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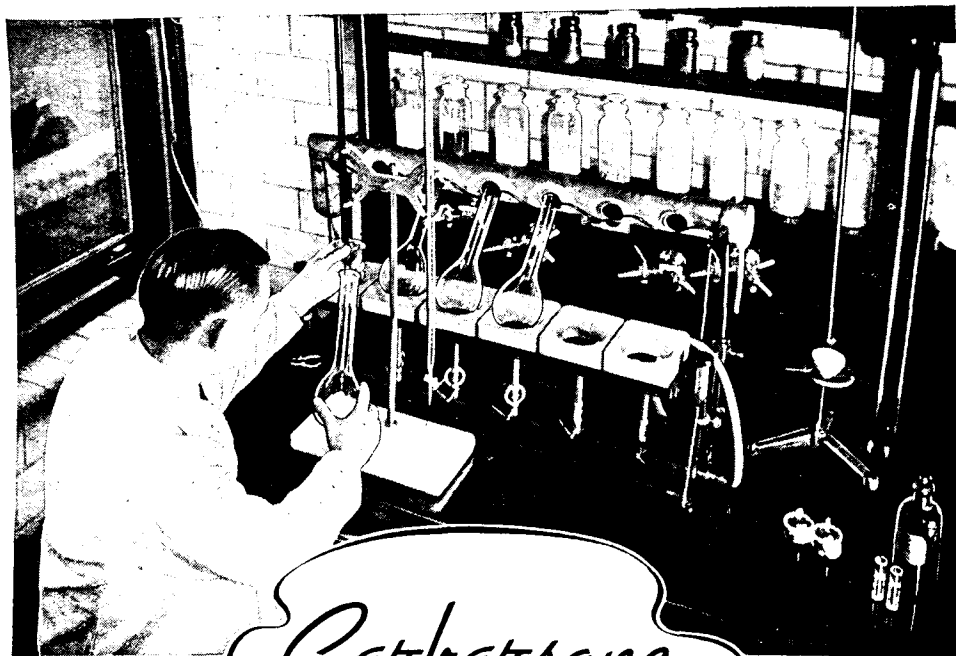
A Monthly Medical Journal

Edited by

Dr. U. Rama Rau & U. Krishna Rau, M.B., B.S.

CONTENTS.	PAGE.
TUBERCULOUS DISEASE OF BONE. By Lt.-Col. M. M. Cruickshank, I.M.S., Prof. of Operative Surgery, Medical College, Madras. ...	129
THE PRESENT POSITION OF SURGERY AND RADIUM IN CANCER. By Dr. E. S. Gopalan, M.B.B.S., Hony. Assistant Surgeon, Govt. General Hospital, Madras. ...	138
THE COMPLICATIONS OF GONORRHEA IN THE MALE AND THEIR TREATMENT. By Dr. M. Rathnavelu, I.M.S., Honorary Assistant Surgeon, Venereal Department, General Hospital, Madras. ...	160
THE TREATMENT OF BURNS. By Dr. B. M. Sundaravadanam, F.R.C.S. Hony. Surgeon, Govt. General Hospital, Madras. ...	170
URETERAL CALCULI AND THEIR TREATMENT. By Dr. N. Mangesh Rao, M.B.C.M., F.R.C.S., Surgeon, Govt. General Hospital, Madras. ...	176
VISUALISATION OF THE URINARY TRACT FOR DIAGNOSIS. By Dr. N. Mangesh Rao, M.B.C.M., F.R.C.S., Surgeon, Govt. General Hospital, Madras. ...	183
VISUALISATION OF LOWER URINARY TRACT. By Dr. N. Mangesh Rao, M.B.C.M., F.R.C.S., Surgeon, Govt. General Hospital, Madras. ...	188
SURGICAL TREATMENT OF FILARIAL INFECTIONS. By Dr. B. M. Sundaravadanam, F.R.C.S. (Eng.) Hony. Surgeon, Govt. General Hospital, Madras. ...	193
SOME SURGICAL EMERGENCIES IN GENERAL PRACTICE. By Dr. D. Subramaniam, M.B.B.S., Civil Assistant Surgeon, Govt. General Hospital, Madras. ...	199
Editorial:— THE MADRAS UNIVERSITY EXTENSION BOARD LECTURES. ...	207

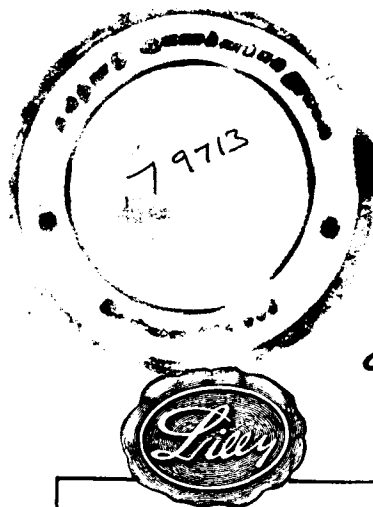
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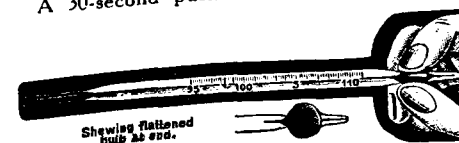
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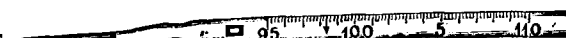
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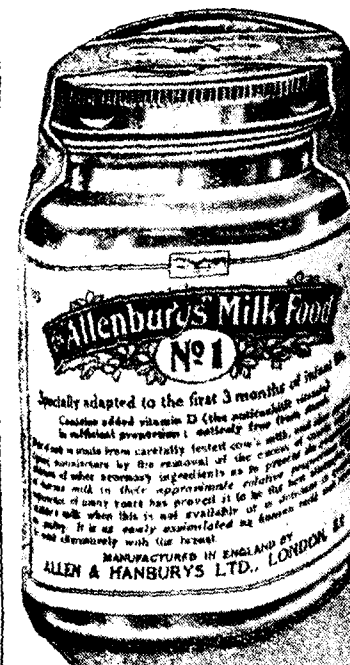
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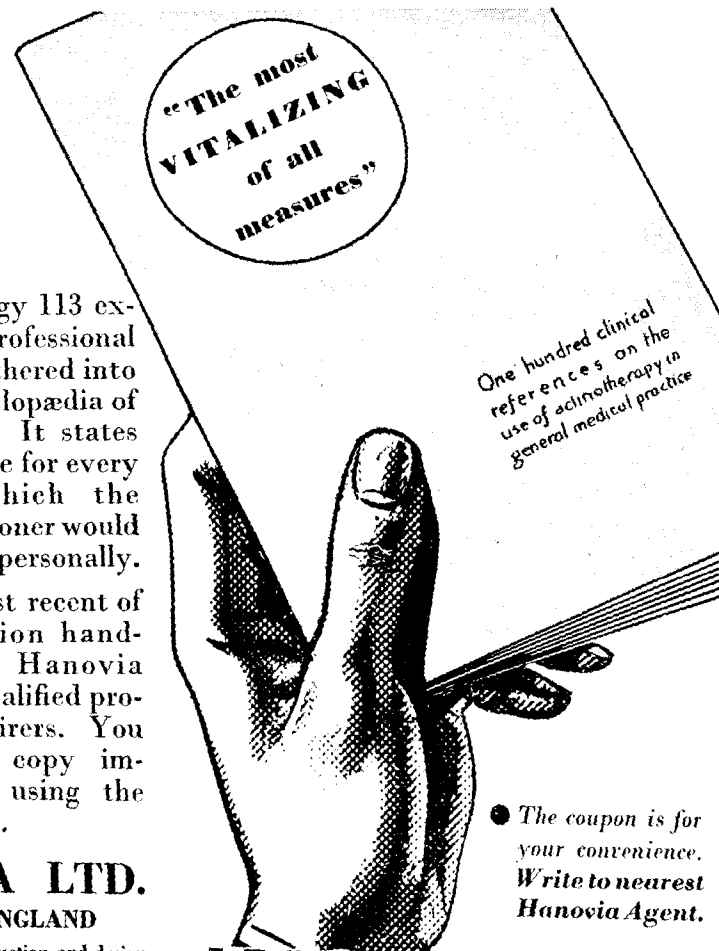
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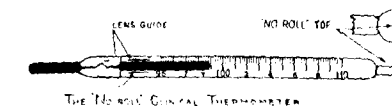


