absorption from the intestines. In a recent case, the writer found an intravenous injection of natural Vitamin K₁ successful when the ordinary preparation had failed. Other vitamin deficiencies related to abnormal bleeding are discussed under "Nutrition" and "Anemias."

Calcium Chloride and hydrated Calcium Chloride (10-30gr. orally), Calcium gluconate (15 -60 gr. orally or 10 - 30 ml. by injection) and calcium lactate (15 -60 gr. orally) all t.i.d., have been used because calcium is essential to clotting.

Dextran and plasmosan are plasma substitutes, which when given intravenously have no ill effect on the circulating blood, though it should be noted that dextran upsets the blood grouping of the patient. They may be used after severe haemorrhage where whole blood is not available, restricting the dose to less than two litres to avoid replacing too many normal plasma colloids with synthetic molecules.

When heparin, dicoumarol and ethyl ^{biscoumaacetate} have been used in the treatment of embolic complications and for patients long confined to bed, oral surgical procedures should not be carried out unless administration of these drugs has been discontinued for five days. (8)

Secondary Haemorrhage.

When wounds are infected, lytic softening of the vessel walls may occur to produce secondary haemorrhage. This usually occurs two days or more following surgery. Antibiotic therapy should be used in conjunction with astringents and haemostatics. Caution of bleeding points is often successful. Bleeding which occurs soon may be due to rapidly developing infections, systemic disease (outlined in following chapter), ligatures and sutures slipping, loose sharp pieces of bone and surgery performed on inflamed or neoplastic tissue. A soft high protein diet supplemented with iron, fluids fortified with glucose given in bulk, and ascorbic acid should be taken. It is vital to control

Chapter 11. Cont'd.Secondary Haemorrhage.

bleeding associated with shock. (See "Shock.")

Intravenous Transfusion. (8,9)

In shock, haemorrhagic anaemias and following severe haemorrhage it may be necessary to restore depleted blood volume by transfusing isotonic solutions of saline or dextrose, sodium chloride, or sodium lactate, stored whole blood, blood serum, citrated plasma or dried plasma to which distilled water has been added. The necessity for transfusion will be indicated by pallor, dyspnoea and a feeble pulse. In small children and the debilitated, a condition of irreversible shock occurs more readily, and it is best not to delay transfusion too long.

Whole blood which is most likely to replace a natural deficiency is best used in cases of severe haemorrhage. In this case it is essential to establish that the donors and recipients blood are compatible. The four main blood groups are based on the agglutinin content of the red cells and the agglutinin present in the serum. In Landsteiner's classification the groups are named, AB, A, B and O whilst in Moss' system the corresponding groups are designated; 1,2,3 and 4. In this country it is customary to give both figures: eg. O 4 the "universal donor, and A B, 1 the universal recipient. In addition about 15% of the people are Rhesus negative, and these people should not be transfused with blood from Rh⁺ donors. As minor sub groups exist it is wiser to cross-match before transfusing. Blood of group AB contains agglutinin in the serum; A has serum agglutinin B; B contains X and O.

Stored blood contains an anti-coagulant such as trisodium citrate which may somewhat diminish its value in controlling haemorrhage. Fresh whole blood is therefore preferable, but its use in transfusion requires a great deal of skill. The injection of 10cc of fresh whole blood intramuscularly is often very effective. It is best stored at 4° - 6°C. and if allowed to freeze, auto-agglutinins cause clotting. Transfusions are carried out at the rate of 20 - 40 drops per minute, this is increased to 60 drops per minute in Haemorrhagic crisis.

The donor should always be a healthy person free of syphilis,

Chapter 11 Cont'd.Intravenous Transfusion. Cont'd.

and any contamination of blood during storage or transfusion produces acute toxæmia.

The amount of transfused blood should be limited at least to one half a pint in excess of the amount lost to avoid overloading the circulation, which may cause heart failure or recurrence of hæmorrhage due to increased pressure. Severe reactions, usually fatal, follow the use of incompatible blood. Milder reactions due to auto-agglutinins, the use of universal donor blood, infected, old or improperly stored blood may occur. In about 1% of cases, allergic reactions, caused by sensitivity to plasma proteins occur. It is possible that there reactions may be avoided by the donor fasting for some time before giving blood.

Owing to the possible complications arising from transfusions, it is well to avoid them by having proper preoperative blood tests and carrying out good surgical techniques. However, transfusions have saved many lives and in doubtful cases, there should be no delay in supplying additional fluid to the blood.

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PART 11.CHAPTER 111.ORAL SIGNS OF THE DISEASES OF THE BLOODIntroduction: CLASSIFICATION OF DISEASES OF THE BLOOD

In this chapter those disorders involving changes in the corpuscular elements of the blood are considered in relation to their effect on the oral cavity.

"Anaemia is a pathological state in which the quality or quantity of the circulating red cells is reduced below the normal level."⁽¹⁾ Most anaemias are secondary to a deficiency or pathological state and can themselves lead to other disease processes. Many methods of classifying anaemias have been used, but the classification according to the cause is the most desirable. Throughout this review, an attempt is made to name and classify conditions according to aetiology. On the following page is a satisfactory classification used by Whitby and Britton.

Deficiencies of iron, copper, the haemopoietic principle of raw liver, vitamins, internal secretions (thyroxin) protein intake, protein absorption and metabolism may lead to dyshaemopoiesis.

In haemolytic anaemias there is excessive intravascular destruction of red cells by infections, poisons or inherent abnormalities. Classifications according to cell size and count are still widely used. They are: macrocytic, normocytic, simple microcytic and hypochromic microcytic.

When there is abnormal proliferation of leucopoietic tissue pouring large numbers of mature and immature leucocytes into the blood stream and tissues, the condition is called leukaemia. Probably neoplastic, but possibly caused by infection, leukaemias are classified according to the predominating cell in the blood stream. Where there are large numbers of primitive leucocytes, without an overall leucocytosis the term aleukaemic leukaemia is used. When myeloid tissue is affected myeloid leukaemia describes the condition.

CLASSIFICATION OF ANAEMIAS.

(Whitby & Britten.)

<u>GROUP.</u>	<u>SUB-GROUP.</u>	<u>DISEASE.</u>	<u>AETIOLOGY.</u>	<u>MORPHOLOGICAL CLASSIFICATION.</u> (based on M.C.V. & M.C.H.C.)
		Idiopathic hypochromic anaemia. Chlorosis. Nutritional anaemia of infancy.	Deficiency of iron.	Hypochromic microcytic.
		Pernicious anaemia. Tropical Nutritional anaemia. Diphyllobothrium latum infection.	Deficiency of haemopoietic principle.	Normochromic macrocytic or Hypochromic macrocytic.
	Deficiency.	Anaemias of pregnancy. Sprue. Idiopathic Steatorrhoea. Gastric Carcinoma. Gastro-intestinal operations. Gastro-intestinal fistulae. Cirrhosis of the liver, yellow atrophy. (subacute.)	Deficiency of a. Iron. b. Haemopoietic principle or both. Failure to store haemopoietic principle.	If (a) Hypochromic. Usually normocytic. May be microcytic. If (b) Normochromic or hypochromic and macrocytic.
Dyshaemopoietic		Scurvy. Pellagra.	Deficiency of Vit. C. " " P.P. factor.	Hypochromic or normochromic. Normocytic or microcytic often macrocytic.
		Myxoedema Thyrotoxicosis	Deficiency of Thyroxin.	Hypochromic or normochromic. Normocytic, microcytic or macrocytic.
Toxic.		Syphilis and chronic infections. Sepsis. Chemical poisons. Nephritis. X-rays and Radium.	Marrow unable to utilize haematinics.	Usually normochromic and microcytic. May be hypochromic.
		Leukaemia Lymphadenoma (of marrow) Malignant disease		

CLASSIFICATION OF THE ANAEMIAS. CONT'D.

GROUP.	SUB-GROUP.	DISEASE.	ÆTIOLOGY.	MORPHOLOGICAL CLASSIFICATION. (Based on H.C.V. and H.C.H.C.)
	Metabolic.	Osteosclerosis.	Unknown. probably general metabolic or nutritional disease.	Hypochromic. Normocytic.
	Dyshaemopoietic	Primary aplastic anaemia.	Unknown. ? Deficiency.	Normochromic. Normocytic.
	Ineffect- ive.	Malaria. Oroya Fever. Cl. welchii.	Haemolytic parasite.	Hypochromic or Normochromic. Normocytic or macrocytic.
	Toxic.	Lederer's Anaemia and other Idio- pathic haemolytic anaemias.	Unknown.	Hypochromic or normochromic. Normocytic or macrocytic.
		Lead and other chemicals.	Direct action on cells and marrow. Often partly dy- shaemopoietic.	Hypochromic. Normocytic or microcytic.
Haemolytic .		Acholia jaundice. Sickle-cell anaemia. Mediterranean anaemia.	Congenital defect in red cells.	Hypochromic or normochromic. Microcytic, but normal volume.
	Intrinsic.	Peroxydase hae- moglobinuria.	Haemolysin.	Hypochromic or Normochromic. Normocytic or Macrocytic.
	Extrinsic.	Erythroblastic anaemias of the newborn.	Acquired Maternal haemolysin.	Hypochromic or normochromic. Normocytic, rarely macrocytic.
		Acute haemorrhage.	Injury.	Normochromic. Normocytic.
		Chronic haemorrhage.	Injury.	Hypochromic. Normocytic or Microcytic.
Haemorrhagic.		Haemophilia Essential thrombocytopenic purpura.	Abnormality of the blood.	As in acute or chronic haemorrhage.

Chapter III. Cont'd.CLASSIFICATION.

- | | | | | |
|----|-----------|--------------------------------|-------|----------|
| 1. | Myeloid | Leukaemia | Acute | Chronic. |
| 2. | Lymphatic | Leukaemia | Acute | Chronic. |
| 3. | Monocytic | Leukaemia | Acute | Chronic. |
| 4. | Atypical | Leukaemia and allied diseases. | | |

- a. Aleukemic Leukaemia.
- b. Eosinophilic Leukaemia.
- c. Neutrophilic Leukaemia.
- d. Basophilic Leukaemia.
- e. Megakaryocytic Leukaemia.
- f. Leukanaemia.
- g. Leukosarcoma.
- h. Chloroma.
- i. Mixed Leukaemias.
- j. Mikulicz's Syndrome.
- k. Leukaemic erythrodermia.

5. Leukemoid blood pictures.

- a. from infection.
- b. Leuco-erythroblastic anaemia from bone-marrow disease,

such as :-

- Myeloma.
- Carcinoma.
- Osteosclerosis.

Chapter III. Cont'd.

1. The purpuric and Haemorrhagic Diseases.

In the control of spontaneous and post-operative haemorrhage, the purpuric and haemorrhagic blood disorders must be considered when making a differential diagnosis. Ideally, blood tests should be carried out before surgical procedures: certainly it is essential where there is a previous history of abnormal bleeding.

Whitby and Britton's classification is based on the deficiency causing the abnormality and is an excellent one to follow:-

A. Purpuras showing quantitative deficiency in Platelets.

1. Essential Thrombocytopenia (Purpura Haemorrhagica.)

2. Symptomatic Thrombocytopenia.

a. Bone marrow defect.

Pernicious anaemia.

Aplastic Anaemia.

Leukaemia.

Multiple bone marrow metastases.

Poisoning from benzol, N.A.B. and metals

Malignant diseases with cohexia.

Kray and radium poisoning.

Fevers in acute stage, especially typhus.

b. Splenic defects.

Banti's disease.

Gaucher's disease.

Felty's syndrome.

B. Purpuras with Slight or no Deficiency in Platelets. (Vascular factors involved.)

1. Anaphylactoid Purpuras.

Purpura Simplex.

Henoch's Purpura.

Schönleins Purpura.

Allergic purpura.

2. Purpura Fulminans.

3. Simple Symptomatic Purpura.

Chapter 111. Cont'd.Purpuras with slight or no deficiency in platelets. Cont'd.

a. Fevers (Platelets often diminished in Acute Stage.)

Typhoid.

Endocarditis lenta.

Influenza.

Scarlet fever.

Nephritis.

Cerebro-spinal meningitis.

b. Toxic

Snake venom.

Drugs such as Copaiba, Bellodonna, Quinine.

c. Miscellaneous.

Avitaminosis and Scurvy.

Mechanical constriction.

Convulsions.

C. Haemorrhagic Conditions with a possible Qualitative Platelet Deficiency.

a. Haemophilia. —

b. Hereditary Haemorrhagic Thrombasthenia (Glanzmann).

c. Constitutional Thrombopathy (van Willebrand)

D. Haemorrhagic Conditions due to Deficiency of Prothrombin.

a. Lack of Vitamin K.

Haemorrhagic disease of the new born.

Obstructive Jaundice.

Biliary Fistula.

Sprue and allied conditions.

b. Liver damage.

Poisoning from Anaesthetic, phosphorus and arsenic.

Acute yellow atrophy.

Atrophic cirrhosis.

Infiltration with malignant cells.

c. Ideopathic Hypoprothrombinaemia.

d. Administration of Dicoumarin.

E. Rarer Haemorrhagic Conditions.

Chapter III. Cont'd.E. Rarer Haemorrhagic Conditions.

- a. Hereditary Haemorrhagic Telangiectasia.
- b. David's disease.
- c. Haemorrhagic Thrombocythæmia.
- d. Congenital and acquired Fibrinopenia.

Essential Thrombocytopenia (Syn: Purpura Haemorrhagica, Werlhof's disease,
Primary Thrombocytopenic, Purpura Haemorrhagica.)

Ætiology:— not certain, possibly infection.

Symptoms: Acute form, rare.

Sudden onset purpuric spots on skin and mucous membranes —
haemorrhages from mucous membranes especially the nose — excessive bleeding
or hæmatoma from trifling injuries — ecchymoses from light blows over
bony prominences — platelets greatly decreased. (20,000 or less) —
bleeding time prolonged. Coagulation time, blood calcium and fibrinogen
normal — markedly positive capillary resistance tests. May result in
death or more often progress to chronic form.

Chronic form: Usually first met with in childhood — persistent but
fluctuating thrombocytopenia with corresponding exacerbations of symptoms.

Capillary resistance tests may be positive at all times.

May be slight malaise, fever and chronic leg ulcers.

Pathology: Possible that the spleen liberates a substance, thrombocytopenin
which inhibits platelet formation.

As platelet reduction occurs in the absence of hæmorrhagic tendencies,
damaged or defective endothelial lining of blood vessels may be important.

Continuous hæmorrhage may lead to hypochromic anaemia — leucocytes
usually unaltered but may increase.

Treatment: Sometimes spontaneously disappears—

Control dangerous hæmorrhage by transfusion — preferably prior to
operation — fresh citrated blood satisfactory.

In chronic cases, splenectomy gives excellent results.

Vitamin C and D sometimes useful.

Chapter 111. Cont'd.

Calcium, liver extract of no value. It is essential that the dentist be familiar with disease and that he realises that no surgical procedure should be carried out without prior blood transfusion.

Two years ago the writer treated a girl, aged 8 years, in whom the first sign of the disease was persistent haemorrhage from hypertrophied gingival tissue in the carious cavity of an upper deciduous molar tooth. Some twelve hours later numerous purpuric spots appeared on the abdomen and limbs. It is interesting to note that the child apparently had measles a fortnight previously. The condition was treated with transfusions, and repeated blood tests since that date have been normal.

Symptomatic Thrombocytopenia.

From bone marrow defects:

In pernicious anaemia and leukaemia excessive erythroblastic or leucoblastic activity may restrict the activity of megakaryocytes and so reduce the platelet count. Metastatic bone deposits have a similar effect.

Platelet production is rapidly reduced in aplastic anaemia.

Xrays, radium, the toxins of acute fever, benzol, arsenic, sulphanilamide, silver and gold preparations all act on the megakaryocytes and reduce platelet formation. Probably the capillary endothelium is also affected.

From Splenic Defects:-

Splenic anaemia or Banti's disease is a chronic condition of unknown cause characterised by splenomegaly, hypochromic anaemia, with neutropenia and hepatic cirrhosis and ascites. Platelet deficiency may result.

Gaucher's disease is a rare familial and congenital disease, most commonly affecting female Jews, in which splenomegaly, hepatomegaly, leucopenia and hypochromic anaemia are characteristic. In the spleen, liver, lymph glands and bone marrow, are "foamy" cells of a distinctive Gaucher type 20 - 30u in size. Some of the cells are multinucleated, the nuclei being at the cell border and often pyknotic.

Chapter 111. Cont'd.

Purpura, haemorrhagic symptoms, gingivitis and epistaxis often occur due to platelet deficiency in the later stages of the disease. Actual bone changes are not common, but Xrays may reveal osteoporosis and thinning of the cortical bone. Spontaneous fractures may occur.

PURPURAS WITH SLIGHT OR NO PLATELET DEFICIENCY.Simple Symptomatic Purpura.

In early and acute febrile conditions there is a marked platelet deficiency due to toxæmia. Later stages of fever produce toxic degeneration of the vascular endothelium.

Allergic toxic reaction of the endothelium may be due to snake venom or drugs (ergot, iodine, phenobarbitols, belladonna and quinine) and the condition may simulate thrombocytopenia.

In simple symptomatic purpura, the main blood tests may give normal results.

Anaphylactoid purpuras.