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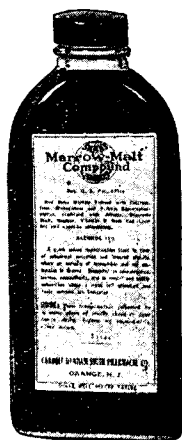


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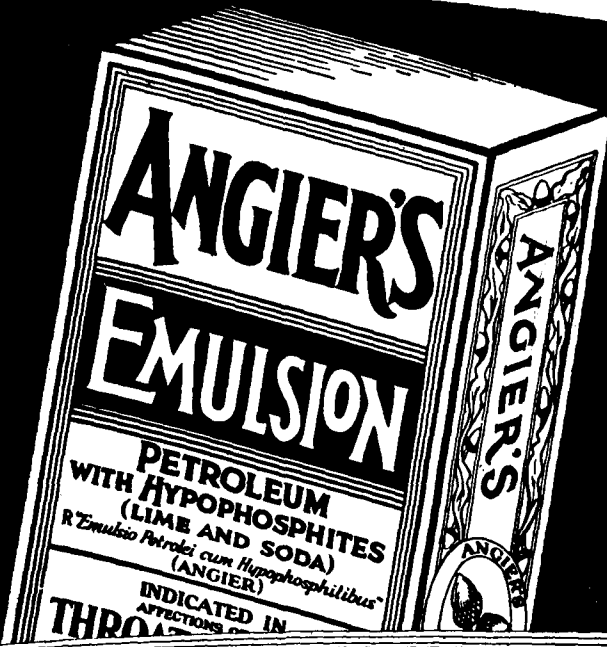
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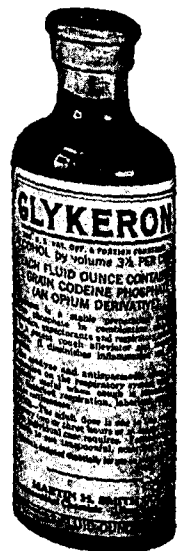
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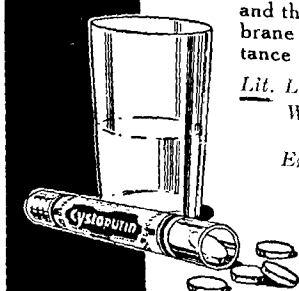
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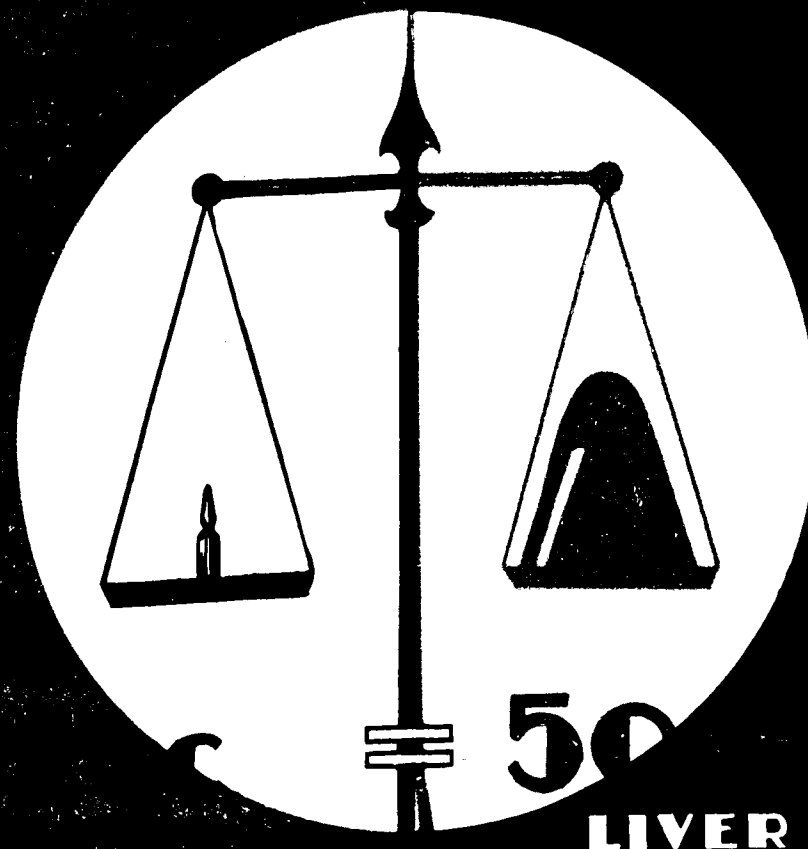
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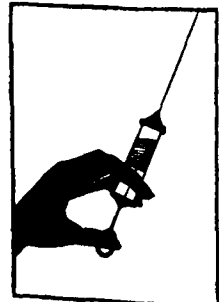
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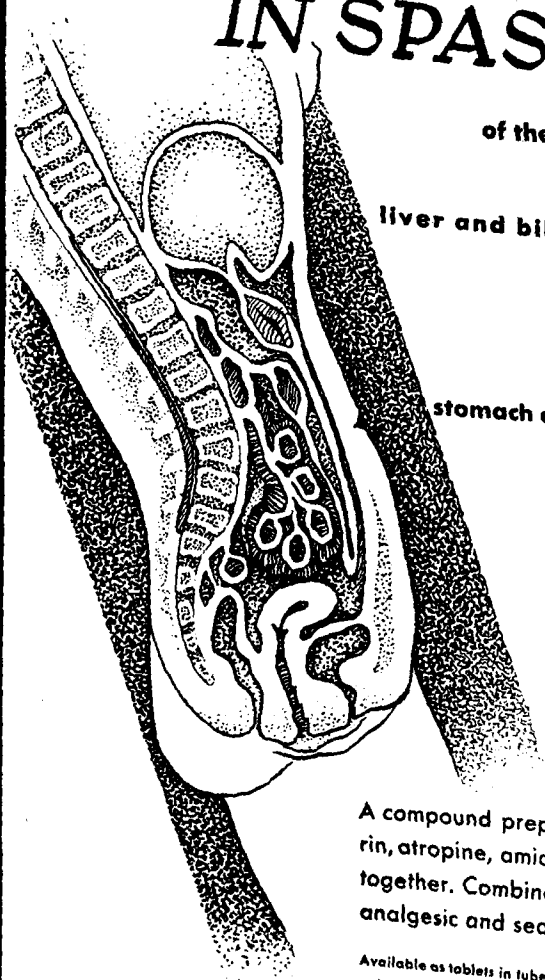
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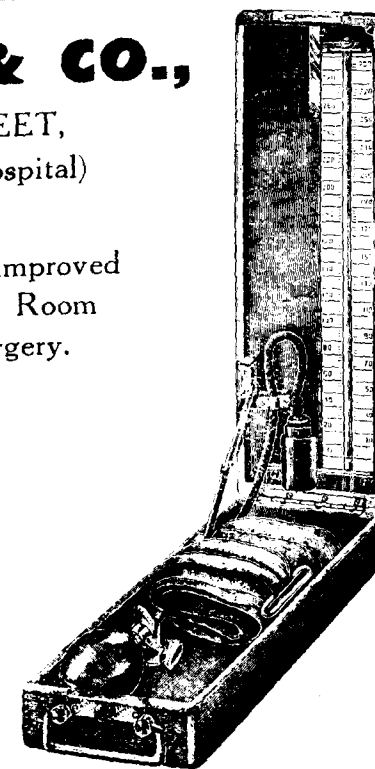
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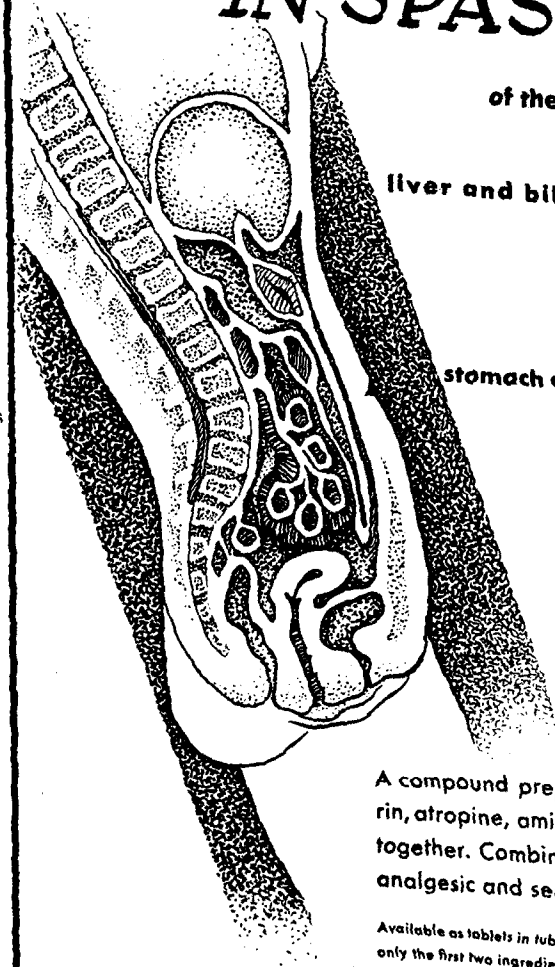
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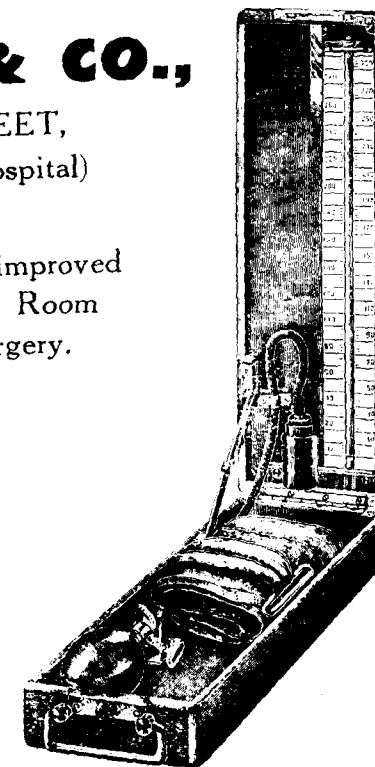
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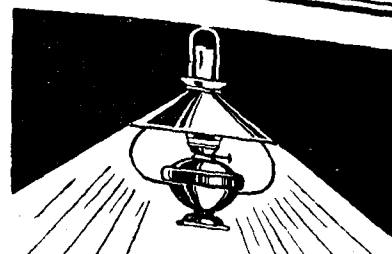
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Berlin, This 10th day of November, 1933.



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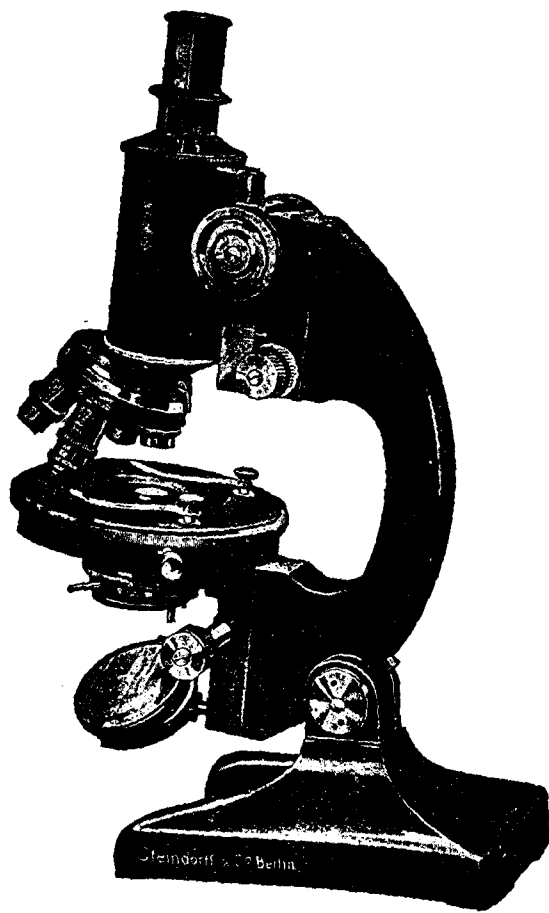
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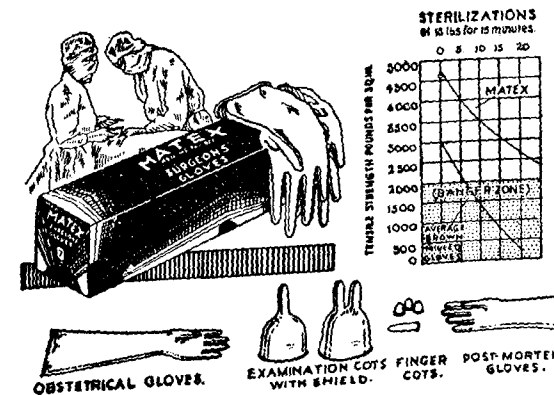
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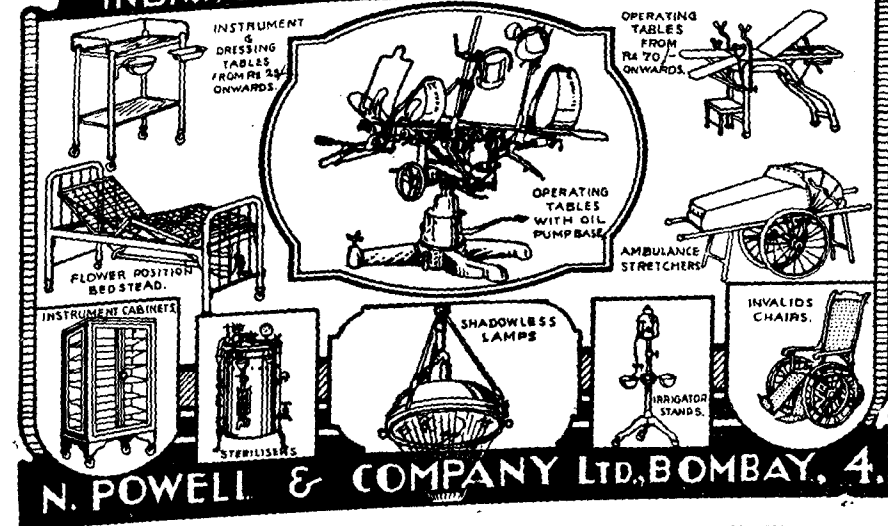
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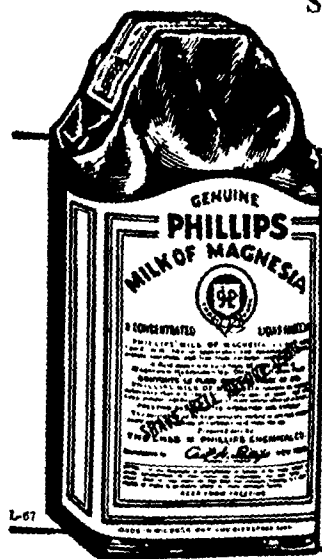
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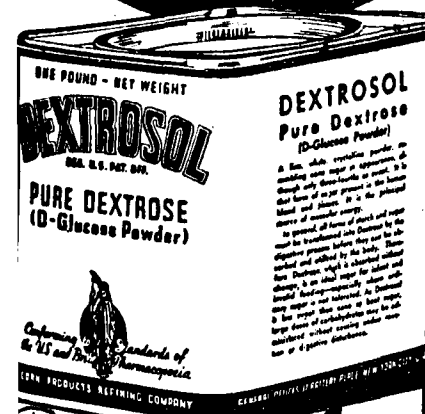
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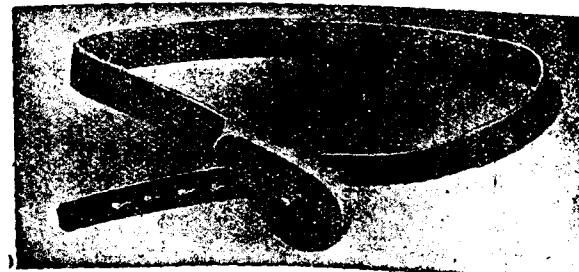
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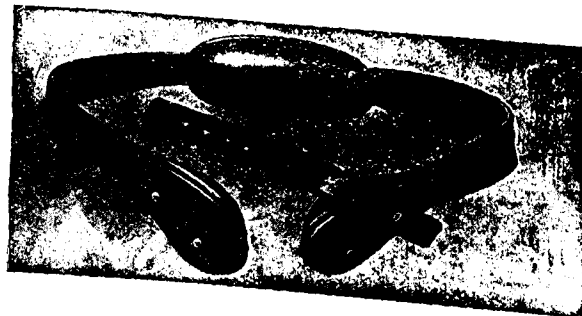
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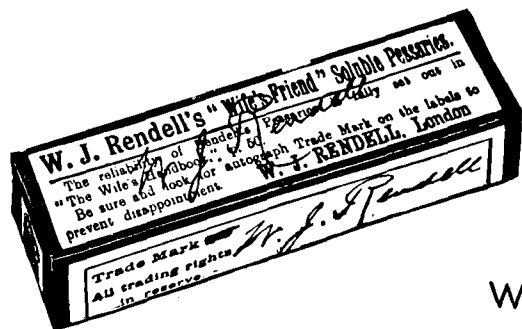
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(Address given by Dr. J. C. Drummond at St. Mary's Hospital, London, 17th May, 1934.)