Included under this heading are purpura simplex, Henoch's purpura, Schonleins disease, (purpura rheumatica) and allergic purpura. With these conditions the capillary endothelium is more permeable due to protein allergy (sometimes food).

Purpura Fulminans is a rapidly fatal purpuric condition which is rare and bleeding does not occur from mucous membranes.

HAEMORRHAGIC CONDITIONS DUE POSSIBLY TO A QUALITATIVE PLATELET DEFICIENCY.Haemophilia.

Haemophilia is a hereditary disease, manifesting itself only in males, but transmitted through females by a sex-linked recessive character. As pointed out by Whitby and Britton it is, according to the Mendelian theory of heredity, possible for a female haemophiliac to be born from the union of a male haemophiliac with a female carrying the recessive haemophilia gene. Merskey claims to have discovered two authentic cases in females.⁽²⁾ When it occurs, haemophilia is found usually in English or Teutonic races.

Chapter 111. Cont'd.

Clinical Signs:- Not evident at birth, but usually appearing at 2 - 3 years of age, there is a lifelong tendency to excessive haemorrhage. it is more difficult to control in early years. The essential characteristic is persistent haemorrhage from the most trivial injury. Bleeding into a joint, with peri-articular swelling is common. When effusions of blood or serum occur in the joints, subsequent resorption is often incomplete and fibrous adhesions with partial ankylosis may result. The gingiva and nasal mucosa are prone to haemorrhage. While epistaxis is characteristic, true purpuric spots are not seen.

Pathology:-

The corpuscular elements of the blood do not show any distinctive change, and there is usually no diminution in the number of platelets. Coagulation time is greatly prolonged and yet the bleeding time is normal. This apparent contradiction is due to the fact that the platelets are able to seal the single puncture made to determine bleeding time.

There is apparently, some deficiency in the quality of the platelets and that they fail to liberate thrombokinase. Birch showed that by damaging the platelets of a haemophiliac's blood, normal coagulation could be induced.⁽³⁾ It is probable that the study of platelets will not completely solve the mysteries of haemophilia. In 1939, Loznar and Taylor produced an euglobulin factor of human plasma, which encouraged coagulation of the blood in this condition. The 'antihaemophiliac' globulin evidently is thrombocytolytic.

Anaemia, secondary to haemorrhages occurs and coagulation time is sometimes almost normal after a bleeding attack.

Treatment:-

Immediate local treatment of a 'spontaneous' (probably from slight injury) consists of removing the blood clot, washing with hot water and applying normal blood on a tampon to the bleeding surface. Local application of prothrombin, plasma and thrombin, and fibrin foam are often effective. Transfusions of fresh whole blood, citrated blood or citrated plasma are usually effective.

Chapter III cont'd.

After numerous transfusions a refractory state often develops, probably due to the host developing an immunity against the introduced plasma globulin.

Prophylactic treatment prior to unavoidable exodontia or surgery, may consist of intramuscular injections of egg white, mucic acid derivatives or 10cc of fresh whole blood. Intravenous transfusion of blood or plasma are undoubtedly sound.

Nutritional factors are important, particular emphasis being placed on proteins, vitamins C and D. Since septic foci may interfere with nutrition, the treatment of infected teeth is important.

Tonio and other suggest the gradual avulsion of teeth using a series of small rubber bands. (3) He also described the use of a thromboplastic substance derived from the brains of cattle. Prefabricated, clear acrylic splints have been used to retain local haemostatics. The use of sutures is probably contra-indicated. (4)

Differential diagnosis is based on family history. In purpura the bleeding time is prolonged and the coagulation time normal. The reverse is true in haemophilia. Purpuric spots are not seen in this condition and a platelet count assists in distinguishing the diseases.

Hereditary Haemorrhagic Telangiectasia is a rare hereditary disease affecting both males and females usually between 20 and 30 years of age. The characteristic feature is epistaxis. Bleeding and coagulation times are normal.

Haemorrhagic Thrombocythemia is also a rare disease, but more likely to be noticed by the dentist as there are commonly haemorrhages from the mucous membranes. Usually affecting elderly people, there is an increase in platelet count. Coagulation time is normal, and the bleeding time may or may not be increased.

Hereditary Haemorrhagic Thrombasthenia and Constitutional Thrombopathy: Similar in nature, are also quite rare. Affecting males and females; the bleeding times is prolonged but coagulation time and platelet count are normal.

Chapter 111. Cont'd.

11. OTHER BLOOD DISORDERS AFFECTING THE ORAL CAVITY.

Idiopathic Hypochromic Anaemia.

This anaemia most commonly affects middle aged women, due to iron deficiency, insufficient absorption resulting from achlorhydria or repeated loss of iron in the red cells from menstruation and parturition. The bone marrow is normoblastic and hyperplastic, and the blood picture is microcytic and hypochromic.

To the dentist, the essential features are those of the Plummer-Vinson syndrome of glossitis, dysphagia and anaemia with mild neurological disturbances. The syndrome occurs in about 15% of the cases. Usually the glossitis is painless, but occasionally the affection is more severe, and shallow ulcers may form. The tongue often shows excessive hyperkeratinization and a rare complication is epithelioma of the tongue or pharynx.

Massive doses of iron are used in treating the condition.

Chlorosis.

Similar to idiopathic hypochromic anaemia, chlorosis affects younger females and glossitis is not commonly present.

Pernicious Anaemia (Addison's Anaemia; Biermer's anaemia.)

A disease of middle and old age, affecting both sexes. Pernicious anaemia must be considered because of its oral signs and also because of the care to be taken in the surgical treatment of affected patients.

Addison's anaemia is caused by a failure to elaborate the haemopoietic principle due to the absence of the intrinsic factor in the bowel. There is a megaloplastic degeneration of the bone marrow and the blood picture varies with the course of the disease, but very low red cell and haemoglobin counts are common. The most numerous cells are macrocytes, but microcytes are present (anicytosis). Varying numbers of polychromatic cells, stippled cells and reticulocytes are seen and in severe untreated cases haemoglobinized megaloblasts are present in the circulating blood. Other important pathological changes are fatty degeneration of the organs, especially the heart muscle; an increase in red marrow of the long bones.

Achlorhydria is almost always present and the colour index high due to an

Chapter III. Con't.

increase in the mean corpuscular volume. There is usually a neutropenia. In severe cases the platelets are decreased and the coagulation and bleeding times may be prolonged. There is a history of fatigue, digestive disturbances, palpitation, dizziness, paraesthesia and pallor is usual.

Of significance to the surgeon, are the mental changes, characterised by melancholia and paranoid delusions of persecution, which are fairly common.

A fiery red "beef-steak" tongue may be an early sign of the disease. Later the mucosa becomes smooth and atrophic. Fissures and ulcers may develop. In contrast to the usually painless glossitis of idiopathic hypochromic anaemia, a sore tongue is present in about 50% of the cases of pernicious anaemia. The symptom may wax and wane, and often precedes other signs of the disease. After each attack of glossitis the mucosa becomes smoother and denuded of more papillae.

Unless treated this anaemia is invariably fatal. Treatment consists of continuously supplying the lacking haemopoietic principle. Raw or lightly cooked liver, liver extracts or proteolysed liver must form part of the diet throughout life. Parenteral therapy using hepater or Bencard's liver extract is most successful.

When the patient's condition permits, septic foci must be removed, to avoid further nutritional disturbance. Before carrying out surgery the ^{cardio-}cardio-vascular condition should be estimated.

Large doses of Vitamin B complex and Vitamin C should supplement the diet. Recently, there have been references to the faulty absorption of Vitamin B₁₂, due to the lack of the intrinsic factor in the gastric juice. This may lead to the disturbances of the gastro-intestinal tract, bone marrow and central nervous system found in pernicious anaemia. Although of a different chemical nature to Vitamin B₁₂, and not deficient in this anaemia, oral administration of folic acid has been found to bring remission of the haematologic symptoms, but it fails to arrest the sub-acute spinal degeneration. The lack of intrinsic substance does not inhibit absorption of folic acid. (5) Evidence is mounting that vitamin B₁₂ is identical with the haematinic principle.

Chapter 111. Cont'd.SPRUE (PSILOSIS. COCHIN-CHINA DIARRHOEA.)

With the increase in air travel, it is possible that the oral surgeon may encounter cases of glossitis due to Sprue. Mainly confined to the tropics and sub-tropics, sprue is disease characterised by chronic diarrhoea, steatorrhoea, glossitis and anaemia. At first the anaemia is microcytic and hypochromic, later becoming macrocytic. The colour index is usually greater than one. Anicytosis is marked. Hypochlorhydria, rather than achlorhydria is usual. The presence of fat in the stools and the fact that the patient has probably visited the tropics help to differentiate the symptoms from those of pernicious anaemia.

Glossodynia and oral ulcerations may appear early in the course of the disease. The tongue is not coated, but may be inflamed, ulcerated, fissured or atrophic.

Aplastic Anaemia and Agranulcytic Angina.

An aplastic or hypoplastic condition of the bone marrow may inhibit the formation of one or more of the precursors of red cells, leucocytes or blood platelets. These hypoplastic conditions (true aplasia is rare) may exist where the primary division of primitive cells is at fault or where the lack of an essential factor or some inhibitory influence leads to defective maturation.

Aplastic Anaemia.

This anaemia may be idiopathic or symptomatic. In the idiopathic form the disease is most common in the young adult, and hypoplastic rather than aplastic bone marrow is found to exist. Symptomatic aplastic anaemia may be produced by certain poisons, most commonly benzol, but also arsenical compounds, X-ray and radium effects and also bacterial toxins (especially in children). The disease may be secondary to pernicious anaemia or be due to tissue replacement in leukaemias, multiple myeloma of the bone, Ewing's sarcoma, carcinomatous deposits and osteosclerosis.

There is a progressive anaemia, but the blood cells that do appear are normal in shape, size and staining. Haematinics do not improve the condition. Early oral signs are seen as haemorrhages from the gums. Later, due to platelet deficiency there may be purpura and if the number of

neutrophils decrease necrotic ulcers of the mouth and gastro-intestinal tract occur.

The bone marrow is watery and fatty; -- agranulocytosis, and thrombocytopenia may be as marked as the erythrocytopenia. The progressive fall in red cell count is due not to haemolysis, but to a failure to replace naturally worn-out cells.

Repeated blood transfusions and sternal marrow transfusions are used in treating the condition and the prognosis is better in the symptomatic forms if the cause can be found.

AGRANULOCYTIC ANGINA (AGRANULOCYTOSIS. GRANULOCYTOPENIA, MALIGNANT NEUTROPENIA, AGRANULAEMIA, GRANULOPHTHISIS, ALEUKIA.

Not only the oral surgeon but the general practitioner in dentistry should be familiar with this serious disease. It is important because oral manifestations are marked, because amidopyrine (amino Pyrine) which may be included in proprietary sedatives is a common cause, and because it is often professional people engaged in roentgenology who are affected.

The essential clinical features of the disease are severe diminution or absence of the cells of the myeloid series and necrotic ulcerations, particularly of the mouth. The necrotic lesions in the oral cavity are usually the first and sometimes the only sign of the disease.⁽⁶⁾

Aetiology: Occuring most commonly between 40 and 60 years of age, the condition has been diagnosed in people of all ages. Females are more susceptible than males.

Probably the condition is primarily a disease of the myeloid tissue in the bone marrow and the resultant leucopenia causes the necrotic ulcerations due to a lower resistance against bacterial invasion.

Polymorphonuclear Leucocytes are formed extravascularly in the bone marrow, and enter the circulation by their active amoeboid movements.

Nucleic Acid^d and its cleavage products adenine and guanine appear to stimulate the maturation and movement of the leucocytes. These products are released in the breakdown of senile leucocytes. Like aplastic anaemia, the disease exists in idiopathic form but it is usually the result of sensitivity to drugs and poisons, Xrays and radium or from severe infections.

Chapter III. Cont'd.

In the light of present knowledge, an acceptable theory for idiopathic agranulocytosis is a lack of the substances pentose nucleotide or reduced glutathione which are necessary to stimulate the production and maturation of polymorphonuclear leucocytes.

Post-mortem examinations reveal that the disease may be aplastic or due to fault granulocyte maturation where faulty maturation of leucocytes is the cause, the bone marrow may actually be hyperplastic and a normal number of myeloblasts and myelocytes are present. In this form of the disease, treatment with nucleic acid or its derivatives is likely to be more successful.

The condition may present as a complication in diseases causing damage to the bone marrow.

Aetiologically the disease may be related to the administration or taking of amino-pyrene, barbiturates, sulphonamide drugs, neorarsphenamine, gold preparations, dinitro phenol ("slimming" drug), benzol, trinitrotoluene thiouracil, bismuth, mustard gas and quinine. Drugs of the aminopyrene group, especially when a barbiturate is used as an adjuvant, are most often found to be a causative agent in individuals who have become sensitized. It is not clear whether barbiturates used alone will destroy granulocytes in sensitized individuals.

Even in normal persons, sulphonamide drugs will frequently cause a reduction in the leucocyte count. There are many reports to hand of agranulocytosis due to sulphapyridine, sulphathiazole, sulphadiazine and especially sulphonilamide.

Xrays and radium in excessive doses, aplastic anaemia, aleukaemic leukaemia and lymphadenoma (where Xray therapy is used) may cause agranulocytosis.

Infections reported to cause agranulocytosis are osteomyelitis, Vincents infection, hepatic abscesses, pneumonia, renal disease and septicaemia. The disease has been known to follow dental extractions. Other infections less commonly associated in aetiology are typhus, typhoid, malaria, mumps, measles, influenza, dengue and kala-azar.

Pathology: Necrotic lesions occur anywhere in the alimentary tract, especially in the mouth and pharynx. Necrosis may occur also in the

Chapter III. Cont'd.

conjunctival sac and vagina. In the aplastic type, cells of the myeloid series may be completely absent, but in the maturation type of the disease myleocytes are present without mature polymorphonuclears being seen.

If death occurs rapidly, there will be no change in the red cell count, but in more chronic cases, anaemia with a low erythrocyte count and a normal colour index will develop. The total leucocyte count is almost always below 2,500 per mm^3 and may be much lower. If the count is in excess of 4,000 per mm^3 it can be taken that the condition is not idiopathic but secondary. The leucopenia is essentially due to a deficiency of granulocytes, but if an absolute count is made, a decrease or increase in the number of lymphocytes and monocytes is sometimes found. Occasionally, in agranulocytosis, the coagulation time may be prolonged.

Due to the low resistance to infection, numerous organisms are isolated from the necrotic lesions. Streptococci and *treponema* Vincenti are especially common.

Agranulocytosis may terminate in pneumonia. In the acute forms of the disease the temperature may be as high as 106°F , but in chronic agranulocytosis the usual range is from 98° — 100°F .

Whitby and Britton report five clinical types of the condition (according to Beak):-

1. Fulminating: acute, rapidly fatal.
2. Sub-acute: lasting 1-3 weeks, with many cases recovering.
3. Recurring or relapsing: death in any attack — sometimes recovery.
4. Sub chronic: slight insidious onset — lasting a year or more — recovery usual.
5. Cyclical: often associated with menstruation.

Diagnosis: As favourable prognosis depends on early diagnosis, blood tests should be made for all necrotic oral and pharyngeal lesion. The oral signs together with the blood picture are diagnostic (cf. aplastic anaemia where all blood cells are reduced.)

Treatment: 0.7 gms of pentnucleotide are injected twice daily to stimulate polymorphonuclear maturation. (7)

Chapter III. Cont'd.

In treating secondary types of granulocytopenia it is important to find and if possible eliminate the cause. The only justification for blood transfusion is that nucleotides from the breakdown of introduced polymorphonuclears may stimulate white cell production in the bone marrow. Some success has been attained in the use of liver extract. Irradiation may help in treating the hyperplastic maturation forms of the disease.

The Leukaemias.

As with agranulocytic angina, the first signs of leukaemia may appear in the mouth and therefore these conditions are important to the dentist. A classification and definition of the leukaemias (leucoses) have already been given and it remains to describe these conditions.

Acute Myeloid Leukaemia. (Acute myeloblastic anaemia, Acute Myelosis.)

Mainly a disease of children and young adults, but occurring at any age, and affecting males more commonly than females, acute myeloid leukaemia is the most common acute leukaemia, but is not seen so frequently as chronic myeloid leukaemia. The characteristic feature is the large predominance of myeloblasts, whereas myelocytes are not so numerous as they are in the chronic form. In view of this, the synonym, acute myeloblastic leukaemia has merit and should be accepted to describe the condition.

Symptoms: Frequently the first sign of the disease is manifested as an oral or pharyngeal lesion. Pain in the back and limbs, fever, prostration and often a sore throat are characteristic symptoms in a sudden onset.

Due to a deficiency in the blood platelets, there is an increasing haemorrhagic tendency, and multiple haemorrhages in the retina, ear, spinal cord, uterus, kidney, bowel but especially ^{from} for the mucous membrane of the mouth are signs for strong suspicion.

In the same way as in agranulocytosis, the necrotic ulcerations of mucous membrane may be due to a deficiency of polymorphonuclear leucocytes.

Acute myeloblastic anaemia is characterised by a rapidly progressing ^{anaemia} anaemia and tenderness over the sternum and bones. If the disease lasts long enough, rarefaction of the bone is seen. Priapism, enlargement of the lymphatic glands, and splenomegaly occur less frequently than in chronic myeloid leukaemia.

Chapter 111. Cont'd.