"The Conference recognises that amounts of cod-liver oil and irradiated ergosterol which contain an equal number of vitamin D units, as determined by tests with rats, may not possess equal anti-rachitic activity when tested on certain other species—e.g. poultry."

(League of Nations, Quarterly Bulletin of the Health Organisation, September, 1934.)

Scientific evidence is now rapidly accumulating to indicate that in the prophylaxis of rickets and other bone diseases, the natural vitamin content present in butter and cod-liver oil is more reliable and effective than that artificially produced by irradiation.

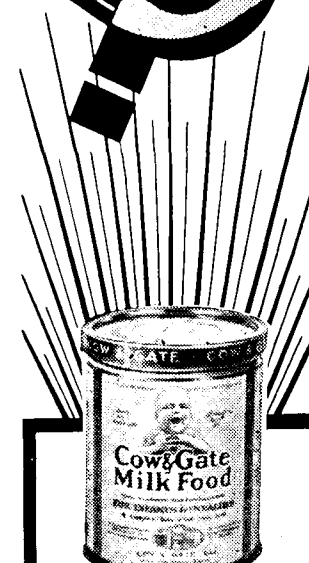
Even Steenbock, the American pioneer of irradiation, has admitted (Jnl. Biol. Chem., July, 1932) that:—

"Ergosterol and yeast when activated anti-rachitically by ultra-violet radiations are inefficient sources of vitamin D for the chicken. Whereas 1 per cent of cod-liver oil of average potency resulted in normal bone formation, it required from 40 to 120 per cent of cod-liver oil equivalence as irradiated ergosterol and from 7.5 to 60 per cent cod-liver oil equivalence as yeast to produce the same result."

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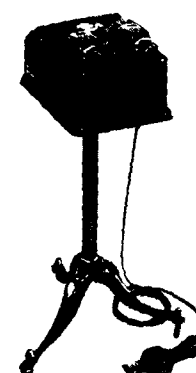
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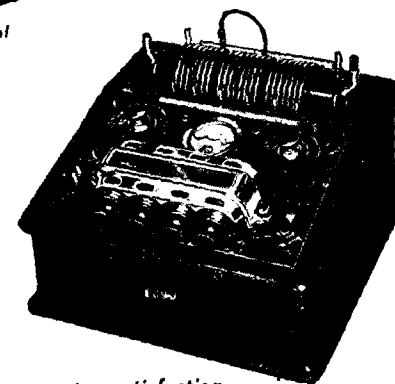
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"Micro" Surgical Diathermy Unit



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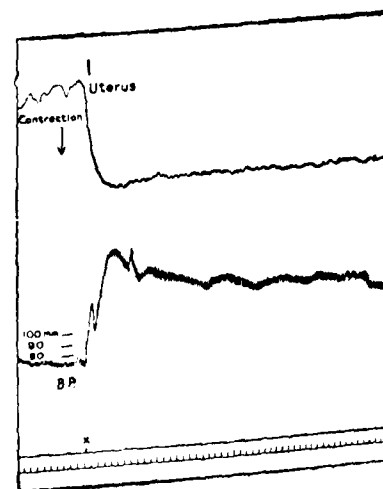
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ESTD. 1904.

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TUBERCULOUS DISEASE OF BONE

BY

LIEUT. COL. M. M. CRUICKSHANK, I.M.S.,

Professor of Operative Surgery, Medical College, Madras,

BONE tuberculosis is a chronic inflammatory condition and an osteomyelitis with secondary periosteal involvement occurring in early life, choosing particularly the ends of long bones, the short long bones and the short bones; displaying as a rule an excess of bone destruction over bone formation and yet with a decided tendency towards limitation of spread and spontaneous healing owing to the same fibrous tissue formation, so characteristic of tuberculous disease in the lungs and other organs.

Though essentially a disease of childhood and of adolescence, it may become manifest at any age, even in senility, but in these older patients it can be proved to be a recrudescence of any affection, latent perhaps for many years.

Route of Infection.—The infection is carried to bone by the blood stream probably in the form of a tuberculous embolus from some other part of the body.

Site of infection.—Tuberculosis commences in cancellous bone, seldom in compact bone.

The most frequent sites are, ends of long bones especially the tibia and femur, the short long bones, the short bones of the tarsus and vertebrae; as all of these are in close proximity to joints, bone and joint tuberculosis are very frequently associated.

The common situation to be affected is usually the metaphysis, occasionally the epiphysis of a long bone.

Both are richly supplied with capillary loops in which an infected embolus may lodge.

The *circulus vasculosus* (of Hunter) containing the vessels responsible for carrying the infection lies in the reflection of the synovial membrane on to the bone. When the reflection includes the metaphysis as at the upper end of the femur, the disease will originate in that part; when on the other hand the reflection lies entirely in relation to the epiphysis as at the upper end of the humerus and to a lesser extent at the lower end of the femur the primary focus will be in the epiphysis, but another factor is present which may well determine which bone is to be attacked. The blood vessels which supply the bone become affected with tuberculous endarteritis, due to the circulating tuberculous toxin.

The nutrient arteries of the short bones are especially so affected, and as a result the bone marrow undergoes a gelatinous or fibromyxomatous degeneration, and in such a bone tuberculous osteomyelitis readily develops.

Occasionally the diaphysis is affected.—Why? Typical tuberculous diaphysitis is seen in the affection of the phalanges, metacarpals and metatarsals and in the bodies of the vertebrae.

There are two considerations which explain the development of this form of the disease.

1. The vascular distribution in the smaller bones is peculiar; the nutrient vessel as soon as it enters the interior of the bone, breaks up into a complete network of vessels and there is therefore a tendency for any circulating tuberculous material to be held up before it reaches the metaphysis.

2. The nutrient vessel is sometimes the site of a tuberculous endarteritis and the peculiar marrow changes which appear secondary to this condition are responsible for the lodgment and development of the tuberculous lesion.

This is the influence which explains the infection of the larger long bones.

The common forms of tuberculous diaphysitis such as "spina ventosa" are practically confined to the earlier years of life, because it is during this period that the nutrient vessel is the main source of blood supply. After growth has ceased the periosteal vascular supply becomes of greater importance than the nutrient and there is a corresponding fall in the incidence of tuberculous diaphysitis.

Occasionally the Epiphysis is affected.—Why? The impres-

sion abroad is that the epiphysis like the metaphysis is frequently the site of tuberculous disease, but this is not so. The error has arisen through erroneous nomenclature and confusion of the terms metaphysis and epiphysis.

There are however conditions in which a tuberculous epiphysitis does occur.

The most common is the secondary infection which extends from a related infected joint.

The second condition is an anatomical one. If the reflection of the synovial membrane is related only to the epiphysis and does not extend on to the diaphysis, then that epiphysis may become the site of a primary tuberculous epiphysitis, because into such an epiphysis a large number of vessels enter from the neighbouring joint and it is therefore liable to be infected from the joint itself or by a blood borne infection from other parts (Fraser). Such a statement might give one the impression that tuberculous epiphysitis is rare but this is not so in long bones.

As Greig puts it, "in long bones the initial tuberculous infection does not occur so invariably at the metaphysis as does the acute septic process; commonly it is epiphyseal and as such, may by early perforation, cause a tuberculous arthritis or more rarely spread towards the marrow cavity. When the tuberculous affection begins in the diaphysis it may be periosteal but more frequently is endosteal or medullary. Of the long bones the tibia is probably the most commonly affected".

Changes which result from the lodgment of the Bacilli. The Primary Bone lesion.

Probably the bacilli become deposited by an extravasation of blood, from a vessel, the wall of which has been previously weakened by Tuberculous endarteritis.

In the effused blood the Bacilli form, just as they do in tuberculous elsewhere and as a result of their growth a typical tuberculous follicle is found with giant cells, epithelioid cells and lymphocytes, a central mass of endothelial cells with a surrounding zone of lymphocytes—a miliary tubercle. A mass large enough to be apparent to the naked eye, a small translucent greyish white area in the centre of the marrow. Changes appear at the centre, caseation occurs and at the periphery there is an attempt at fibrosis and localisation of the follicle—the grey tubercle has now become a yellow tubercle. Independent of the growth of the miliary tubercle changes appear in the various constituents which comprise the bone.

tuberculous granulation tissue and in virtue of the granulation tissue is undergoing rapid decalcification. It never forms a true sequestrum, a dead homogeneous entity, unless sepsis be super-added.

In the absence of sepsis any dead osseous tissue will be dealt with by the inflammatory process and will ultimately disappear, its decalcification providing an immense amount of excess calcium which goes to form the light porous fusiform involucrum, standing well away from the necrotic shaft, so characteristic of tuberculous dactylitis. It is misleading to speak of this granulation—impregnated necrotic osseous tissue as a "sequestrum", it is not isolated, but retains its attachment to the extremities of the metatarsal and is connected freely with the new porous bone in which it is encased. If closely examined the "sequestrum" if large will be seen to be porous.

Tuberculous Periostitis

While usually associated with tuberculous osteomyelitis, it may occur as a separate entity. It is usually found in superficially placed bones but may occur in the long bones. The pathological process is due to the presence of tubercles and their toxins, producing a hyperaemia in the periosteum with slight serous exudation with resulting rarefaction of cortical bone: this is later replaced by light porous subperiosteal bone. Excess of this porous spongy bone on one aspect of the bone as compared to another is due to posture, the exudate raising the periosteum further from the bone over the dependent parts.

Superficial bones such as clavicle, sternum, ribs, vertebrae, skull, occasionally show this new bone formation. It is much less frequently seen in the long bones of the limbs.

In superficial bones such as the sternum the formation of tuberculous granulation tissue in the deeper layers of the periosteum and its subsequent caseation and liquefaction is attended by the insidious development of a doughy swelling which is not as a rule painful, although tender on pressure. While the swelling often remains quiescent for a time, it tends to increase in size, to become boggy or fluctuating and to assume the characters of a cold abscess.

In deeply seated bones such as the upper end of the femur the formation of a cold abscess in the soft parts is often the first evidence of the disease.

The Progress of the Disease—Pathological Varieties

Tuberculosis may behave in various ways in bones as in

other organs. It is unnecessary to introduce a special series of names to denote different varieties. It is sufficient to recognise

BOYD	FRASER
1. a localised form.	1. encysted.
2. a spreading form.	2. infiltrating.
3. an atrophic form or caries sicca	3. atrophic.
	4. hypertrophic ? mixed with syphilis.

The localised form is much the commonest and most chronic. The defence is sufficiently strong to hold the disease in check and this form corresponds to a localised nodule in the lung. The lesion, which is about the size of a marble presents a centre which is either caseous or converted into a semi-fluid material.

Around this is a pale pink zone blending with the surrounding marrow. This is the limiting band of new fibrous tissue. The condition is essentially chronic so that the slow process of rarefaction results in complete absorption of the lamellae. If the lamellae are not absorbed completely, then they separate as and form small sequestra.

The spreading form.—Where the fibrosis is insufficient to limit the spread of the disease, it corresponds to a diffuse tuberculosis of lung. The central caseous mass is surrounded by a zone of gray infiltration representing tuberculous granulation tissue which has not yet become caseous. Around this there is a red zone of reaction.