Blood picture: The total leucocyte count, usually between 20,000 and 50,000 per c. mm may vary considerably from day to day and consists of 90% myeloblasts. The red cell count may fall to less than 1,000,000 per c.mm. and reticulocytes polychromatic cells and normoblasts are usually found. the anaemia is usually macrocytic and blood platelets are greatly reduced. Differential Diagnosis: In aplastic anaemia, there is not the evidence of red blood cell regeneration and in distinguishing glandular fever a sternal puncture may facilitate diagnosis. Even in the severest forms of glandular fever, significant anaemia is not present. (7)

Prognosis: The condition is fatal, usually within a few days.

Transfusions may delay the inevitable outcome.

CHRONIC MYELOID LEUKAEMIA (SPENOMEDULIARY LEUKAEMIA, CHRONIC MYELOSIS.)

Chronic myeloid leukaemia usually occurs at a later age than the acute disease, and is most common between 30-50 years of age. Rarely occurring before the age of twenty, about 60% of those affected are males.

Symptoms.

Very early symptoms of fatigue, dyspnoea and pallor are features of an insidious onset. The spleen is enlarged, and nodules due to infarcts may be palpated. Pressure effects cause gastro-intestinal disturbances, diarrhoea and vomiting; progressive anaemia results in myocardial symptoms, and there may be tenderness on percussion over the sternum. In women amenorrhoea is common. One of the earliest signs in men is priapism. Haemorrhages occur in the later stages, but purpura is less common. The oral signs are not so dramatic as in acute leukaemia, but gingivitis stomatitis and pharyngitis occur. Frequently there is an isolated painful swelling about one tooth, usually a becuspide or molar. Healing after simple exodontia is often greatly retarded. Haemorrhages into the semicircular canals may cause tinnitus, vertigo and deafness.

Blood changes.

An extremely high leucocyte count of from 250,000 to 750,000 per c.mm is the essential feature. Cells of the granular series constitute 90% of the white cells, there being giant and dwarf forms of polymorphonuclear cell;

Chapter III. Cont'd.

15 — 50% of the cells are myelocytes and this is the diagnostic criterion. Most of the myelocytes are neutrophilia. A much lesser number of myeloblasts are present. Both myelocytes and myeloblasts are present. Both myelocytes and myeloblasts divide in the peripheral circulation.

Occasionally there is a polycythemia in the early stages of the disease, but anaemia soon develops. In the final stages of the disease the anaemia is severe, and is usually of the hypochromic normocytic type, although macrocytic and aplastic forms are seen. At first the platelet count rises, but as the disease progresses the number decreases and may be less than normal.

Pathology:

In all the long bones, the yellow fatty marrow is replaced by greyish-red tissue. Owing to the leucoblastic actions there may be a purulent appearance. In addition to the myeloid elements, megakaryocytes are numerous, and islets of erythropoietic foci are present. The spleen is greatly enlarged, and contains white infarcts. The liver also is greatly enlarged but to a lesser extent. Its tissue is pale when cut. There may be some enlargement of the lymph glands.

Prognosis and Treatment:

The disease is progressive and is usually fatal within six years. Irradiation is the most effective form of treatment, and its mode of action may be the destruction of mitotic cells. Arsenic, taken in the form of Fowler's solution often gives good palliative results.

ACUTE LYMPHATIC LEUKAEMIA. is a rare disease in which the total leucocyte count (which varies greatly) consists of 99% lymphocytes, cells mostly lymphoblasts. The platelets are greatly reduced and purpuric symptoms in any part of the body are marked. ^{Stomatitis} Stomatitis with necrotic ulceration of the fauces and a rapidly progressive anaemia are present.

Death rapidly occurs.

Differential diagnosis; In agranulocytosis the lymphocytes are more mature; mononucleosis has less severe oral signs and there is no anaemia. Essential thrombocytopaenia is distinguished by the fact there is increase in lymphocytes.

Chapter III. Cont'd.

CHRONIC LYMPHATIC LEUKAEMIA (CHRONIC LYMPHADENOSIS.)

Less common than the myeloid leukaemias, chronic lymphatic leukaemia is most frequently seen in males from 45—60 years of age. Women of the same age group are affected less frequently.

Symptoms: The insidious onset of the disease is similar to that of chronic myeloid leukaemia, but in this condition, swelling of the lymph glands is usual and the lacrimal and salivary glands may enlarge simulating Mikulicz's syndrome. As with myeloid leukaemia there may be neurological lesions, gingivitis, abducens palsy and developing anaemia with haemorrhages. ^{Priapism} ~~Priapism~~ is rare in this condition.

Pathology: The lymph glands are discreet, painless firm and moderately enlarged and microscopically consist of masses of lymphocytes. The lymphatic tissues of the tongue, tonsils and pharynx are hypertrophic, the spleen, while enlarged, is not prominent as in myeloid leukaemia. Nodules may appear on the skin and tongue due to localised lymphoid masses. The bone marrow is grey red and extensively infiltrated with lymphocytes.

Blood picture: The total leucocyte count may be marked. 85% or more of the white cells are lymphocytes, which appear to be fragile because smear and basket cells are often seen. Excepting in the final stages, lymphoblasts are rarely seen. Because the bone marrow is not the original site of affection, anaemia is later developing and usually is mildly hypochromic with slight anicytosis and poikilocytosis.

Prognosis: The patient usually lives about three years and the treatment is much the same as for chronic myeloid leukaemia.

MONOCYTTIC LEUKAEMIA: Although rare is now recognised as a definite entity. The dentist should note that an extension of the oral lesions found in other types of leukaemia to the tonsils and soft palate may be important in differential diagnosis.

In monocytic leukaemia the total white cell count is usually lower (15,000 — 45,000 per cmm.) of which 50 — 90% may be monocytes. In the latter stages of the disease the monocytes are of a more primitive form, and the larger the cell, the more acute the disease.

A normochromic hypochromic anaemia is always present.

Chapter 111. Cont'd.ALEUKAEMIC LEUKAEMIAS.

When leukaemia is present without the pathognomic blood picture, the diagnosis may be extremely difficult. The term aleukaemic leukaemia is used where the peripheral white cell count is not abnormally high and yet there is a leukaemic infiltration in many organs. A leucopenia may even exist. In these cases a sternal marrow puncture may assist.

In acute aleukaemic conditions, primitive white cells are seen in the blood although the count is within normal limits. The spleen may be enlarged.

There is usually a generalised glandular enlargement in chronic aleukaemic leukaemia. In these cases a biopsy of an enlarged gland will assist diagnosis.

EOSINOPHILIC LEUKAEMIA, exists as a separate form, distinct from the appearance of large numbers of eosinophils which may appear in chronic myeloid leukaemia.

The leucocyte count is usually between 20,000 -- 80,000 per c.mm. of which 60 - 80% may be eosinophils. The spleen is enlarged, and the lymph glands may be palpable. The bone marrow is hyperplastic and contains excess eosinophils and their precursors.

Differential diagnosis: Eosinophilia may occur in Hodgkin's disease when the glands are enlarged, but here the eosinophilia is more constant and definite, whereas the cells in eosinophilic leukaemia vary in size and are usually very large.

LEUKANAEMIA is a term used to describe a condition where the blood picture suggests both pernicious anaemia and leukaemia. It is probably not a distinct clinical entity, and can be associated with neoplasms of the bone, ovary or breast.

CHLOROMA. is a rare leukaemia occurring in association with single or multiple green coloured tumours. These lesions are found on or in the bones of the skull and thorax and are usually subperiosteal, the orbit being the most common site. Chloromata may also be found in the soft tissues of the breast, kidney, liver and muscles. The green pigment is probably photo-porphyrin which fades on exposure to light.

Chapter III Cont'd.

The leukaemia is usually acute and in all other respects the disease is indistinguishable from acute myeloblastic anaemia.

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P A R T II.

CHAPTER IV.

DISEASES WHICH HAVE BEEN ATTRIBUTED TO THE LIPOID METABOLISM.

These are rare diseases, mainly affecting Jewish people⁽¹⁾ which are associated and probably due to a disordered lipid metabolism. Their exact aetiology is a fascinating subject of conjecture. Usually included in the group are Gaucher's disease, the Niemann -- Pick disease and Hand -- Schuller -- Christian's disease. A symptomatic group which are not more than manifestations of an upset lipid metabolism include, diabetes, chronic renal disease, and chronic jaundice.

HAND -- SCHULLER -- CHRISTIAN'S DISEASE. (Lipogranulomatosis.) (Seotosis, or Cholesterolosis.)

The disease which appears to be confined to males is congenital and familial and is most common among Jews, is stated by Whitby and Britton (op. cit.) to be due to a disturbance of the lipid metabolism. This theory is based on the appearance of lipoids in the bone marrow. Stone⁽²⁾ quotes another theory that inflammatory reactions due to infection cause the radiolucent areas and that the lesions in the first place are characterised by the presence of numerous histiocytes; the three conditions being merely different manifestations of an unknown basic disease with a predilection for the haemopoietic system.

Symptoms: Occurring usually in childhood or adolescence, the classical symptoms are: exophthalmos, bony defects and diabetes insipidus.

Frequently there are disturbances of growth, dyspnoea, cyanosis with moderate splenomegaly, hepatomegaly, and enlargement of the lymph glands. Usually there is a yellow discolouration of the skin. Thoma & Robinson,⁽³⁾ also mention gingivitis, cessation of growth (dwarfism) malnutrition, anaemia and adiposogenital dystrophy. They state the disturbed lipid metabolism leads to a storage of cholesterol in the cells of the liver, spleen, lymph nodes and bone marrow. The accumulated lipid material is associated with the formation of granulation tissue followed by fibrosis in the presence of cholesterol crystals.

Chapter IV. Cont'd.

The skull and the jaws frequently contain the bony lesions but they may occur in any of the bones especially the flat ones. The lesions commonly appear under the developing teeth causing displacement and ultimate exfoliation. When the lipoid granulomata occur in the orbit, they first cause exophthalmos, then invade the accessory sinuses, pushing up the base of the skull to press upon the pituitary body. Thus occurs the diabetes insipidus. All lesions, contain characteristic 'foam cells' storing cholesterol. These cells are derived from the reticulo-endothelial system.

When the bone marrow is extensively involved, secondary anaemia develops. Blood cholesterol is high.

The prognosis is grave but Stones (op. cit.) states that radiotherapy checks the course of the disease. Dealy and Sosman⁽⁴⁾ report that small doses only (200 - 250 kilovolt with medium filtration) are necessary to bring remission. Because of the small dosage, they are able to use radiotherapy again when necessary.

EOSINOPHILIC GRANULOMA OF THE BONE.

This is a benign, self limiting osteolytic process appearing as haemorrhagic or cystic areas containing some granulation tissue. There is a predominance of eosinophils and histiocytes. The lesions are round or oval areas which perforate the cortex and when occurring in the jaws cause pronounced resorption of the tissue. The histiocytes are phagocytic and may contain ingested debris. In addition to involving the bones the granulomata may appear in the skin, lungs and reticulo-endothelial system. When multiple the Xray picture of the bones resembles Hand - Schuller - Christian's disease. It could be that there is a relationship between these granulomata and lipogranulomatosis analogous that exists between hyperparathyroidism and osteoclastomata.

In treatment curettage, supplemented by radio therapy is effective.

Chapter 1M. Cont'd.LETTERER - SIWE'S Disease - (non - lipoid histiocytosis.)

This disease is apparently a more highly malignant variant of Hand-Schiller-Christian's disease. Occurring usually in infants before four years of age, the disease is characterised by a dispersion of histiocytes throughout the skeleton and nodular foci of these cells are found in the soft tissues (Stones, op. cit.) There is a predilection for the viscera.

The destructive lesions of the bone contain numerous eosinophils and in the later stages there is fibrosis with the histiocytes being replaced by 'lipophagic foam cells' (c.f. Hand - Schiller - Christian's disease). The course of the disease is acute or subacute and is usually fatal within a few months.

A severe secondary hypochromic anaemia with purpuric eruptions develops.

It is probable that the opinion held by Whitby and others that the above disease is due to lipoid disturbances was unfounded. The foam cells and lipoid deposits, however, are not fully explained. Shira (5) definitely classifies them as reticulo-endothelial disturbances.

GAUCHER'S DISEASE.

Gaucher's disease is extremely rare, is congenital and familial and presents with splenomegaly, hepatomegaly, leucopenia and hypochromic anaemia. At present, it is conceded that this is due to a disturbance of the lipoid metabolism.

More common in early life, Gaucher's disease may also occur in later years. Even though the spleen and liver are greatly enlarged, the symptoms are not marked excepting for a fever. Yellow-brown pigmentations of the skin appear early in the course of the condition and later as the anaemia develops there occur haemorrhagic symptoms of purpura, epistaxis and menorrhagia.

Bone lesions are not common, but when they occur, they contain typical Gaucher cells as do the liver and spleen. Kerasin, the phosphorus-free cerebroside, and haemosiderin collect in all organs.

In addition to the anaemia, there is a leucopenia; and death is usually due to infection. As with Hand - Schiller - Christian's disease, Jewish people are susceptible.

Chapter 13. Cont'd.

NIEMANN - PICK DISEASE.

Also a congenital familial disease mainly affecting Jewish people (females, in this case), this disease can probably be regarded as a true exanthema.

An early symptom is a loosening of the teeth with ulcerative gingivitis. There is a rapid enlargement of the spleen, exanthematous patches on the skin, oedema and bronchitis. The lymph glands are always enlarged.

There develops a mild hypochromic anaemia associated with a leucocytosis in which the white cells of all types contain large vacuoles of lipid material. The spleen, liver and lymph nodes contain diagnostic 'foam' cells which are different from Gaucher cells. — No keratin is present. There is a fatal termination before two years of age.

It is probable that the practising dentist will never see these conditions, yet they present an interesting study in physiology and pathology.

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PART II.CHAPTER V.NUTRITION.

A general outline of basic facts is first given:- This brief survey is in note form and provides a background for the later discussion of oral manifestation of nutritional deficiencies and the importance of diet in the surgical patient. "Human Nutrition," written by V. H. Mottram and published in 1948, by Edward Arnold & Co., London, being a concise analysis of post-war concepts in nutrition is the text surveyed.

Metabolism: changes in food after absorption.

Anabolism.: those changes in food which build up tissues.

Katabolism: those changes which result in breaking down food and tissue substances.

(Exogenous Katabolism changes in food.)
(Endogenous " " " tissue.)

Food: is any matter taken into the system to enable growth or maintenance of the organism.

Energy Production:	Growth and repair of tissues:	Trace elements
		which stimulate
		energy production
		or growth process.

Energy from -	{	Oxidation of Sugars, fats
		and amino acids.
		Measured in calories.

Building and Repair ----- minerals and proteins.

Catalysts for building and repair. ----- Hormones ----- Vitamins -- Trace elements.

Food may contain any or all of the following:-

1. Proteins.
2. Fats.
3. Carbohydrates.
4. Mineral Elements.
5. Vitamins.

Chapter V. Cont'd.

NUTRITION.CHART OF BASIC ESSENTIALS AND ELEMENTARY FACTS.

Purpose of Food	Their Chemical Nature.	Facts Obtained from:-
1. Energy Production.	Fats, Starches, Sugars, (lesser extent proteins.	Dripping, lard, Suet, margarine, Oils, Cereals, Sugar, Dried fruits, nuts and pulses.
2. Growth and Maintenance.	Mainly proteins. (lesser extent Ca, Fe.)	Milk, Eggs, Cheese, Fish and meat.
3. Control, Regulation and direction of the processes of the Body.	Mineral Elements, e.g. Ca, I ₂ , Fe, P ₄ and vitamins.	Dairy Foods, Certain fruits, Vegetables and fish fats.

CALORIES.

Measurement of energy produced by food.

It is the amount of heat energy which will warm one (1) litre of water through 1°C.

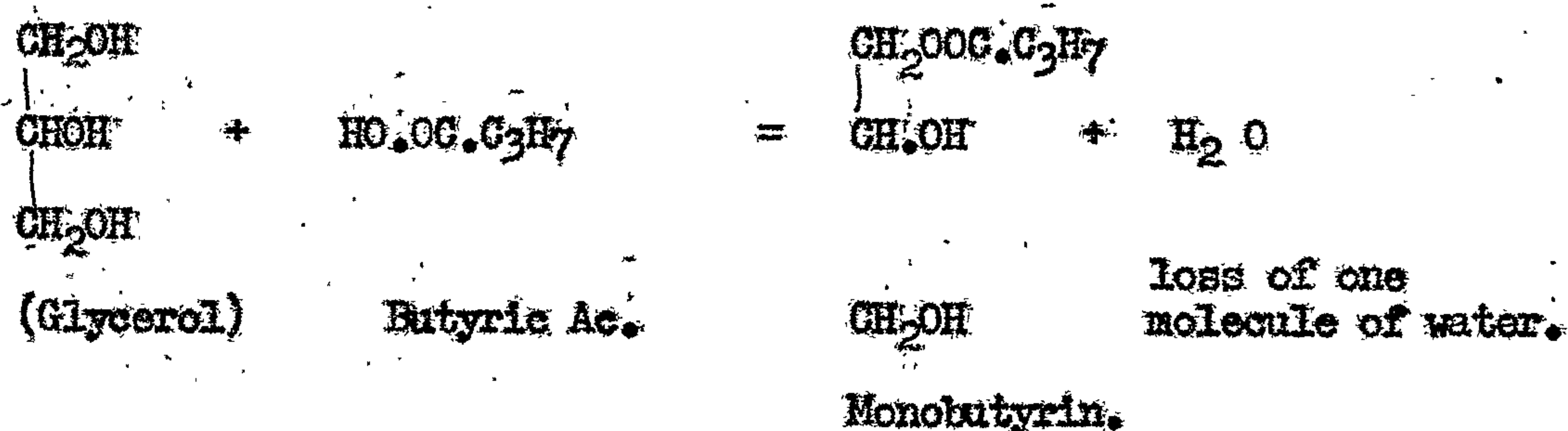
The heat the body gives out (daily) is measured in calories and the power of giving out heat by foods when consumed is given in calories.