Thrombosis of vessels which occur early greatly weakens resistance. Rarefaction is not so marked, because active processes are arrested and necrosis supervenes, with the formation of comparatively large sequestra. The disease may spread down the medullary cavity until the greater portion, or the whole of the shaft is involved. It may spread to the cartilage of conjugation and involve the epiphysis and neighbouring joints. It may spread to the periosteum and form a sub-periosteal abscess. It may ultimately discharge on the skin. Where the medullary spread is marked, expansion of bone with deposition of new bone is seen as in tuberculous dactylitis.

The atrophic form.—Caries sicca is a rare condition chiefly affecting the upper end of the humerus. The deeper portion of the bone becomes rarefied owing to the formation of granulation tissue and new bone is deposited on the surface which itself in turn becomes eroded. Finally the granulation tissue becomes dried and fibrosed.

With the replacement of marrow by granulation tissue, the bone lamellæ undergo a rapid absorption. The process begins in the centre of the medulla and gradually extends to compact bone at the periphery: the lacunae are increased in size and the whole appearance is one of extreme porosity.

True suppuration never occurs.

The changes may extend to articular cartilages but never involve it.

The absorption is due to the activity:

- (1) of osteoclasts; (2) of granulation tissue.

A periosteal hyperaemia brings about a deposition of subperiosteal new bone which tends to become absorbed near the original shaft, so that a ring of granulation tissue lies between the new bone and the original shaft. This goes on and on giving an increased but unstable circumference.

"Tuberculous osteomyelitis as seen in the long bones and short long bones has no counter part in the bones of the cranium and face. In the membrane, bones of the skull tuberculosis is of the greatest rarity, yet tuberculoma of the brain and tuberculous meningitis are common occurrences.

There is a vast difference between the anatomical and functional relations of the pericranium on the outer table and the dura mater on the inner table, to the cranial bones, and the periosteum and endosteum in the long bones, and the parallelism between the diploe and the marrow cavity.

In the long bones the central canal is naturally evolved as being an essential part of the mechanism of stability under the stress and strain to which such bones are subjected by function and by muscular strain; but the diploe is a covered way whereby the venous intracranial circulation finds ready transference by an alternative route in the event of unilateral temporary obstruction, be it postural or from extraneous pressure.

In the limbs temporary obstruction to the venous return is met by the system of superficial subcutaneous veins, but in the calvaria, the physical features of the scalp and of the galea aponeurotica make impossible a similar arrangement of such superficial cisterns for venous overflow. The prime importance to the organism of the intracranial contents make it imperative that venous congestion be avoided and for this no more efficient plan than the venous canals of the diploe could be devised. The occurrence of true intraosseous tuberculosis is practically confined to the zygomatic bone. When tuberculosis occurs the osseous changes

are due to the hyperaemia it provokes and they conform to the changes found in the milder inflammatory conditions and are sooner rather than later complicated by the addition of sepsis.

When tuberculosis does occur in the skull it begins in the diploe and extends outward so as to perforate the outer table. It is found most commonly in children and in the frontal, parietal and temporal bones, and usually with the formation of a fine, worm eaten, circular sequestrum.

The pathology of Pott's Disease cannot be discussed here, but two points with regard to tuberculous disease in a vertebrae must be borne in mind:

- (1) that the varieties of the disease in a vertebrae depend on the blood supply of a vertebrae;

- (i) Medullary; (ii) Epiphyseal; (iii) Periosteal; (iv) Anomalous;

- (2) that while compression of the cord with paraplegia may be due to

- (i) oedematous membranes; (ii) tuberculous granulation tissue; (iii) abscess formation; (iv) sequestrum or tissue debris; (v) pathological dislocation;

yet paraplegia may arise apart from mechanical compression as a result of toxic and vascular changes, which often account for transitory paraplegias; this is due to repeated minor circulatory damage by chronic disease going on year after year with little outward sign.

THE PRESENT POSITION OF SURGERY AND RADIUM IN CANCER

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PART I

I PROPOSE to discuss the subject under the following sub-headings :

- (1) The problem of cancer in Madras ;
- (2) Evolution in the treatment of cancer ;
- (3) The cancer cell ;
- (4) Pathological basis of the modern surgical treatment ;
- (5) Scope of pure surgery in cancer.
- (6) Properties of radiation.
- (7) Pathological basis of the action of gamma rays ;
- (8) Scope of radio-therapy in cancer,
 - (a) to the exclusion of surgery,
 - (b) combined with surgery.
- (9) The clinician and the technician.
- (10) Future of cancer management.

1. The Problem of Cancer in Madras

To those of us, medical men and medical students, who attend the surgical out-patients of any large hospital in Madras, it is easy to find at a glance the tremendous amount of humanity of cancer is one of the most interesting, fascinating but elusive studies in the realm of human pathology, the problem of disposing these patients, major portion of them being hopelessly inoperable and untreatable, in the surgical out-patients, from day to-day is really disgusting to the medical man concerned. The poor wretches, objects of pity, come from long distances, after spending their meagre fortune in railway fare, practically penniless. Some who could not afford even the railway fare, manage to reach Madras after protracted and interrupted journey, receiving attention from the ticket examiners at practically all junction stations, as honorary guests of the railway companies. If the medical man sitting at the out-patient refuses admission, he is driving a poor man out, who requires immediately food rather than treatment. If he admits them he incurs the displeasure of the higher

authorities for increasing the number of mat-patients (by mat patients I mean, extra-patients who are accommodated in Korai mats on the grounds). At any rate, some of these poor fellows can be prevented from getting in for a few days. A few of them learn the trick of tearing the old out-patient ticket and presenting themselves before another medical man as a new case with varying success. But the patient coming from a district, under the authority and advice of a D. M. O., travelling at government expense, with a covering letter to the R. M. O., no matter how advanced or incurable he is, has to be admitted for obvious reasons. This cancer problem so far as Madras is concerned is really very serious. The influx of patients in the General Hospital has recently, markedly increased after the advent of radium in the institution. The illiterate people talk of radium as magnetic needle (காந்தப் பூக்காய்), meaning thereby not in the physicist's conception of magnetism, but in the lay man's conception of the wonderful and supernatural. Really radium is wonderful and demoniac in the destruction of some of the cancers and sarcoma cells. A demoniac disease like a sarcoma or carcinoma requires an equally or more powerful demon. If the properties of the radium demon are properly understood, harnessed, and utilized to destroy the cancer demon before it assumes proportions, and spreads its nests and colonies, the exorbitant price paid for purchasing the radium demon, is money well spent.

In Hindu mythology the ten headed monster of Lanka was said to have been indestructible in human hands. It is said that if one head is cut off, another head immediately sprouts. So also is radium which is practically indestructible, said to lose 50% of its potency in 1690 years, a valuable possession for any one who knows its use, perhaps more valuable than the Kohinoor diamond or the peacock throne of Shajehan. All of us will die, so also our children, our children's children, etc., the General Hospital or the Barnard Institute of Radiology may not exist but the radium purchased by the Government of Madras, should exist even after two thousand years, if not thrown into inaccessible places wantonly or by terrestrial cataclysms like Bihar and Quetta earthquakes. With this little digression, more to illustrate what a mighty weapon we have in radium, I shall just enumerate some figures taken from the records of Col. Pandalai's cases for the year 1934 in the General Hospital. These figures are taken just to give us an idea as to the magnitude of the cancer problem in Madras.

Total number of in-patients—1,779.

employment of safer anæsthetics, the surgical treatment of cancer, in regions accessible to surgery, has grown and grown till at the early decades of the present century, one can almost say that perfection has been attained in the technique of operative surgery. Lord Moynihan in his inimitable style has been saying repeatedly that the technique of operative surgery has reached its zenith though this statement has been questioned by Lord Dawson of Penn and others. To a certain extent Moynihan's statement is true though one cannot have a conception of what is going to happen in the next decade. The science of Medicine did not stop with Hippocrates, Galen, Charaka or Susruta. Though hero-worship did stop the clock of human progress and Galileo had to pay the penalty for daring to say the stars could be seen by his telescope; the sacerdotal classes prohibited surgeons from practising in the middle ages, Harvey's *De motu Cordis* and Lister's carbolic spray earned the derision of their contemporaries, the scientific truths have come out unalloyed after having passed through the fire of destructive criticism and derision. No region in the body is inaccessible to the modern surgeon. Even cases of Mitral stenosis have been attempted by some surgeons. The mitral valve has been cut and enlarged by valvulotome, in the same way as a stricture of the urethra is cut by an internal urethrotome. Excision of the thoracic œsophagus has been attempted with success for carcinoma. Torck's patient in America lived for 14 years after an excision, with a rubber œsophagus. Another patient is still living in Great Britain under similar circumstances. Though such heroic surgery is sometimes successful it may not be applicable to the average patient under average circumstances. In my student days, the operation for cancer of the Breast was in my opinion, not correctly performed. The teaching was that the breast and the large area of skin should be removed. The patient was practically flayed alive. Sampson Handley's technique embodying the principle of the removal of the tumour, with a reasonable but not too wide a margin of skin with the growth as the centre, undermining the skin to a diameter of roughly ten inches, excision of the subcutaneous fat, deep fascia, pectorals, digitations of the external oblique, fascia over the serratus magnus and latissimus dorsi; subscapulars Teres Major, the axillary lymphatic contents, areolar tissue and fascia in one continuous piece with the growth, was not adopted. Recurrences were common. So also excision of the maxilla, a frequent sight in my student days, with a preliminary laryngotomy or tracheotomy was one of the bloodiest and mutilating operations. Excisions of the mandible were also

frequently done though they were not so bloody. But the most outstanding achievement in cancer therapy of this century is the discovery by Röntgen in 1895 of X-rays and by Mr. & Mrs. Curie of Radium in 1898. The discovery of the surgical uses of radium was accidentally made, in 1901 from the famous "Bacquerel burn". Bacquerel carried a glass tube of radium in his waist-coat pocket for some hours and about a fortnight later a severe inflammation appeared on his skin. Besnier attributed this to the action of the radium and the caustic effect of the rays was proved by Curie who made a similar experiment on himself. In 1902 on Besnier's suggestion, Curie lent a small quantity of radium to Danlos for clinical experiments at the St. Louis Hospital in Paris; and in 1904 Danlos published an account of the work, which showed that valuable therapeutic results might be obtained with larger amounts of radium. So the application of radium to clinical medicine and surgery, progressively increased in its scope until, at the present time, treatment of certain lesions is practically standardised and others are in the melting pot and perhaps may be standardised in the very near future. The use of short wave hard Röntgen X-rays (the so-called deep X-ray or penetrating rays) is also proving very useful as an accessory to Radium and Surgery. So also surgical diathermy and use of high frequency cutting current by the electro-surgical knife or loupe, is a necessary and a timely addition to our surgical armamentarium specially useful in cancer therapy. Attempts to cure cancer by streptococcus *Erysipelatus* vaccine (Coley's fluid), lead silemide, cobra venom, etc. though reported successful in some cases, have not stood the test of time and may be ignored for all practical purposes. The newer conception of the pathogenesis of cancer and the grading of malignancy should prove very useful to the clinician in his attack. Thus the science of medicine, enriched by the auxiliary sciences of physics, chemistry, biological pathology, etc. and enriching the pure sciences in turn and which has grown from success to success and from tower to tower, will in time, if it has not done so already, be so unwieldy as to stagger the future student of medicine. Just as in the present cancer surgery is dominated by pathology and radio therapy, in the future, Biochemistry, a virile growing science, will have to play a prominent part.

3. The Cancer cell

In the realm of pathological medicine, no subject is more fascinating, and no subject has so far eluded the clinician or research worker as regards its causation and proximate nature.

and specific factor eliminating one and preserving another. Two products, in one of which only the virus was still present and the other only the specific factor, were separately incapable of producing the tumour when injected with fowls, but when mixed and injected together, they did so. The specific factor was said to be thermolabile being destroyed at 55°C. Other workers were not able to confirm the above findings and the virus theory is not seriously maintained at present.

Then the *theory of irritation* exemplified by the Tar cancer of Yamaguchi (1915) came in. It is still holding its own. Numerous irritants such as coal tar, Paraffins (shale-oil), lubricating oil (mule-spinner's cancer), Soot (chimney-sweep's cancer), Aniline (carcinoma of the bladder in dye works employees), Arsenic, light, heat (kargiburn), X-rays and radium, etc., are shown to be carcinogenic. In South India, the so-called chunam cancer is said to be carcinogenic. I do not believe so. Pan is so universally used with chunam that if it were the cause of its frequency must be more. Perhaps tobacco may be the culprit but tobacco is equally used in the Tamil districts as in Malabar and why should there be greater incidence of buccal cancer in Kerala than in Tamil Nadu?

Then there is the *theory of heredity*. As a result of Maud Slye's researches in mice, it is known that susceptibility to cancer behaves as a mendelian recessive character. If it were not so, the whole human race will be extinct. By selective breeding and sub-breeding it was shown that cancer-free and cancer susceptible strains can be bred. If one has to put this theory in practice so far as human cancer is concerned, man, in the words of Lockhart Mummery, "should begin intelligently to control the breeding of his own stock as he has for long been doing with his domestic animals. But the world does not appear to have yet reached a general level of intelligence which renders possible such a step. True, some slight efforts in this direction have been made in America, and just recently in Germany, but it is likely to be many more years before any general advance will be made in controlling the breeding of human beings on scientific lines".

Then there are the genetic theories. The first attempt to construct a *genetic theory of tumours* was made by Theodore Boveri, the Zoologist in 1914 and might be described as the *chromosome transmutation theory*. He had observed abnormal mitosis in sea-urchin's eggs due to transmutation and had noticed that the cells which underwent abnormal division continued to exhibit the same behavior in subsequent generations,

He suggested that tumours resulted from accidental transmutation of chromosomes in the cells of the somatic tissues. A great deal of work has been carried out on this theory, but there is overwhelming evidence that the ordinary tumour cell does not contain abnormal number of chromosomes in the nucleus, so that although Boveri's theory may be the correct explanation of a few rare tumours, it is certainly not correct for the majority.

The latest is the *genetic theory of tumours* as propounded by Lockhart Mummery (1932). The vital factor in a cell is its chromosomes. Says he "It is evident that the original cells from which the adult organism started, the fertilized ovum to which nothing has been added except food materials, must contain units within it for each different kind of cell found in it in the adult organism, and for their behavior in response to changes in the environment what may be called their character and constitution. Thus one adult organism is less subject to certain diseases than others, one is less affected by cold and heat than the other, one is braver and one more cowardly, one is clever and another is stupid. All the physiological differences, as well as the morphological differences, are controlled by unit factors which must be present in the nucleus or cytoplasm of the original cell from which they all arose. We must visualize millions of distinct characters all of which are contained in the one cell, but there are not necessarily units for each. Several different units or genes are involved in such a single character as blue eyes or fair hair. The manner in which the genes control the differentiation of cells and characters is very complicated and quite beyond our present understanding, but that all necessary unit characters are present in the original cell is certain, for, in no other way can we explain the complexity of the adult structure which has developed from a single cell with no addition except food material. Biologists have christened these units "genes". These units or genes bear the same relationship to the living structure that atoms bear to the elements in physics".