The calories is a suitable measure of the mechanical work of the body because:

- (a). Conveniently sized units.
- (b). All body mechanical work is ultimately changed to heat.

Fats. Compounds of glycerol with Fatty Acids such as butyric, oleic, palmitic and stearic acids.

Typical formula:-



Fat $\longrightarrow$ rancid or digestion $\longrightarrow$ Glycerol and Fatty Acids.

Fat $\longrightarrow$ Heat and NaOH $\longrightarrow$ Glycerol and Soap.

Fats $\longrightarrow$ Oxidised in body. $\longrightarrow$ Heat 9.3 av. cals/gramme.

Chapter V. Cont'd.

Nutrition Cont'd.

Carbohydrates composed of C.H. & O: H:O = 2 : 1 always.

Nutritional C. OH: Sugars: Sucrose -- cane or beet.

Lactose -- milk.

Fructose -- fruit.

Glucose -- grape.

Starches: Cereals.

Pulses.

Potatoes.

Unripe bananas.

Negligible amounts in other vegetables.

Glycogen:

Glucose and Fructose in: Fruits

Some vegetables.

Honey and golden syrup

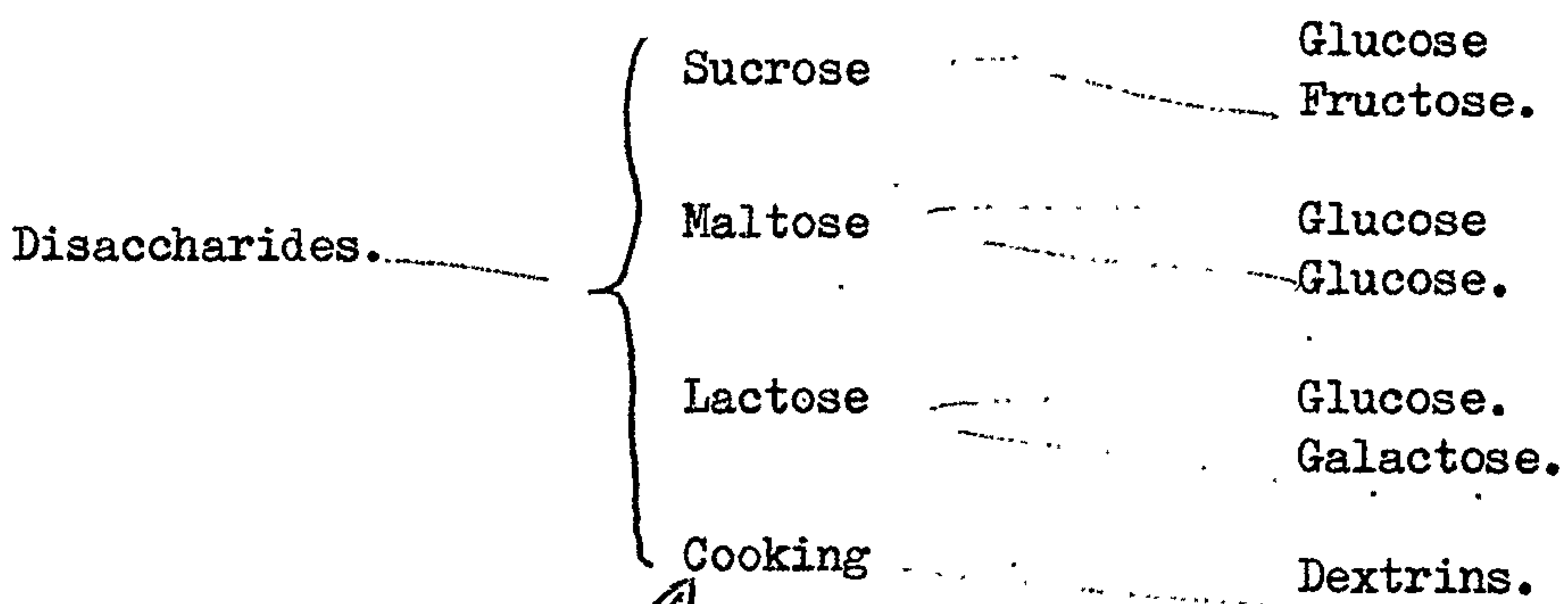
Some confectionary (commercial glucose.)

Lactose in: Milk.

Commercial lactose.

Maltose: Malts and its extracts.

All complex C.OH's must break down into simple sugars, (glucose, fructose or galactose) before utilised by the body. (Hexoses or monosaccharides with six chain C. Atoms.)



Polysaccharide -- Starch

Monosaccharides contain 3.75 cals/gramme.

Disaccharides " 3.95 cals/gramme.

Starch " 4.15 cals/gramme.

Average 4.1. for all C.OH's.

Protein yields 4.1 cals/gramme.

Chapter V. Cont'd.

Nutrition Cont'd.Calculation of Calories in Food Intake:

1. From Fats, C.H.N. and protein by weights of different foods.
2. From Respiratory Quotient — estimation of calories from oxygen intake and CO_2 output.

Scale of Calorie Needs.

			<u>CALORIES.</u>	
			Men.	Women.
Sedentary Occupation			2,500	2,100.
Moderately Active			3,000	2,500.
Very Active			4,000	3,000.
Children:	1 — 3 years		1,200	
	4 — 6 "		1,600	
	7 — 9 "		2,000	
	10 — 12 "		2,500	
Boys.	13 — 15		3,200	
"	16 — 18 "		3,800	
Girls.	13 — 15 "		2,800.	
	16 — 18 "		2,400.	

Dental Soft Diet following surgery 2,500 calories (1)

PROTEINS.

Proteins are of particular interest to the oral surgeon, being essential in the healing and repair of soft tissues and bone.

The molecules are composed of long ^{chains} chains of chemically united amino-acids (organic acids containing the group NH_2). In the stomach and intestines, digestive processes break down food proteins into their respective amino-acids, where they can be utilised by the body. Whole proteins, if they do enter the blood stream are toxic, producing protein shock. The digested amino-acids are reassembling in the body to build human body protein in growth and repair.

Essential amino-acids are, ^{arginine} arginine, ^{cystine} cystine, isoleucine, leucine, tyrosine, methionine, phenylalanine, threonine, tryptophane and valine.

Plant proteins, especially those in cereals, contain less of the

Chapter V. Cont'd.NUTRITION. CONT'D.

essential amino-acids than animal protein. Tryptophane and methionane have been shown to have special importance in growth, bone repair and post-operative repair and following burns. In these conditions the human mobilises ²⁹ a great deal of protein, and loses a great deal of nitrogenous material in the urine.

When the diet is low in protein, especially if tissue repair is taking place, there may be extensive damage to the liver. This can be obviated by supplying sufficient amounts of methionine, found in milk foods.

Depending on the type of amino-acid they contain, there is a considerable wastage of proteins. This is particularly so with animal proteins and is accentuated in ^{hot} that warm climate. The ingestion of carbohydrates at the same time as the protein is taken checks this wastage, that is, it prevents the liver from metabolising the amino-acids into glucose and fatty acids. If warm humid nights are experienced there should be less protein in the evening meal and the protein could then be of vegetarian source to minimise wastage.

The normal requirements of protein have been calculated at one gramme per kilogramme of body weight. An average of 60—70 grammes approx. 2½ oz. has been considered sufficient for the average adult. In childhood and adolescence, pregnancy and post-operative convalescence the requirements are higher. More than half of the required (37gms) amount should be first class protein (of animal source,) containing a preponderance of the amino-acids listed above.

Foods containing 37 grammes of animal protein:-

Cheddar, Cheddar.

4½ oz.

Eggs

5-6

Fish.

8-11 oz. Cooked 4½ oz. - 5½ oz.

Meats.

Bacon.

11½ oz.

Beef. Corned.

4½ oz.

Chicken.

8½ oz.

Ham Smoked.

9 oz.

Liver.

5½ oz.

Mutton.

6½ oz.

Pork.

7½ oz.

Milk.

1 Quart.

Fried. 3½ oz.

Roast 4½ oz.

Roast 4½ oz.

Chapter V.THE MINERAL ELEMENTS.Various Mineral Elements in the Body:-

	Total Body Content.	
Calcium	1,050	grammes.
Phosphorus	700	"
Potassium	245	"
Sulphur	175	"
Chlorine	105	"
Sodium	105	"
Magnesium	35	"
Iron	2.8	"
Manganese	0.21	"
Iodine	0.208	"
Cobalt	Trace	
Silicon	"	
Aluminium	More Trace	
Arsenic	"	"
Copper	"	"
Fluorine	"	"
Nickel	"	"

Most elements can be absorbed as salts but sulphur must be obtained in organic composition (e.g. from eggs and onions.)

THE TRACE ELEMENTS.

The elements found in traces, if they are essential to life at all, act only as catalysts. Copper, though it does not form part of haemoglobin is essential for its production. ⁽²⁾⁽³⁾ It appears to be mobilised in the blood, in pregnancy; in the liver and spleen of the foetus and generally assists in converting inorganic iron into haemoglobin. Cobalt is undoubtedly necessary to life in some animals and plants and traces are probably essential to man. Its value in treating anaemias is doubtful. (Whitby and Britton, op. cit.) but Dobbs (op. cit.) states that it is apparently necessary for the activity of Vitamin B12.

Chapter V. Cont'd.

Manganese in traces may be necessary in the production of sex hormones.

Fluorine has been the centre of attention in recent years in the study of preventive dentistry. Its important role in this sphere is not in the scope of this review, but it is worth mentioning that a significant reduction in the caries rate in the next generation would undoubtedly diminish the incidence of lesions concerning the oral surgeons. Fewer periapical infections would occur and a decrease in the number of edentulous patients should reduce the cases presenting with manifestations of nutritional deficiencies. Relevant too, is Foltman's report ⁽⁴⁾ which describes ^{es} one percent incidence of undesirable side effects from ^{apparently normal} fluorine therapy in 1100 cases. The side effects consisted of skin rashes, headaches and epigastric disturbances which disappeared when fluorides were withdrawn. The author repeats the suggestion formerly made that the trace element, fluorine, may inhibit thyroid function, accounting for late eruption of the dentitions. The oral surgeon should be aware of the signs of acute fluorine poisoning. At present there is on the market a preparation of tablets containing an optimum daily dosage of sodium fluoride. Cases of children locating and ingesting large number of these tablets may occur which would in a few hours cause dysphagia, vomiting, diarrhoea, cyanosis, pallor, pain in the limbs and cranial nerve palsies. ⁽⁵⁾ Courco, Collins and Crane ⁽⁶⁾ state, "A delayed effect is the production of tetany from its combination with calcium to form calcium fluoride. In fluoride poisoning, death may occur in a matter of minutes. ^{Gastric} Gastric lavage, calcium, glucose and saline intravenously are life saving."

Skeletal sclerosis, particularly affecting the ear bones, may result from dosages exceeding the optimum.

Of the other trace elements, zinc is worthy of mention being essential in the production of insulin.

The study of trace elements is fascinating and dentists, who have perhaps concentrated their attention on fluorine, begin to be aware of the wide ramifications which this study involves.

Chapter V. Cont'd.

CALCIUM AND PHOSPHORUS.

Of the remaining mineral elements calcium and phosphorus have the greatest significance in this review.

Calcium is of major importance in a number of bodily functions. It is essential in the formation of bones and teeth and consequently is important in post-operative diets; it plays a significant part in the conversion of prothrombin to thrombin; it is important in controlling muscular and nerve irritability; it may ^{diminish} ~~diminish~~ the permeability of cell membranes and decrease allergic manifestations.

The body contains more calcium than any other element. About 99% of the body calcium is stored in the hard tissues and in adults 9 to 11 mgs. are carried in every 100ccs. of blood. Variations in the latter have a diagnostic significance (vide chapter ^{VI}). The parathyroid glands control the metabolism of calcium and it is absorbed from the bowel as calcium chloride whatever its form in the diet. ^{Vitamin D,} ~~Vitamin D,~~ by increasing the acidity of the intestines, facilitates the conversion of calcium compounds to calcium chloride and is therefore an essential in their ingestion.

It is difficult to ponder the role of calcium in nutrition and metabolism without considering its partner phosphorus. Apart from the fact that this element is a constituent of the nucleoproteins and the phospholipines, phosphorus, elaborated as phosphate ions combined with calcium to form the carbonate apatite of bone. Jolly ⁽⁷⁾ described the possible mechanism of this process and outlined the part which alkaline phosphatase, liberated by the bone and cartilage cells, may play in precipitating this salt in the repair and formation of bone. Mottram (op. cit.) estimates the daily requirement of phosphorus as 1360 mgs. per day. It is contained in dairy foods, meat and fish and rarely is a diet deficient in the element. Page and Brooks ⁽⁸⁾ maintain that correct calcium phosphorus levels are disturbed by the ingestion of sugars; that excess calcium absorption over a long period may lead to the ^{formation} ~~formation~~ of arthritic deposits, cataracts, kidney stones and salivary calculus.

Chapter V. Cont'd.

^{Excess} while excess phosphorus may cause inflammatory lesions such as appendicitis and acute arthritis. Jenkins, (9) however states that serum calcium is remarkably constant and not materially affected by carbohydrate intake.

Rowe and Killey (10) suggest a ratio of two parts of phosphorus to one of ^{calcium} calcium-salts. Spinach which contains ^{oxalic} oxalic acid may form calcium oxalate while cereals ingested at the same time as calcium foods will cause the formation of insoluble calcium phytate. 600 mgs. of calcium should normally be ingested each day. Milk, eggs, greens and cheese are the most reliable sources, and a deficiency can occur. Such a deficiency is, if possible, best corrected by change in diet than by adding various compound preparations.

IRON:

This element is a component of haemoglobin, the blood pigment which transports oxygen. 95% of the body iron is contained in haemoglobin. The average normal ^{female} female contains 12.4 gms of iron per 100cc. of blood and the average adult 13.3 gms per 100c.c. This figure may be reduced in anaemias, and from post operative or menstrual haemorrhage. It is the duty of the oral surgeon to prescribe iron after severe haemorrhages to restore the haemoglobin to normal afterwards and to be alert for oral signs of the iron deficient anaemias.

IODINE.

Of certain significance is the element Iodine. A necessary constituent of thyroxin, the thyroid hormone. A low intake ^{causes} causes enlargement of the thyroid gland especially at puberty, pregnancy, lactation and menopause. Myxoedema and cretinism due to thyroid deficiency may be primarily caused by an insufficient iodine intake.

THE VITAMINS.

Catalysts are essential in the widely diverse processes of metabolism and catabolisms. Some are mineral elements which are present only in traces, some such as the hormones are complex organic compounds manufactured within the body; other, ^{exogenous} exogenous organic compounds acting in the body as catalysts are known as vitamins. Generally, they occur in the

Chapter V. Cont'd.

food already elaborated, but sometimes vitamin ^{precursors} precursors are contained in the diet and are known as provitamins.

The story of the discovery of vitamins is a fascinating one which has captured the public's imagination, so that many, without advice from their physician or dentist, artificially supplement their diet with these exogenous catalysts. Excepting possibly the excessive ingestion of A and D, the habit will do no harm.

When the role of catalytic substance was first discovered, they were given the name vitamins, that is an amine essential to life; but since all these compounds are not amines, the final 'e' has been dropped. As it became evident that there was more than one vitamin, each was distinguished by the use of a capital letter and the compound named for the function it performed. For example, the water soluble vitamin B was the 'anti-neuritic' vitamin. This original nomenclature has become unwieldy and as laboratory research is revealing the true composition of these compounds, more suitable modern names are evolving. The present period is transitional; for example the term 'ascorbic acid' is supplanting 'Vitamin C' although both names are still in use.

The quantities of vitamins required for the maintenance of good health have now been estimated but therapeutic doses of vitamins are administered in multiples of five to ten times the normal requirements. (11)

As stated in "Accepted Dental Remedies," (loc. cit.) lesions of the oral mucosa related to a prolonged inadequate supply of water soluble vitamins may occur in the absence of other recognised manifestations."

The same ^{article} ^{mentions} mentions the possibility of vitamin deficiency occurring as a result of poorly functioning dentures leading to an improper selection of diet.

AXEROPHTHOL - fat soluble Vitamin A; the anti-infective or anti-^{opthalmic} ophthalmic vitamin.

As a provitamin: ^{Carotene} Carotene α, β, γ , the yellow pigment of fruits, pumpkin, squash, carrots, oranges and green vegetables where chlorophyll masks the yellow colour.

Cryptoxanthin, the red colouring matter in cape gooseberries and

Chapter V. Cont'd.

papillae.

In the liver, the provitamins are changed to axerophthol, which is a pale yellow alcohol. Medina (12) states that the presence of some bile and a certain amount of fat are necessary for the proper absorption of provitamin A, while Mottram (op. cit.) warns that mineral oils, such as medicinal paraffin may dissolve the carotene substances and carry them through the bowel. It is usual to calculate that only one third of the provitamins will be absorbed and finally elaborated by the liver, which also stores the body reserves of Vitamin A. Dobbs (op. cit.) considers that thyroxine contributes in the conversion of provitamin A and that increased quantities of axerophthol are required in hypothyroid states.

Axerophthol itself occurs in fish liver oils, milk and eggs.

Unlike many of the other vitamins, axerophthol is still measured in the international unit which is the activity of 0.68% of B carotene.

The daily requirements for adults are 5,000 I.U., in pregnancy, 6,000, in nursing mothers 8,000 and in children 5,000 to 6,000 I.U.'s.

The effect of deficiencies:-

Night blindness: Because vitamin A is a constituent of visual purple, a deficiency causes defective vision in lights of low intensity.

Epithelial changes: The normal regeneration and resistance to infection of the epithelial surfaces depend on an adequate supply of axerophthol. In a deficiency, the eye shows marked manifestations, the tear glands losing their power of secretion resulting in xerophthalmia. Secondary infection then occurs easily and blindness may result. Medina (op. cit.) describes the changes occurring in certain epithelial structures of the body. There is atrophy of the cells and replacement by stratified keratinising epithelium and similar keratinising metaplasia may occur in the salivary glands. The process may be repeated in the linings of the respiratory and urogenital tracts. Widespread infections in any or all of these may follow.

Most authors report atrophy and metaplasia in the enamel forming organs of the incisors of rats. As rat's teeth grow throughout life,

Chapter V. Cont'd.

they offer an excellent opportunity for the study of the effect of various deficiencies on the formation of tooth structure. Medina quotes the work of Boyle who described changes in the enamel organ of tooth germs in infants with Vitamin A deficiency.

Bone Changes:- An absence of vitamin A during growth inhibits the normal formation of bone and underdeveloped bones of the skull and spinal column cause compression of the nerves which pass through them.

Periodontal lesions:- Gingival hypoplasia has been stated to develop in puppies fed on a Vitamin A deficient diet.

Hypervitaminosis A may result from excessive ingestion. The symptoms are anorexia, loss of ^{weight}, irritability, a low grade fever, sparseness of the hair, tenderness over the long bones and hepatomegaly. (13)

Therapeutic dosage:

Capsulae Vitamini A. (B.P.C.) — 4,500 units of Vitamin A activity.

Liquor Vitamini A Concentratus (B.P.) contains 50,000 units in one gramme.

Dose:- I - 10 minims (2,500 to 25,000 units) daily.

Vitamin A is not a general anti-infective, as the infections occurring in deficiency states are secondary to the epithelial metaplasia.

Vitamin D.

A group of related sterols are effective in the prevention and control of rickets.

Calciferol or Vitamin B₂ is produced by the irradiation of ergosterol and Vitamin D₂ by the irradiation of 7-dehydrocholesterol.

Fish oils are the only rich sources of vitamin D, but small quantities are found in butter and eggs. Vitamin D₃ is produced under the skin of humans by the action of the ultra-violet rays of the sun.

Vitamin D is the catalyst which facilitates the absorption, retention and metabolism of calcium and phosphorus. Medina reports Follis' opinion that calcium only, and not phosphorus absorption is assisted by Vitamin D. It is now well known that it is essential in the formation of bones and teeth. Infants and children require about 400 I.U. a day but in normal adults the necessary intake is minimal. Even in the

Chapter V. Cont'd.

treatment of fractures in adults Rowe and Kieley (op. cit.) do not consider it necessary to supplement their usual convalescent diet with vitamin D. During pregnancy and lactation however 800 units are required daily.

Overdosages: Excessive dosage of calciferol can cause intoxication in man; pathological ^{changes} in the oral soft tissues usually presenting. Hypercalcification of the alveolar bone and cementum may occur. (14)

VITAMIN D DEFICIENCY STATES

Rickets:— A nutritional disorder of infancy and childhood — a deficiency disease due to an insufficiency of Vitamin D, calcium or phosphorus — an interference with the epiphyseal development of long bones.

Aetiology:— Calcium deficiency.
Phosphorus deficiency.
Insufficient Vitamin D.
Lack of sunlight (15)

A disease of the limbs, inadequate nutrition and sunless cities.

Thom (op. cit.) has surveyed a series of significant experiments demonstrating the effects on rats and dogs of diets deficient in one or more of the calcium — phosphorus — vitamin D. triad. Where normal proportions of calcium and phosphorus salts without vitamin D were administered, subsequent sections of the alveolar bone revealed osteoporosis, with yellow fat replacing the red marrow. Diets low in calcium and vitamin D produced fibrous and cystic reactions reminiscent of von Recklinghausen's disease. There was a degeneration of the periodontal membrane. Weismann and Scheurs experiments which showed an improvement in rachitic changes following intra peritoneal injections of phosphates would seem to indicate that the vitamin does assist the absorption of vitamin. Thom concluded from the experiments that correct proportioning of calcium and phosphorus was more important in the absence of vitamin D. Traces of magnesium in the diet are important.

Signs and Symptoms of Rickets.

The general signs are those of anaemia, irritability and restlessness, with the patient perspiring freely. French and Douthwaite (op. cit.) summarise the general affect: "In infantile rickets there is a general softening of the skeletal system in addition to the disorganisation of

Chapter V. Cont'd.

of ossification occurring at the ends of the long bones resulting in bending of those bones subject to weight-carrying or other pressures". Occasionally, spontaneous fractures occur. The costochondral junctions are enlarged, and all affected joints are painful. As the condition progresses spinal deformities and dwarfism can be expected to develop.

The skull and jaws, when affected, offer an interesting study in the effects of muscular pull in the development of facial deformities. The distortion is aggravated by a reduced resistance of the bone to the forces of mastication and a more pronounced damage from habits such as mouth breathing, thumb and pencil sucking. Due to compression the upper maxilla is constricted, producing a high vault and the resultant narrowing of the arch forces the upper anterior teeth into protrusion. The mandible is usually underdeveloped and mental protuberance may be absent. The pull of the muscles of the floor of mouth would seem to be important in producing this deformity.

If the disease has developed early in life there is hypoplasia of the enamel.

Pathology:- In the poorly calcified soft bone, there is evidence of the formation of trabeculae without calcification. Zones of osteoid tissue are seen. Neither osteoblastic or osteoclastic activity is pronounced whereas in osteitis fibrosa cystica the latter is a prominent feature. In Paget's disease areas of osteoclastic activity will be found, and where apposition of new bone is taking place, small osteoblasts will be detected. The bone marrow is fibrous. The cartilage cells in the epiphysis lose their systematic arrangement and are grouped irregularly.

Blood Pathology:- There is a marked increase in the blood phosphatase and the inorganic serum phosphorus is lowered. Not so marked, but interesting in comparison with hyperparathyroidism where the figure is always high, the blood calcium level in rickets is usually lowered.

A leucocytosis with a relative eosinophilia may occur. Due to faulty formation of red marrow, anaemia is common (Whitby and Britton op.cit.)

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Treatment:- The basis of treatment is careful attention to diet and if possible, the patient should increase outdoor activities. The diet should be supplemented with milk, calcium phosphorus and 1,000 I.U. of Vitamin D. daily.

OSTEOMALACIA.

This disease is now universally regarded as an adult form of rickets. Since normal adult requirements of vitamin D is minimal, the disease usually occurs in women, especially during pregnancy and lactation. In adults, calcium deficiency may be more significant in aetiology than lack of vitamin D. The disease is more common in the densely populated eastern countries than in those where the living standard is high.

Thoma mentions true osteomalacia (adult ricket), pregnancy osteomalacia and hunger osteomalacia.

In sprue and coeliac disease where the fat content of the bowel is high, the fat soluble Vitamin D may not be absorbed, so that even with an adequate diet, nutrition may be deficient and osteomalacia can result. Similarly the lack of bile salts in chronic obstructive jaundice may produce an osteomalacia even though the ingested diet be adequate.

Clinical features:- The disease is generally not recognised in its early stages. An examination where blood chemistry tests are carried out may lead to a diagnosis before clinical signs are evident. When the condition is established the bones are deformed and the vertebrae depressed due to the pressure of body weight. The patient becomes shorter.

General symptoms and signs are fatigue, muscular wastage, pains in the back and joints and tetany. The bones are soft and flexible but not brittle. Thoma points out that pathogenesis may be confused by an enlargement of the parathyroid glands.

Pathology:- The normal labile state of the bone is disturbed. Normal bone is replaced by new uncalcified osteoid zones which are wider than those seen in infantile rickets. Adipose tissue fills the spaces of the spongiosa. Thoma (op. cit.) states that uncalcified osteoid is characteristic of osteomalacia, whereas the bone trabeculae are entirely

CHAPTER V. Cont'd.

absent in osteoporosis.

Blood changes: Serum calcium is as low as 5 to 7 mgs. per 100cc. and phosphorus from 1.8 to 3.8 mg.

Secondary anaemia is common and a slight eosinophilia may occur.

The treatment follows the lines that were outlined for rickets.

THE VITAMIN B COMPLEX.

When Vitamin B was first discovered, it was thought to be a single substance, present in the germ and outer layers of cereals which would prevent beri-beri. As Dobbs (op. cit.) states: "It is now known to be of a complex mixture of at least fifteen substances and 'vitamin B complex!'" Dilling and Hallam's Pharmacology⁽¹⁶⁾ classifies the various members of the group thus:-

Heat labile Faction:	Aneurine Pantothenic Acid
Heat Stable faction.	Riboflavine Nicotinic Acid Folic Acid Cyanocobalamin Pyridexine Para-amino-benzoic Acid Choline Inositol Biotin

Of these, only five, thiamine, riboflavin, folic Acid, cyanocobalamin and nicotinic acid have been proved important in therapeutics (Dobbs op. cit.) but the 1956 edition of Accepted Dental Remedies states that data is accumulating on the significance and therapeutic possibilities of the other members of the complex.

ANEURINE (Thiamine Chloride, Vitamin B₁)

A colourless crystalline powder with a yeast-like odour and taste, soluble in water and hygroscopic, aneurine is found in yeasts, whole grain, nuts, lean pork and liver. The daily requirement for infants is 0.5 mgs. and for adults 1. 2 mgs. Therapeutic doses are from 2 to 50 mgs. per day, given orally or by subcutaneous injection. One milligramme of thiamine equals 333 I. U.

Aneurine is the catalyst essential to the oxidation of glucose in nervous tissue. Mottram (op. cit.) states, when the glucose metabolism

Chapter V. Cont'd.

has reached the point of producing ^{pyruvic} pyruvic acid, the process ceases and for that reason pyruvic acid is found in the blood of patients suffering ^{metabolism} from beri-beri. As the vitamin is associated with the metabolism of carbohydrates, larger quantities should be taken where the patient has a high carbohydrate diet, after strenuous muscular exercise and in any condition where tissue metabolism is increased. The vitamin assists in the treatment of hyperthyroidism, ^{nausea} nausea and neuritis of pregnancy and febrile conditions. In addition to being unstable at high temperatures, it is destroyed by alkalis. Regular daily intake is important as the vitamin is not stored well in the body.

RIBOFLAVIN (Lactoflavin, Vitamin B₂, Vitamin G.)

Riboflavin is a yellow-orange powder, only sparingly soluble in water, but slightly more so in saline solution and alkalis. The vitamin is obtained from milk as lactoflavin, from egg as ovoflavin and from liver as hepatoflavin.

All these substances contain a flavin nucleus with a pentose chain. Riboflavin is a general name.

The average adult requirement is 1.8 to 3 mgs. daily, but it is greater during pregnancy, lactation and periods of increased metabolism.

A deficiency of riboflavin produces some or all of the following signs: stomatitis, glossitis, cheilosis, seborrheic dermatitis, parosmia, ^{photophobia} photophobia and corneal dystrophy. There is little point in treating any of these signs with riboflavin unless they have been caused by a deficiency of this vitamin.

Therapeutic doses range from 2 to 20 mgs. daily by oral or subcutaneous route. Riboflavin is successfully stored in the body.

NICOTINAMIDE (Nicotinic Acid, Nicotinamide, P.P. factor.)

Nicotinic acid may be taken to be the essential vitamin, but it is probably used by the body in the ^{-amide} amide form to synthesize an active tissue enzyme in carbohydrate metabolism. The vitamin probably acts in conjunction with others of the complex.

Nicotinic acid is an odourless white crystalline powder, soluble in water and alcohol. It is extremely heat stable and not damaged by light.

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or air.

The vitamin is important in the prevention and treatment of pellagra. Secondary Vincent's infection in patients suffering from this disease is common, and a deficiency of nicotinic acid may be a predisposing but not an active cause of acute ulcerative stomatitis. A painful glossitis, inflammation of the mucosa and a scaly dermatitis may result from a deficiency of nicotinic acid. Indigestion, constipation, anorexia, erythema, tachycardia and neuritis may be manifestations of a mild deficiency.

The vitamin is found in yeast, liver, lean meat, greens, peas, canned salmon and wheat germ.

The daily requirement is probably 15 mg., but therapeutic doses of 50mg. t.i.d. are in order.

FOLIC ACID.

In the discussion on pernicious anaemia in Chapter III, it was mentioned that Folic acid may do the work of vitamin B₁₂ in alleviating symptoms of recent years, more and more references to this vitamin have been made, Dobbs (op. cit.) is quoted: "Folic acid restores the red cell count and haemoglobin levels in pernicious anaemia, sprue and nutritional macrocytic anaemia. It does not correct the neurological symptoms in sprue and pernicious anaemia, and is, therefore used as an adjunct to treatment."

This vitamin is a yellow crystalline powder, insoluble in water and occurs widely in nature. Under normal conditions it is synthesized in the bowel by bacteria but should these bacteria be destroyed absorption is inadequate.

Therapeutic dosage is 10 mg. daily.

PYRIDOXINE HYDROCHLORIDE (Vitamin B 6.)

Only recently has the value of pyridoxine been appreciated. Found chiefly in meat, fish, molasses, whole wheat and cabbage, pyridoxine is also synthesized in the presence of the intestinal bacteria.

A deficiency of vitamin B₆ may produce cheilosis, glossitis, conjunctivitis, lymphocytopaenia or polymorphonuclear leucocytosis, hypochromic anaemia, and dermatitis. The patient may lose weight.

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Therapeutic dosage: 5 mg. daily per oris.

CYANOCOBALAMIN (Vitamin B₁₂).

In recent years, it has become increasingly evident that this vitamin is closely associated with the intrinsic factor in the formation of blood. It may well be that it is the intrinsic factor.

In sprue and pernicious anaemia, there is a failure to absorb cyanocobalamin from the bowels and therefore parenteral therapy is indicated.

Injections may be used in the treatment of glossitis of pernicious anaemia and sprue, diabetic and other neuritides, neuralgia and atypical facial pains.

Dosage: preferably by injection; 1 mg. daily.

PARA - AMINO - BENZOIC ACID.

When the antagonistic action between this substance and the sulphonamides was first discovered, its importance as a metabolite was realised. Although it is now often included among the Vitamin B group, there is as yet no evidence that it is an essential constituent of the diet.

It has been used with some success in the treatment of pulmonary tuberculosis, scleroderma and leukaemia.

The roles of Biotin, choline, Inositol await elucidation. Pantothenic acid deficiency has been associated with glossitis.

GLOSSITIS, and abnormalities of the tongue.

In this review, an attempt has been made to discuss oral lesions under the headings of probable systemic causes. Generally, glossitis cannot be regarded as a disease in itself; rather is it usually a sign and glossodynia a symptom of perhaps a blood dyscrasia or nutritional deficiency. The dentist is frequently asked to determine the cause of an inflamed tongue and it appears to the writer that it is appropriate to discuss this subject after dealing with the vitamin B complex.

It is emphasised however that the approach must be systematic. Taking a blood count, the medical history, followed by a careful recording of the

Chapter V. Cont'd.

GLOSSITIS. CONT'D.

patient's diet are the steps necessary.

A Classification of Abnormalities of the Tongue. (French (op. cit.),

Thoma -- Robinson, (17) Whitby and Britton (op. cit.).

Trauma and

Irritations: mechanical; carious cavities, broken teeth, artificial dentures, fish bone.

chemical; drugs such as chromic acid, condiments, ginger cayenne pepper.

bitten tongue; after general anaesthesia, in epilepsy, while eating, during sleep.

smoking, hot foods, hot drinks.

Congenital:

congenital fissures: usually definite pattern near midline.

macroglossia

microglossia

aglossia

ankyloglossia, (short frenum)

hypermobility, posterior fraenal attachment.

cleft tongue.

lobulated tongue; -- additional tongue formation on surface.

median rhomboid glossitis, rhomboid shaped area devoid of papillae in midline, anterior to circumvillate papillae.

Infections: Syphilis, Primary chancre, mucous patches of secondary stage and tertiary gumma.

Varicella

Tuberculosis.

Herpes simplex and zoster.

Scarlatina (Strawberry tongue).

Cellulitis and abscess.

Chronic streptococcal glossitis.

Foot and mouth disease.

Chapter V. Cont'd.Moniliasis.

Actinomycosis (not usual) and blastomycosis.

Allergy: Meeller's glossitis — glossitis marginalis exfoliata —
superficial irregular atrophy, may
be due to allergy, neurological or
vitamin deficiency.

Xerostomia: Glossitis, — due to atrophy.

Aetiology
Unknown:

Benign Migratory

Glossitis.

(Geographic tongue), psychic factor?
← pemphigus, lichen planus.

Coated

Black hairy

Tongue.

May be due to anaemias, leukaemias,
avitaminosis, antibiotic therapy
or no systemic cause.

White
Coated.

Moniliasis

Antibiotic therapy, hypersensit-
ivity.

Acute lack of

Vitamin B.

Allergy.

Black
tongue.

Lymphatic leukaemia,

Lollies.

White
Patches.

Leukoplakia

Moniliasis

Mixed in congestion of liver.

Systemic:

in Anaemia:

Idiopathic hypochromic: hyperkeratinization usually
atrophied may be ulcerated.

pernicious anaemia

red fiery 'beefsteak' tongue.

Plummer Vinson Syndrome:

glossitis, dysphagia and anaemia,
usually idiopathic hypochromic.

Sprue:

clean inflamed tongue. In
pregnancy, probably due to anaemia.

Chapter V. Con'd.

ANEMIC DYSPEPSIS.

Vitamin deficiency:

- Riboflavin
- Nicotinic Acid
- Folic Acid
- Pyridoxine
- Cyanocobalamin
- Pantothenic Acid.

Swellings.

Acute Swelling:

- Insect sting.
- Traumatic and Chemical injuries.
- Angioneurotic oedema — not common but may ^{embarrass} ~~embarrass~~ respiration.

Indurated tongue.

Chronic enlargement.

- Macroglossia
- Myxoedema
- Acromegaly
- Chronic dyspepsia.
- Cretinism and Mongolian Idiocy.

Localised Chronic Swellings.

Tumours:

- | | |
|-----------------------|--------------------------|
| Benign:— | malignant;— |
| Fibroma | carcinoma (most common.) |
| papilloma | |
| Myoblastic myoma | |
| myoma | fibrosarcoma |
| lipoma | adenosarcoma. (rare). |
| Lymphangioma | |
| haemangioma | |
| struma. | |
| gumma | |
| Glossopharyngeal cyst | |
| tuberculosis | |
| actinomycosis | |
| mucous cyst. | |

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Diagnosis: With such a large number of possible causes, it is almost useless to treat lesions of the tongue empirically. A patient presenting with a glossitis should be requested to have a blood cell count and a nutritional analysis. Should one of the anaemias be diagnosed, the treatment may be left in the hands of a competent physician. When it is decided to use therapeutic doses of vitamin B, it is preferable to use the vitamin B complex. Attempts to identify the particular deficiency may lead to failure. It is now evident that vitamin B deficiency and blood dyscrasias may not be separate aetiological factors, and that folic acid or cyanocobalamin may alleviate a condition of glossitis by improving an anaemic condition.

Wasserman and Kahn tests, and chest X-rays may help in differential diagnoses. When there is a white coating, scrapings should be taken and bacteriologic examination made for *Candida albicans*. Actinomycosis occurs more frequently at the angle of the mandible than in the tongue but it must be included in diagnostic considerations. Where a whitened surface is completely adherent and diagnosed as leukoplakia complete surgical excision followed by biopsy should be carried out. In dyspepsia the tongue is enlarged, pale and flabby in appearance, and the margins are usually marked with indentations from the teeth.

CHEILITIS.

Cheilosis or cheilitis may be due to the actinic rays of the sun, pyralism, overcrowded dentitions, sensitivity (cheilitis Venetosa) or riboflavinosis. Medina (op. cit.) described an angular stomatitis as the labial commissures which may be secondarily infected as the cracks extend into the underlying tissues and cheilitis where the lips are excessively dry, and there is exfoliation of the superficial epithelium and later superficial and deep fissuring.

Treatment consists of prescribing emollients, from 2 to 20 mgs. of riboflavin a day and correction of any defect in the vertical dimension of the jaws.

PELLAGRA. (elephantiasis italica; Lombardy leprosy.)

A disease due to a deficiency of aneurine and nicotinic acid

Chapter V. Cont'd.

which may result from an inadequate diet, alcoholism and some organic diseases such as, tuberculosis, diseases of the gastro-intestinal tract lines and heart and diabetes. In these latter cases riboflavin absorption may be impeded.

The clinical signs are erythema and pigmentation of the skin, gastrointestinal disorders, glossitis and cerebrospinal disturbances. General symptoms include loss of appetite, diarrhoea, abdominal pain, vertigo, headache, nervousness and depression. Lesions of the mouth, tongue and oesophagus are common. The oral signs are haemorrhagic gingivitis and stomatitis, cheilitis and often secondary Vincent's infection. The characteristic tongue is known as the bald tongue of Sandwich which is caused by desquamation of the lingual papillae. Commencing at the tip and sides of the tongue the entire surface may become eroded. The tongue is painful, fiery, swollen and bears the indentations of the teeth. (Thoma, op. cit.)

Treatment is dietary, multi-B complex being used rather than thiamine or nicotinic acid.

BERI = BERI.

A disease of the East caused by aneurine deficiency due to the ingestion of a diet of polished rice.

The symptoms are diarrhoea, muscular cramps, peripheral neuritis with cardiovascular disorders ultimately developing.

Oral manifestations are not marked but there may be gingivitis and oedema with atypical facial pain.

Injectons of 5 to 20 mgs. of aneurine daily are effective in treatment.

ASCORBIC ACID (Vitamin C.)

Ascorbic acid, first synthesised in 1933, is present in citrus fruits, tomatoes, black currants, turnips, paw paws, strawberries, rock melons, passionfruit, persimmons and most berries. (18)

The vitamin is present in all tissues of the body but occurs in the highest concentration in the adrenal cortex, pituitary gland, the liver

Chapter V. Cont'd.

and kidneys (Dilling and Hallam, op cit.). The daily adult requirement is 30 mgs. and the rate of excretion is high. Children require 5 mg per kilogram of body weight.

The vitamin appears to be important in the formation of collagen in the connective tissues. It seems to be especially necessary in the preservation of blood vessel walls. In the repair of bone the formation of osteoid tissue depends partly on an adequate ascorbic acid intake. By reason of its part in the formation of collagen and intracellular material, ascorbic acid is important in the healing of soft tissue wounds. In diagnosing a deficiency, ascorbic acid estimations of the blood can be carried out (normal 0.3 — 1.3 mg. per 100 cc.

In all surgical cases, routine administration of vitamin C is logical and large doses are well tolerated.

Deficiencies of Vitamin C may cause anaemia, increased capillary fragility, gingivitis, cataract and scurvy.

Ascorbic acid is most conveniently used in 50 mg. tablets which enables the prescription ^{of} varying dosages. Tablets of 25 and 100 mgs are also supplied.

Packet (19) describes an additional anti-scorbutic factor found in citrus fruits in association with vitamin C and claims improved results in therapy from its use as an adjunctant with ascorbic acid. His work evidently refers to the P - factor flavonols. Martindale's text reports favourably, but most authors are still sceptical.

SCURVY.

Frank cases of scurvy are now rare, but relative deficiencies of vitamin C may cause some of the symptoms.

Resulting from a complete lack of vitamin C, scurvy has marked oral manifestations. The gingivae become swollen, maroon coloured and finally dark blue or purple. Actual ulcerations are not uncommon. Haemorrhages are characteristic occurring in the submucosa, at the gingival margins and subperiosteally. Similar bleeding may take place in any part of the body. Haematomas and haemarthroses are common.

Martindale 1961

Chapter V. Cont'd.

Secondary Vincent's infection is common. Infarcts are often formed in the lung and spleen and a normocytic hypochromic anaemia usually develops as a result of repeated haemorrhages.

Treatment is effected by very heavy doses of ascorbic acid. At first 500 to 1,000 mgs are used daily and the amount tapered gradually to maintenance levels.

THE IMPORTANCE OF DIET AFTER SURGERY.

From the above notes and discussions, it will be seen that the ~~value~~ of a good post-surgical diet should contain:-

Calories; 2,400: This should be adequate for a sedentary patient; an additional 400 calories should be provided in the last three months of pregnancy; calculate at approximately 4 calories per gram of carbohydrates: to be ingested at same time as proteins. Increase to 2,500 when patient becomes ambulatory.

Proteins; 60-80gms: Important in body repair and bone regeneration. Increase with body weight and up to 100 gms in last trimester of pregnancy. Try to have 40 gms of first class protein (37 gms normal optimum) requirement.

Minerals. Calcium: Normal adult requirement 0.8 gms daily; 1.5 to 2.0 in late pregnancy and lactation; for children 1.0 - 1.3 grams: In bone repair, possibly may be increased.

Phosphorus: Normal adult requirement about 1.4 gms; greater in pregnancy and childhood.

Iron. Normal adult requirements are 12 mgs. daily: Larger amounts are required after haemorrhage, during pregnancy and in childhood.

Vitamin A. 5000 I.U.: Normal adult requirements of value in epithelial and bone regeneration. Slight supplementation

Chapter V. Contd.

permissible, but excess dosage is toxic.

Folic Acid and Cyanocobalamin:

May be significant if patient anaemic.

No special reason for therapeutic

dosage of other members of vitamin B complex.

Ascorbic Acid; up to 400 mgs.
daily:

Large therapeutic doses are not

contraindicated and should be beneficial;

75 mgs. are normal requirements

Ascorbic acid tablets or orange drinks

preferably from fresh fruit: Shop

oranges have lost some, but not all of their vitamin content.

Fluids; 3,000 cc. fluid daily
(Acher, op. cit.)

Tendency for inadequate intake of fluids

after oral surgery; cells require

adequate fluid surroundings to allow

cooling during metabolism; insufficient

fluid may cause 'dehydration fever.'

If unavoidable use intravenous 5% glucose solution.

DIETS SUGGESTED BY NOTABLE AUTHORITIES.

Rowe and Koley (op. cit. P. 694.)
Semi - solid diet.

Breakfast.

Calories.

$\frac{1}{2}$ oz sieved porridge with milk and glucose
 $\frac{1}{2}$ pt. milk with beaten egg
 $\frac{1}{2}$ pt. tea with sugar

120.
300.
20.

10.00 am.

$\frac{1}{2}$ pt. milk with Horlicks or Ovaltine

300.

12.00 noon.

$\frac{1}{2}$ pt. sieved soup
 $\frac{1}{2}$ oz sieved mince with vegetables
 $\frac{1}{2}$ oz. sieved mustard with jelly
 $\frac{1}{2}$ pt. milk
 $\frac{1}{2}$ pt. tea with sugar

50.
350.
120.
200.
20.

3.00 p.m.

$\frac{1}{2}$ pt. milk with beaten egg
 $\frac{1}{2}$ pt. tea with sugar

300.
20.

Chapter V. Concluded.

	<u>calories.</u>
6. 00 p.m.	
$\frac{1}{2}$ pt. sieved soup	50.
$\frac{1}{4}$ oz sieved mince with vegetable	330.
$\frac{1}{4}$ oz. sieved custard with jelly	120.
$\frac{1}{2}$ pt. milk	200.
$\frac{1}{4}$ pt. tea with sugar.	30.
9. 00 p.m.	
$\frac{1}{2}$ Pint milk with Horlicks or Ovaltine.	300.
Total	<u>2,800 calories.</u>

Total fluid intake 5 pints (approx. 2,000 c.c.)

In a totally fluid diet given to patients whose maxillae have been immobilised in the treatment of fractures, milk must form the basis of the diet. One half pint of milk has a calorie value of 250 to 300. First class protein can be incorporated in the milk by using eggs and the fluids may be supplemented with vitamins.

Varco's Diet for tube feeding (diet Manual of prince Alfred Hospital p. 13.)

6 whole eggs.
2 egg whites.
 $1\frac{1}{2}$ pts liquid skim milk.
100 g. dried skim milk.
300 g. lactose.
Salt.

Calories 2,380 :: approximately 3 pints.

Archer's Dental Soft Diet (Oral Surgery op. cit. p. 230.)

Breakfast.

Fruit juice — 100g.
Cooked cereal
Soft cooked egg.
Cream — 2 oz.
Milk — 8 oz.
Coffee — Sugar.

10 am. Fruit nectar — 200 g.

Noon meal:

Cream Soup.
Eggnog.
Fruit juice — 200 g.
Jello or vanilla ice cream.
Tea or coffee.
Cream — sugar.

3 p.m. Milkshake.

Chapter V. Concluded.Evening Meal:

Fruit juice.
Cooked cereal.
Soft cooked egg.
Mustard.
Tea or coffee.
Cream — sugar.

8 p.m. "Pep" cocktail.

Total of proteins :: 73g. Calories 2, 500.

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PART II.CHAPTER VI.ENDOCRINE STATES RELATED TO DISEASE OF THE MOUTH AND JAWS.THE PITUITARY GLAND.

Situated in the sella turcica at the base of the skull, the pituitary gland is composed of three parts; the anterior lobe, the 'pars intermedia' and the posterior lobe.

The functions of these parts are:- (1)

The Anterior Lobe:- Chromophobe cells; devoid of granules and of two types, which ultimately form the chromophil cells of both types.

Basophil Chromophil Cells: 10% of anterior lobe cells - probably produce the gonadotropic hormones, A.C.T.H. (vide Part I, Chapt. 1) and the lactogenic hormones.

Eosinophil Chromophil cells: 40%, sources of the growth stimulating hormone and the thyrotropic hormone.

Pars Intermedia (2)

and Posterior Lobe:- produce pitressin; a substance antagonistic to insulin, a vasopressor with anti diuretic action (3) and pitocin (oxytocin); Thoma (4) adds a chromatophore stimulant. (5)

Diseases due to pituitary dysfunction.a. Hyperpituitarism:

Acromegaly.

Giantism (gigantism)

Pituitary basophilism. (Cushing's syndrome.)

b. Hypofunction.

Simmond's disease (pituitary cachexia).

Frohlich's syndrome (dystrophia adiposo-genitalis).

Pituitary dwarfism.

Diabetes insipidus.

Chapter VI. Cont'd.GIANTISM.

Due to hyperfunction of the anterior lobe of the pituitary gland ^{is caused} before ossification is complete, giantism by an excessive but proportionate growth of the individual due to very active bone formation at the epiphyseal lines. The hyperactivity is usually due to an adenoma of the anterior lobe, but sometimes cystic structures have been found. Should the hyperfunction continue after complete ossification some of the features of acromegaly may be superimposed. At an early age, the giants are precociously powerful and are sexually potent, but feebleness, impotence and mental impairment may develop later. More recently the condition has been ascribed to hyperplasia of the eosinophil cells; X-rays may reveal an enlarged sella turcica.

In eunuchoid giantism the signs are associated with hypogonadism which may result from underactivity of the basophil cells.

The maxilla, mandible and teeth are proportionately enlarged.

ACROMEGALY (Marie's disease.)

Acromegaly is due to an hyperactivity of the eosinophilic cells after ossification of the bone and epiphyseal lines has been completed. Enlargement takes place in the extremities mainly on the part of the soft tissues, though thickening of the bones may later occur especially in the phalanges and head. The nose, mandible, ears, hands and feet are usually enlarged and the lips are thick and prominent.

General symptoms are severe bitemporal headaches, faulty vision, cephalgia and photophobia. As with giantism, there may be glycosuria and polyuria. If there is additionally an ^{over}secretion of the thyrotropic hormone, the thyroid gland may be enlarged, increasing the metabolic rate. Spacing of the teeth, which of course are not enlarged, may help in early diagnosis.

Roentgen examination may reveal that the sella turcica is enlarged or destroyed by tumour formation. The sinuses are enlarged and there is usually sclerosis of the mandible especially about the ascending ramus.

Irradiation of the pituitary gland is sometimes effective in controlling the condition, while Wolf and Hightower (3) state, that

Chapter VI, Cont'd.

oestrogens and androgens have been used because they suppress pituitary function.

PITUITARY BASOPHILISM (CUSHING'S SYNDROME).

This is a disease caused usually by a basophil adenoma of the pituitary gland, not sometimes by an overactivity of the adrenal cortex. Symptoms similar to those of Cushing's syndrome may develop with prolonged administration of A.C.T.H.

The body is painfully adipose but the limbs are not affected. Often there are purple striae on the skin of the abdomen. Other symptoms are excessive perspiration, excessive growth of masculine type hairs, high blood pressure, polythaemia, glycosuria and osteoporosis.

Simond's disease is the most usual example of anterior lobe hypofunction and is sometimes due to necrosis of the lobe following ischaemia. Usually occurring in middle life, weakness and emaciation are the typical signs. The features become sharp, the lips thin and the skin wrinkled.

Prothlis syndrome and Dercum's disease are not especially significant in oral surgery. Adiposity and underdevelopment of the sexual glands are the essential features. Pain in the joints and muscles may occur.

Pituitary dwarfism is due to hypofunction of the anterior lobe and the patient, though dwarfed, is in proportion. The teeth are usually small, but Thoma (op. cit.) states that if the condition does not develop until the age of 4 to 6 years the crowns may be of normal size. In other cases the deciduous dentition may persist. Hypoplasia is common. In all pituitary hypofunctional disease there is delayed eruption of the teeth. It will have been noticed already that there is an hormonal interaction between the glands. Further instances will be noted.

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THE THYROID GLAND.

This gland, consisting of two lateral lobes and a connecting isthmus is situated at the upper end of the trachea. The thyroid gland develops as an evagination of the primitive pharynx. Acting through its hormone, thyroxin, the thyroid gland regulates the rate of metabolism. Thyroxin contains about 64% of iodine (6) and is the active constituent of

Chapter VI. Cont'd.

thyroglobulin contained in the cells of the gland. Thyroxin assists in the metabolism of proteins, fats and carbohydrates and possibly facilitates the excretion of calcium and magnesium. A lowered secretion of thyroxin reduces resistance to infection.

Excessive thyroid function results in sweating tachycardia, a greater heat production, increased protein and fat consumption. There is an interactivity of the gland with the pituitary, thymus, gonads, the islets of Langerhans in the pancreas, the parathyroid gland and the suprarenal cortex. Thyroid hyperfunction, therefore, produces abnormal changes in the secretion of the other endocrine glands.

NON - TOXIC OR COLLOID GOITRE.

Endemic to certain localities where there is a deficiency of iodine and occurring more commonly in women due to loss of iodine in blood in menstruation, this is an enlargement of the gland due to the excessive storage of collagen.

The symptoms are disfigurement due to enlargement of the gland and pressure on the trachea, oesophagus and glossopharyngeal nerve.

DIFFUSE TOXIC GOITRE (Grave's disease), EXOPHTHALMIC GOITRE (Barry's disease, BASEDOW'S DISEASE, PRIMARY HYPERTHYROIDISM.).

Most commonly affecting women Grave's disease is characterised by an excessive secretion of thyroxin. Young adults are the most susceptible, but the age group varies from 15 to 50 years.

Oversecretion of the thyrotropic hormone of the pituitary glands has been suggested as a cause, but the aetiology is not yet fully understood.

The gland is abnormally large and firm. There is diffuse hypertrophy and hyperplasia of the cells of the alveoli and colloid material is deficient. The blood iodine level is raised (4 - 8 mcg. per 100cc normal), but the iodine content of the gland itself is low. There is a marked increase in calcium excretion but the blood calcium level is usually not raised.

While enlargement of the gland is usual, it is not always visible as the enlargement may extend downwards into the mediastinum. Exophthalmos is the other classical sign. Fairly common additional symptoms are glycosuria, hyperglycaemia with low glucose tolerance. There is a general increase in the metabolic rate.

Chapter VI. Cont'd.

Some of the clinical features are important in dentistry. The patients are almost invariably emotionally unstable; cardiac embarrassment and heart failure are not uncommon. Excepting in the direct emergencies, all surgical procedures should be avoided in patients afflicted with Grave's disease, as a thyroid crisis characteristic by tachycardia, nausea, vomiting, fever, semi-consciousness and weakness, may be precipitated.⁽⁷⁾ The caries rate is extremely high and the gingivae may be hyperaemic or suppurative. Thoma (op. cit) describes a loosening of the teeth due to an osteoclastic type of resorption of the alveolar bone. It is not illogical to suspect hyperthyroidism in cases presenting with rampant dental caries.

In Toxic Nodular Goitre known as secondary hyperthyroidism or toxic thyroid adenoma the symptoms are similar but exophthalmos is not common.

Hyperfunction of the thyroid gland can usually be diagnosed by the classical signs supported by tests of the basal metabolic rate, the serum protein bound iodine value, thyroid absorption of radio active iodine in the urine (Comroe and co-authors op.cit.)

Surgical removal of the gland has for some time been the treatment of choice, but recently the thiouracil compounds have been used in controlling glandular secretion. Thiouracil, unfortunately may cause agranulocytosis (q.v), but the compound propyl and methathiouracil are not so dangerous in this respect. Tapazole has also been found to be an effective anti-thyroid drug but it is very toxic.

MYXOEDEMA (Adult Hypothyroidism, Gull's disease.)

The term myxoedema is usually reserved for the condition resulting from hypothyroidism in the adult. It is seen most often in female patients from 40 to 60 years of age.

Metabolism is lowered (40 - 50) and there is atrophy of the hair follicles causing loss of hair. The skin becomes smooth, firm and dry. There is some swelling. A lowering of the pulse rate and temperature is accompanied by sluggish movement, slowness of speech and lethargy. Sexual desire is diminished and when the disease occurs in young women, amenorrhoea is common. In middle age menorrhagia frequently results.

Chapter VI. Cont'd.

Histologically, there is a fibroid atrophy of the thyroid gland. There is an extensive lymphocytic infiltration; the acini are small and the colloid diminished.

Dessicated thyroid gland is efficient in therapy which must be continued throughout life.

CRETINISM.

Muir (op. cit.) describes a sporadic and endemic type and Thoma (op. cit.) distinguishes a congenital and juvenile form. The conditions are due to an absence or hypoplasia of the thyroid gland. Sporadic cretinism may occur in any locality and the cause is not known. The endemic form is common in iodine deficient areas. Muir illustrates that in sporadic cretinism sufficient thyroxin is obtained through the placental circulation and the hypofunction cannot manifest itself until after birth. Thoma on the other hand describes an inherent inactivity of the thyroid gland with a decreased supply to the foetus. Presumably, this state would apply in endemic areas.

The completely absent or very small atrophic gland. The absence of thyroxin and a resultant low level of metabolism seriously inhibits growth and development. The mentality is retarded. There is usually a generalised oedema. Owing to a deficient ossification of cartilage, the base of the skull is shortened, the nose depressed and the lips thickened. Muir uses the apt. description 'pig-like appearance.' The hair is scanty and coarse, and lipoma often occur around the shoulders and neck.

The dentist will observe delayed eruption of the dentition and could be the first to suspect those conditions of slower onset. The chin is receded with maxillary protrusion. Malocclusion is common and the writer has treated a cretin with six supernumerary teeth. The deciduous teeth are persistent. Typically, the caries incidence is high. Structurally, the teeth are defective, with faulty union of the cusps and hypoplasia. The cuspid teeth are frequently not present.

Iodine and thyroid hormone medication are effective only if the state is diagnosed early.

Chapter VI. Cont'd.THE PARATHYROID GLANDS.

Usually situated posteriorly to the thyroid gland, the parathyroid glands consist of four small yellow red bodies and secrete parathormone which profoundly influences the metabolism of calcium and phosphorus.

Sometimes the parathyroids are embedded in the thyroid gland and aberrant glands may be located in the thymus or mediastinum. They are especially significant in oral surgery. The disease entity, generalised osteitis fibrosa cystica or von Recklinghausen's disease (1891) is now recognised as a syndrome of hyperparathyroidism.⁽⁸⁾ Muir (op. cit.) states that parathormone 'acts on the calcium essentially as a mobiliser,' but Greenwood, Best and Winston⁽⁹⁾ quote Albright's opinion that the primary action is a lowering of the renal threshold for the secretion of phosphorus. As pointed out by Jenkins,⁽¹⁰⁾ changes in inorganic serum phosphates are accompanied by changes in the opposite direction by serum calcium. The extra calcium can come only from the bones or the diet.

TETANY.

Tetany is essentially due to hypocalcaemia resulting from an upset in the calcium-phosphorus balance. In rickets, a deficiency of vitamin D causes inadequate absorption of calcium. During pregnancy and lactation an excessive drain on calcium resources may induce the condition. Any of these conditions associated with achlorhydria may inhibit the calcium intake and produce typical signs of tetany. Parathyroidectomy (including accidental removal of the glands!) and idiopathic hypoparathyroidism may lead to a lowered serum calcium level and produce the condition.

The signs and symptoms are painful muscular spasms involving the extremities and sometimes the larynx and bronchi. The patient may lose consciousness. There is an increased irritability of the peripheral nerves. Blood chemistry tests reveal a lowered serum calcium level and an increased phosphorus content.

If hypoparathyroidism develops early in life, aplasia or hypoplasia of the teeth and defects of the eyes, nails and hair occur.

Dihydrotachysterol, a parathyroid like derivative of egesterol and parathormone are used in treatment.

Chapter VI. Cont'd.

HYPERPARATHYROIDISM.

Greenwood and his co-authors (loc. cit.) describe acute parathyroid intoxication and chronic parathyroid intoxication.

The acute condition follows the removal of or injury to the glands in surgery or excessive dosages of calcium or parathormone. There is intense nausea, vomiting, lethargy and finally coma. They describe the chronic condition under three headings: bone, kidney and blood.

Blood: hypercalcaemia is usually present the usual figure being 12-14 mgs per 100 c.c.s. but the calcium level has been known to rise as high as 18 - 19 mgs. The high blood calcium level may cause anorexia, nausea, vomiting and cardiac muscular disturbances. In secondary hyperparathyroidism due to renal disease or osteomalacia, the hypercalcaemia may not be marked. Plasma phosphorus is low and particularly when there is bone involvement the alkaline phosphatase is high.

The Urinary tract: with excessive secretion of calcium, renal calculi are usual, and there may be an infiltration of the entire kidney.

^{and}
Haematuria ~~or~~ polyuria are frequent symptoms.

Bone changes: essentially osteoporosis, due to a fibrous dysplasia.

As stated by Brightman (loc. cit.) the term 'fibrous dysplasia' has, over the years, been used to describe a wide variety of conditions. On recent years it has become evident that a number of diseases are manifested by fibrous dysplasia and numerous terms, sometimes overlapping, have been applied to try and sort out the puzzle. All has not yet been said, but with advances in endocrinology and blood chemistry the problem is gradually being solved.

It seems that the term suggested by Albright and others, 'osteitis fibrosa generalisata' will ultimately be adopted for Von Recklinghausen's disease. 'Osteitis fibrosa fibrosa cystica' is inadequate because cysts are not always formed. The basic bone lesion in hyperparathyroidism is fibrous dystrophy with osteoclastic bone resorption and fibrosis of the marrow. Osteoclastomas and cysts are secondary complications. Thoma, Greenwood and others emphasise

Chapter VI. Cont'd.

that bone lesions may be entirely absent in hyperparathyroidism.

Histopathology. (Thoma op. cit.)

The principle feature is an active osteoclastic resorption along the enlarged blood vessels in the Haversian system of the cortex and more particularly in the spongiosa. Where there is apposition the bone trabeculae are replaced by woven bone. Fibrosis of the marrow spaces is an important feature, and there is associated hyperaemia and oedema. Thrombi may be seen in the blood vessels. Cysts when present contain an albuminous fluid with or without red cells.

Osteoclastomas are commonly present and their principle characteristic is the presence of large foreign body giant cells and spindle cells. They contain numerous nuclei (up to 50). In all conditions haemosiderin is abundant and there may be numerous extravasated red cells. Osteoclastomas vary greatly in size and may be multiple. Due to the presence of haemosiderin there is a yellow or brown colour. In large lesions the cortex may be involved, the bones enlarged but the periosteum remains intact. Although they may occur in any bones, the jaws are a very common site.

General Symptoms may not be marked but tenderness and pain over the bones and loss in weight and height may occur. Calculi may form in any part of the body. Osteoporosis may cause a loosening or spacing of the teeth. Once formed they are not decalcified. In long standing cases, the patient may be crippled and pathological fractures have been reported.

Primary hyperparathyroidism is at present treated by surgical removal of the gland; adenoma or carcinoma are a common primary cause.

Diseases to be considered in differential Diagnosis.

Von Recklinghausen's Disease.

Usual age: middle years.

Sex: more commonly in women 3 : 1.

General Symptoms. often not marked: pain, stiffness of joints.

Osteoporosis: general.

Roentgenology: diffuse decalcification: often cysts and osteoclastoma, milairy mottling.

Chapter VI. Cont'd.Von Recklinghausen's disease Cont'd.

Percussion of Skull: Tender's 'watermelon sound.'

Histopathology: Giant cell osteoclastoma, fibrosis of spongiosa, often with osteoid tissue.

Blood: haemosiderin. Raised blood calcium; reduced phosphorus. Usually alkaline, phosphatase raised.

Urinalysis: Increased Ca - P₄ - Alkaline.

Aetiology: Hyperparathyroidism.

Polyostotic fibrous dysplasia (Allright's Disease). Osteitis fibrosa disseminata.

Usual age: Under 35: Childhood and early adult life.

Sex: No reference.

General Symptoms: Affects one (monostotic) or many bones, 'café au lait' pigmentation of the skin, precocious sexual development - may be no pain; often swelling.

Osteoporosis: is unilateral.

Histopathology: essentially fibrous connective tissue (spindle cells) with osseous and cartilaginous. Elements - connective tissue whorled and relatively avascular.

Roentgenology: long standing lesions show some expansion with thin cortex and intact periosteum - trabeculated appearance - mottled and stippled - Brightman (loc. cit.) states that periosteum may be thinned where bones are expanded may be circumscribed areas of radiopacity; cysts not common; but Xray deceptive.

Blood Chemistry: Serum calcium, phosphorus and phosphatase normal.

Urinalysis: Normal.

Aetiology: 'perverted activity of specific bone forming mesenchyma' (thoma) may be an associated glandular factor.

Osteitis deformans. (Paget's disease.)

Usual Age: Middle years.

Sex: More common in females.

General Symptoms: slow progressive course at first no symptoms excepting gradual enlargement of bones. - Enlargement or necessarily

Chapter VI. Cont'd.Osteitis deformans. (Paget's disease.)

symmetrical -- as bones enlarge and soften those bearing weight become curved ('bow-legged') -- As with polyostatic dysplasia, long most frequently involved; but skull and jaws often affected.

Percussion of skull: high-pitched cracking sound.

Roentgenology: thickening with fluffy cotton wool appearance; often roots of teeth resorbed.

Histopathology: resorption and apposition of bone; In areas of resorption, osteoclasts; in apposition, coarse irregular bone; well defined demarcation between old and new bone ('mosaic' appearance.)

Blood Chemistry: Alkaline phosphatase raised but calcium and phosphorus normal.

Aetiology: Unknown.

Rickets is a disease of childhood with thinning of bone: the blood calcium level is lowered.

In Osteoporosis of old age the pain is similar to that of hyperparathyroidism but the blood chemistry is normal.

In multiple myeloma sternal puncture and haematological picture are pathognomic.

THE ISLETS OF LANGERHANS.

Numbering some hundreds of thousands or even millions, the islets of Langerhans lie in ~~the~~ sections throughout the tissue of the pancreas. They are composed of two types of cells the ~~the~~ and B cells. Since they release an internal secretion, insulin, the islets form part of the endocrine system. Trypsin amyllopsin and steapsin are external secretions of the pancreas itself.

Insulin the anti-diabetic hormone maintains the blood sugar at a normal level. Normally about 0.1% of the blood is glucose (70-110mg. per 100 c.c.) and if the figure rises to 0.18% excess glucose is excreted in the urine. When there is fibrosis or degeneration of the islets of Langerhans, the output of insulin is decreased and the patient develops diabetes mellitus.

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DIABETES MELLITUS.

The disease can occur at any age but most commonly the first manifestations occur between 40 and 60 years of age. There appears to be an hereditary factor, and Jewish people are particularly susceptible. Liability to the disease is increased by obesity.

The deficient secretion of insulin prevents the patient from utilising all the carbohydrate ingested, and the excess passes into the urine. Because fats are metabolised in the presence of carbohydrate combustion, incomplete oxidate results so that the body accumulates an excess of acetone, diacetic acid and beta hydroxybutyric acid is accumulated in the body. This accounts for the acetone breath of diabetics. In addition to the inefficient metabolism of glucose the body is unable to store reserve so that the rapidly formed hyperglycaemia (sometimes 0.4%) leads to polyuria, which in turn causes the excessive thirst of diabetes. Following upon the incomplete oxidation of fatty acids, a toxic state of acidosis may develop.

Due to the presence of sugar in the urine, there is often bacterial activity about the genitalia causing pruritus. This is especially common in women.

Prior to diagnosis the patient may have been aware of neuritic pains in the extremities, a loss of weight and energy, faulty healing after injury, suppurative gingivitis and carbuncles. However the condition is often not suspected until routine urinalysis is carried out.

The resistance to infection is always greatly reduced. This is because the blood contains excess glucose, thus providing an excellent culture medium for bacteria. Diabetics, not infrequently are infected by tubercle bacilli and all inflammatory reactions are likely to be severe. Pneumonia is a frequently reported complication.

Because of a high blood cholesterol level marked atheroma and arterial thrombosis often results, and the thrombosis in its turn may cause gangrene or coronary artery thrombosis.

Constantly produced diacetic and oxybutyric acids impose a drain on the alkali reserves of the body and divert some of the ammonia of

Chapter VI. Cont'd.

protein that was destined to form urea. These alkalis are used to neutralise the acids described. Sodium is also used in this neutralising process so that there is an excessive loss of chlorides through the kidney resulting in a dehydration and a fall in blood volume. This latter state reacts on the respiratory centre to produce the asphyxia of a diabetic coma. (Muir op. cit.)

The symptoms of diabetic acidosis are polydipsia, drowsiness, nausea, vomiting, abdominal pain, constipation, restlessness, leucocytosis and finally asphyxia, unconsciousness and death (Gomroe and co-authors, op. cit.)

In diabetics there is frequently a deficiency of the vitamin B complex which may account for the symptoms of peripheral neuritis. Other complications are cataract formation, and perhaps ultimate blindness, renal lesions, and arteriosclerosis. Vascular changes eventually cause cardiac damage.

Diagnosis: Ohler⁽¹¹⁾ emphasises that a single positive urine test does not constitute a positive diagnosis of diabetes mellitus. The provisional diagnosis may be confirmed by using the 'glucose tolerance' test. After fasting for 12 hours, the patient is given 100gr. of glucose. Comparative blood and urine tests are made before and after the glucose is taken. In a non-diabetic person the blood sugar will not rise above 180mg. per 100c.c., and the figure will return to normal after 2 or 3 hours. In so-called 'renal diabetes' the reaction is normal but in diabetes mellitus, the glucose concentration remains high.

Treatment: The aim in treatment is to restore and maintain normal blood sugar levels and to keep the urine free of glucose. By carefully balancing the proportions and quantities of fat, carbohydrates and proteins, a considerable improvement can be achieved. Best results are achieved when the patient's weight is maintained a level slightly below average. There must be total abstinence from alcohol. The average daily carbohydrate taken is 150 g. but the ideal varies in different patients.

When the glucose level cannot be standardised by diet alone, insulin is prescribed. As yet, no satisfactory form has been evolved for oral

Chapter VI. Cont'd.

administration and injections must be used. The amount of insulin required varies greatly and must be determined for each patient. The hormone acts strongly for about one hour and has lost its effect after 8 hours. Frequent injections with pure insulin are therefore necessary and the ideal time of administration is about 20 minutes before meals or the performance of unavoidable surgery. Recently Hagedorn of Denmark has evolved protamine zinc insulin and N.P.H. insulin whose actions are longer but are absorbed more slowly. They are frequently mixed with ordinary insulin. Insulin shock, characterised by nervousness, trembling, nausea, abdominal pain, periods of unconsciousness and even convulsions, coma or death, may result from exertion, overdosage or too little food. In these cases, sugar and orange juice are given to the patient.

The Significance of Diabetes Mellitus in Dentistry.

In diabetes there is an increased tendency to form salivary and subgingival calculus, and an acute suppurative gingivitis is frequent. The condition is associated with a soft dark red swelling of the nearby mucosa, while pocket formation with loosening of the teeth may be pronounced. Possible to a concomitant Vitamin B deficiency, the tongue is frequently enlarged and fissured.

Because resistance to infections is low periapical infection should be removed as soon as the general condition is under control.

In uncontrolled diabetes every effort should be made to avoid even the simplest surgical procedure. Very frequent and thorough examinations of the mouth will help to achieve this. Archer (op. cit.) points to the reduced peripheral circulation due to the presence of cholesterol and reminds his readers that the high sugar level in the body fluids encourage bacterial growth. He strongly advises against surgical procedures in uncontrolled diabetes. It is wise to assess the serum glucose level prior to operating.

THE OVARIES.

Two flat oval shaped bodies composed of an outer cortex and a medulla the ovaries produce the hormones oestrin and progesterin (from the corpus luteum). Ovarian function is closely related to the pituitary

Chapter VI. Cont'd.

gland and as a further demonstration of the interaction of the endocrine hormones. Most of the disorders arising from pathosis of the ovaries fall outside the scope of this review, but a few significant conditions are outlined.

Ziskin has shown experimentally that both oestrogenic and male sex hormones act as specific tissue stimulators producing hyperplasia of the prickle cells and hyperkeratinisation (Comroe and co-authors op.cit.)

A form of gingivitis is not infrequently associated with pregnancy. There is a bluish-red enlargement of the gingivae especially at the interproximal papillae. It occurs most commonly near the upper lateral incisor teeth. Haemorrhage from the tissues is easily induced and hygienic measures without the use of a toothbrush usually have to be instituted. Gingivitis may be observed prior to menstruation, after menopause and in association with gynaecologic disturbances. (Thoma, op. cit.)

In extreme cases, gingivitis gravidarum progress to form the pedunculated tumours of pregnancy. These tumours usually grow from an interdental papilla and are often multiple. They may occur on both the labial and lingual aspect and may become so large as to interfere with occlusion. Deep red-blue in colour, the lesions are extremely liable to haemorrhage. Most authors agree that surgical removal should be avoided until after parturition and if the tumours are removed during pregnancy, recurrence is likely. It is the writer's experience that gingivitis gravidarum is not at all uncommon but are more likely to occur when there has been a preexisting gingivitis.

Histopathology: There is hydropic proliferation of the epithelium and the subepithelial tissues resemble a fibro-angroma (Thoma).

Treatment: The condition regresses with the termination of pregnancy, but there is seldom a complete return to normal. Surgery can then be successfully carried out.

The aetiology is not at all clear but Thoma suggests that the immediate cause is a diminished utilisation of oestrogen. Bain⁽¹²⁾ considers the stress plays an important part in aetiology and considers that

Chapter VI. Cont'd.

the prolonged stress of pregnancy may cause a mild adrenal cortex deficiency enabling the processes of inflammation to develop.

The state of knowledge in this condition will serve to illustrate that continued research in endocrinology is needed. Certainly the discovery of new facts about A.C.T.H., and adrenal hormones discussed in Part I, will probably be regarded as significant when clinical trials are completed, but undoubtedly Medicine and Dentistry need to know more of the facts as yet hidden from its ken.

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PART II.CHAPTER VII.SYSTEMIC CONDITIONS PROVIDING ADDITIONAL PROBLEMS IN ORAL SURGERY.

In the preceding chapter some attention was given to the importance of diabetes in Dentistry. It is now proposed to discuss some other significant general conditions which may alter the prognosis in oral Surgery.

SHOCK.

Muir⁽¹⁾ defines shock as a 'condition of profound depression of the body functions'. The definition is a broad one but, Rowe, and Killey⁽²⁾ describe the term 'shock' as a vague expression embracing a wide variety of causes to produce a definite clinical entity which varies but slightly. Knowledge of the condition was greatly increased during World War II, and all authorities now distinguish a 'primary' and 'secondary' shock. Rowe and Killey (ibid) use the better terms 'Neurogenic' and 'Oligaemic Shock.'

Neurogenic shock is in the nature of a vaso-vagal reaction probably due to over-stimulation of the carotid sinus reflex. Pain and psychogenic factors are the principle causes. The patient shows symptoms of pallor and sweating, the pulse and blood pressure are low. Often after vomiting, the patient may feel faint and syncope ensues, due to cerebral anoxia. The condition may be precipitated by a depletion of glycogen reserves in non-diabetic nervous individuals with a high metabolic rate.⁽³⁾ The blood pressure rarely falls below 90 m.m.

During the war, the opinion was formed that the general fall in blood pressure was due to a sudden loss of arteriolar tone, especially in the skeletal muscles resulting in a peripheral pooling of blood. Rapid recovery is usual. Smelling salts may be used where the patient is faint and the administration of antacid powders quickly relieves nausea and vomiting. Relief of pain and the assurance of the apprehensive are

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important steps. When resulting from accidents Rowe and Killey (op.cit.) advise removal of any wet clothing wrapping in dry blankets, rest and morphia (excepting in head injuries).

Oligaemic Shock: Winter⁽⁴⁾ and Muir (op. cit.) give similar descriptions of the series of vascular changes which produce oligaemic shock. Primary shock may precede the development of secondary shock which, excepting in the cases of very severe sudden haemorrhages, takes some hours to be apparent. Tissue trauma (Lewis H. substance) or burns increase the capillary permeability resulting in a loss of plasma and a reduced blood volume. The resulting reduction in blood volume leads to a decreased venous return and a decreased cardiac output. This, in turn causes the arterial blood to drop and a carotid sinus reflex increases the heart rate and the reduced blood pressure results in a peripheral vaso-constriction. A 'vicious cycle' is now established. Because of this vaso-constriction and the initial peripheral pooling of fluid there is an anoxaemia of the organs, and the heart though working hard, has insufficient blood volume to rectify the situation. Excepting where there was an initial heavy haemorrhage there is haemoconcentration. The Anoxaemia is considered by some to increase the capillary permeability and to cause the liver and muscles to liberate increasing amounts of vasopressor substances. This further impedes the return of fluid from the tissue spaces and the shock may become irreversible.

Both Winter and Rowe — Killey emphasise the importance of recognising early signs, as treatment becomes more and more difficult in the later stages. The former describes Blalock's finger test against the sternum, noting the time required for colour to return to the blanched area. The latter authors rely on blood pressure determination and regard 70% of normal (less than 160mm.) as the critical level. Should the level remain this low for an hour, transfusions are commenced.

As the chain of reactions just described occur, some or all of the following signs and symptoms are seen:-

1. Grey - blue colour of the nails, the tips of the fingers, lips and the ear lobes.

Chapter VII. Cont'd.

2. Pale, cold, clammy skin:
3. Weak, rapid pulse; irregular, shallow, rapid respiration. (5)

Rowe and Killey describe a purposeless tossing of the head and arms.

Treatment: The first step is to provide for complete rest and relief from pain. As already mentioned, morphia may often be used for rapid results. Where this is not possible, local injections of Xylocaine will be beneficial. Psychic factors are important. It is vital to control haemorrhage promptly.

Efforts should be made to maintain body temperature, but applied external heat will only cause further loss of blood plasma into the tissue spaces. To counteract the deleterious anoxaemia, 100% oxygen is often administered. This improves metabolism and the production of endogenous heat. Winter advises that the patient lie in a horizontal position with head lowered, but Rowe and Killey warn against causing further congestion and haemorrhage. All clothing that is tight around the neck should be loosened.

Fractures should be immobilised as soon as possible to relieve pain to control further fluid loss. The latter may occur from haemorrhage or rhinorrhoea from middle third fractures.

It is best not to delay long if transfusions are necessary and the precautions outlined in Part II, Chapter II, should be observed. Plasma or whole blood should be chosen according to the principal type of fluid loss.

Death from irreversible shock can usually be avoided if the surgeon is thoroughly conversant with the condition.

Anaphylaxis.

Supersensitiveness is a condition of abnormal susceptibility to articles of diet or drugs acquired by an initial sensitising contact with the particular substance; the term, idiosyncrasy is best used when the sensitiveness may be natural. The development or presence of antibodies against the offending substance would appear to be the cause of the phenom^{on}.

When such antibodies have been produced against normally harmless varieties of foreign protein, the patient has become anaphylactic

Chapter VII. Cont'd.

(Muir, op. cit. p. 194). There is a close analogy between immunity and anaphylaxis. The antigen -- antibody reaction may take place within the cells (cellular theory), but there is a possibility that the toxic reaction takes place in the blood stream.

Heterologous serum (e.g. the horse serum of antitetanus injections) may cause a human to be anaphylactic and cases are occasionally reported of anaphylactic shock occurring following penicillin injections. Symptoms are dyspnoea, pallor, pain in the back and a rapid fall in blood pressure. Within minutes the patient may die. (6) Some have ascribed the accidents to the procaine of some preparations, (7, 8) but it is wise to perform sensitivity tests on patients who have previously had antibiotic therapy or who are suspected of having an allergic state.

Emergency measures in anaphylactic shock consist of applying a tourniquet above the site of injection, or administering adrenalin.

Rheumatic heart disease is significant in dentistry. 'Rheumatic Fever' accounts for nearly half of the total heart conditions and usually occurs early in life. The disease is so named because an acutely painful arthritis is a characteristic symptom but it is essentially a pancarditis, that is, the endocardium, ^{myocardium} myocardium and pericardium are involved. The exact aetiology is not fully understood but there is a close relationship to chorea and streptococcal diseases such as scarlet fever and tonsillitis. Oral sources of streptococci have been suspected. It appears that the original lesion is frankly streptococcal but that other systemic manifestations are allergic. Coombs, Crane and Martin (op. cit.) state that rheumatic heart disease is the result of damage to the heart during and following rheumatic fever. It is essentially a disease of childhood and adolescence.

The onset is usually rapid, with severe constitutional symptoms -- acute arthritis appearing first at the knees and soon becoming manifest in other joints. At times, these symptoms are felt merely as 'growing pains' but severity is the rule. There is a fever and 'a mild encephalitic meningitis produces St. Vitus' dance or chorea' (Muir op. cit. P. 343). About 30% of the patients recover fully; death often occurs, and in the

Chapter VII. Cont'd.

remainder the heart is permanently damaged and recurrences occur. The endocardium covering the valves is affected with ^{vegetations} vegetations and as the condition becomes chronic they thicken with scar tissue to produce mitral and tricuspid stenosis. The mitral valve is more regularly affected. Aortic valve recurgitation imposes an increased load on the myocardium. A diastolic murmur develops. The inflamed pericardial surfaces produce the sound of 'pericardial friction rub.'

In those cases where permanent heart lesions remain, recurrence is likely.

Sub-Acute Bacterial Endocarditis.

Caused by organisms of low virulence, usually streptococcus viridans, this condition has significant dental implications. Sometimes the lesions on the valves are acute with large masses of crumbling vegetations but the sub-acute form is far more common. Muir (op. cit.) accepts dental sepsis as a factor in aetiology. A preexisting congenital defect or valves damaged in rheumatic fever provide the ideal site for bacterial lodgement. Vegetative fragments may then become detached to be transported in the blood stream to other parts of the body. Thus, septicaemia, embolism and heart disease are the three manifestations of infective endocarditis. There is usually an irregular pyrexia, anaemia and a variable leucocytosis. Embolic nodules in the skin are a painful sign, and focal nephritis is another important complication. A fatal termination is common.

The value of penicillin in preventing this condition when surgery is performed for patients with existing heart lesions serves to illustrate that antibiotic therapy should be reserved for such important functions.

CARDIAC INSUFFICIENCY.

When cardiac reserves are greatly diminished, an inadequate venous return causes venous congestion, manifested by breathlessness on mild exertion. There is an insufficient oxygenation of the blood and in the more severe cases cardiac failure may result from the toxæmia of infections, exertion or some special incident. 'Do you become breathless with mild exercise?' should be a routine question in the oral surgeon's office. It is not his responsibility to treat these conditions but he should avoid

Chapter VII. Cont'd.

precipitating cardiac crises. Full medico-dental co-operation is required in the treatment planning of all patients with a history of heart disease.

CARDIAC CRISES IN THE SURGERY.

Auricular fibrillation in which the auricles tremble rather than contract may occur in a number of cardiac diseases and is one of the most common arrhythmias. There is a varying interval between ventricular beats, and the number of apex beats often exceed the number of pulse beats. The beats vary in intensity. Emergency treatment consists of administering 3 - 10 grains of digitalis.

Acute congestive heart failure.

Right-sided failure, is recognised by a marked cyanosis, palpitation and precordial pain and dullness on percussion over the liver. The area is painful. In an emergency, $\frac{1}{4}$ grain of morphine sulphate may be injected subcutaneously and oxygen administered.

In left sided failure, with pulmonary congestion and 'cardiac asthma', prompt administration of oxygen may relieve the condition. A subcutaneous injection of $\frac{1}{2}$ grain of morphine sulphate can be used. The Adams - Stokes syndrome results from ventricular failure, with unconsciousness, and convulsive seizures. The surgeon may detect an abnormally slow heart rate or there may be rapid venous pulsations. Death may occur very suddenly. In severe crisis, 0.5 to 1.5 ccs. of 1 : 1000 adrenalin solution is injected directly into the heart muscle. In less severe attacks subcutaneous injection of $\frac{1}{2}$ to 1 ccs of the solution repeated if necessary at half hourly intervals will usually succeed.

Paroxysmal tachycardia may often be relieved, by pressing over the carotid sinuses.

Morphine sulphate may be used in coronary occlusion and pulmonary embolism.

The surgical risk in cardiac patients need not be over emphasised but operations should be avoided in angina pectoris, renal heart disease and following coronary thrombosis. (Coomes et al., op. cit.)

Patients with Angina pectoris are the poorest surgical risk.

Chapter VII. Cont'd.

EPILEPSY.

Epilepsy is a condition of nervous instability characterised by fits and convulsions. Not infrequently there is a family history. French ⁽⁹⁾ states that the convulsive attacks vary in extent and duration. In the minor form, 'petit mal,' there are usually brief tonic or tetanic spasms without loss of consciousness. In the severer cases, 'grand mal' or 'major epilepsy', the attack usually occurs in stages. First, there is the aura or warning which follows a definite form for each patient and lasts only a few moments. The patient usually becomes pale, utters an involuntary cry and loses consciousness. In the tonic stage, lasting from five to thirty seconds, the patient falls to the ground and remains rigid. Then follows the convulsive or clonic stage with jerking movement, frothing at the mouth and violent movements of the arms and legs. At this stage the tongue is often bitten, and should the attack take place in a surgery, a gag may be used to prevent such damage. Occasionally there is incontinence of the ^efacies or urine. Finally, there is a period of 'automatism' perhaps lasting for some hours during which time the patient is in a stupefied state. The patient should be allowed to sleep.

Until recent times, epileptics were treated with sedatives and a ketogenic diet. Recently, however dilantin sodium (dose $\frac{3}{4}$ to $1\frac{1}{2}$ gr.) has proved to be a valuable therapeutic agent. Unfortunately toxic effects are frequent. They include dizziness, nausea, tremors, fever, blurring of the vision, ataxia, mental confusion and hallucinations. ⁽¹⁰⁾

Skin rashes and gingivitis are common. Thoma-Robinson ⁽¹¹⁾ estimate that it occurs in over half the patients being treated with sodium dilantin. A sore mouth is noticed within a few weeks of the first administration. This may disappear to be followed by a hypertrophy beginning at the interdental papillae. The enlargement is then firm, painless and of normal colour. The fibrous tissue may be covered and surgical excision may be necessary.

In this and other conditions described in this review, the oral surgeon, though not able to assume sole responsibility for treatment, is an important member of a team co-operating to relieve human distress.

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