A change in one or more of genes which are in the chromosomes is called gene mutation. If a single cell in an adult organism mutated no obvious result would occur, since the result in a single cell would be negligible and adult cells though they divide do not increase in numbers. But as the rate of mitosis of cells must also be a gene character, then it follows that if a mutation for an excessive rate of mitosis occurred or could be produced artificially, the result would be seen, even if the mutation took place in only one adult somatic cell, because the number of cells carrying the mutant genes would in course of time increase until a visible and

effective result was produced. So mutation for "excessive rate of growth" produces a benign tumour and secondary mutation for more rapid division and infiltration of connective tissue produces a malignant tumour. In spite of this plausible ingenious explanation it is difficult to understand why there should be a mutation of a gene.

There is an attempt at the Biological explanation of the origin of malignant tumours. This is the phenomenon known as aerobic glycolysis first observed by *Otto Warburg*. "Glucose can be utilized by the cell for the production of energy in either of two ways. It may be oxidised with the formation of carbon dioxide and water, a process which is only possible when oxygen is available, or it may be broken down into lactic acid (glycolysis), an alternative to which the cell may resort when oxygen is lacking. The normal cell gains the greater part of its energy by the former process and resorts to glycolysis only in consequence of oxygen lack. Warburg's discovery was that malignant tissue utilizes glucose by glycolysis whether oxygen be available or not. All cells are capable of glycolysis, some perhaps in any given tissue more than others, whether as the result of vascular changes, pressure, sclerosis, or infection, those cells in it whose glycolytic power is weak will die: the survivors already capable of and forced to employ glycolysis, assume the habit of it, and the type of metabolism characteristic of the malignant tumour is established in that tissue.

The frequency of vascular changes tending to diminish the blood supply in tissues in which cancer commonly arises lends colour to this idea. The endarteritis which so often succeeds long continued chronic infection and the fibrosis which may follow injury or infection of any kind are examples. This is therefore one of the more plausible hypothesis which attempts to explain the genesis of cancer". Attempts to explain on the basis of direct pH determination by means of electrodes into tumours, the reaction being said to be on the acid side; chemical analysis showing a reduced calcium and increased potassium content; the enhancement of lecithin cholesterol ratio; changes in the sulphur metabolism; diminution in the protein content as also the antitryptic and lipolytic activity of blood—all these are in an experimental stage and no finality has been reached.

Amongst the recent of experimental cancer researches the following are of special interest:—

- (1) Malignant cells can be grown in vitro in the presence of

the necessary frame-work, inorganic salts, embryonic tissue juice and serum.

- (2) Specific test for cancer of the sex cells. The Zondek Ascheim test, as evidence of the presence of Prolan A is present in the urine of patients with testicular tumours. Recurrence of metastases is diagnosed by finding prolane A in the urine following operation.
- (3) McCarty and Haumedar lay considerable stress upon the relationship of the ratio of the nucleolar area to a nuclear area. In malignancy the ratio is 1 : 5 to 1 : 17. For non-malignant cells the ratio is 1 : 13 to 1 : 45.

PART II

4. Pathological Basis of the Modern Surgical Treatment

It is common knowledge that except in a few instances like the prostate, thyroid, kidney, etc. the key to the surgical pathology of cancer is the lymphatic drainage and connections of the organ or tissue involved. The theory of embolism of cancer cells organ or tissue involved. The theory of embolism of cancer cells wafted by the lymphatic current to the regional lymph glands holds good in a good many instances especially buccal and pharyngeal cancers, penis and alimentary tract. The theory of permeation propounded in a fighting way by Sampson Handley holds good especially in cancers of the breast. It should not be supposed that embolism does not play in the dissemination of breast cancer or permeation does not occur in other cancers. In one case the predominant method of dissemination is by embolism and in the other permeation, in which the cancer cells grow by mitosis along the lymph channels irrespective of the direction of the current of lymph flow. If I want to go to Bombay I can reach there by walking on foot, by a cycle, motor car, train, sea-voyage over water or fly through air. Perhaps the predominant method of travel to Bombay is by train. If I want to go to London, I may perhaps take a boat, the predominant mode of travel being sea-voyage. In embolism the embolic cell reaches the lymphatic gland and sets up colonies by mitotic division. In permeation the starting cancer cell's remote progeny perhaps the thousandth or ten-thousandth reaches the lymphatic gland. The process of permeation is slow, steady, continuous and progressive.....The process of embolism is quicker. Every embolic cell has no chance of implantation. Perhaps the majority die on account of tissue

response. A few may escape destruction and set up colonies. Then there is the method of transcoelomic implantation by which Krukenberg's tumours are produced secondary to gastric carcinoma. Instances have been known where cancer cells from the stomach have passed through the lumen of the gut and got implanted in a lower portion of the gut. Recently I had a case where the pyloric portion of a stomach was the seat of a growth apparently operable with no deposits in the liver. But the terminal ileum, caecum, appendix and ascending colon was the seat of a malignant mass manifestly inoperable. In this particular case it is difficult to say whether the two lesions arose simultaneously or one is the result of the other. At any rate intracavity implantation is a process of spread which must be kept in mind. There is the method of dissemination by blood stream as exemplified in cases of cancer of the thyroid, prostate, kidney and rarely breast. In such conditions bone metastases are common. Sampson's explanation of metastasis in bone based on the theory of permeation is considered by some as stretching the permeation theory too far. Of course I need not remind you that in the immediate neighbourhood of the lesion and metastasis cancer spreads by local infiltration and expansion with detriment to all structures.

Another very important factor which has a bearing on the natural history of cancer in the several regions of the body, is the type of cancer cell of which the tumour is composed.

Is the tumour composed of specialised cells as an adenocarcinoma of the rectum or an undifferentiated cell like the carcinoma simplex in the breast or back of the tongue? A well differentiated tumour in any situation is less malignant, progresses slowly, forms metastases few in number and is more amenable to radical extirpation by surgical methods. With rare exception, it is radio-resistant. On the other hand an undifferentiated or de-differentiated tumour is very malignant, spreads rapidly, forms metastases quickly even in remote parts, and destroys life. It is radio-sensitive, but surgical extirpation is well-nigh impossible.

The most important recent contribution to the elucidation of the degree of malignancy and prognosis in cancer is the grading of cancers into 4 types by Broders. In his work on cancers of the lip basing his conclusions on 537 cases he says that 15.82 per cent were in Group I with no mortality, and 1.11 per cent in Group IV with cent per cent mortality. Group I consists of well-differentiated cells and Group IV of undifferentiated cells. In Group IV, the cancer cells may be so undifferentiated that they lose practically all evidence that would tend to identify them with the organ of

tissue from which they arose. One may find Grade IV cancers with lymphocytic and eosinophilic infiltration, also fibrosis and hyalinization. Usually the more malignant the neoplasm the more irregular and ill-defined are the nuclei, mitotic figures are numerous, irregular and bizarre. Cells with large nucleoli when present in large numbers are significant of active malignancy.

Broder's grading of malignancy depends on the proportion of differentiated and undifferentiated cells.

Grade.	Differentiated cells.	Undifferentiated cells.
I.	75%—100%	0%—25%
II.	50%—75%	25%—50%
III.	25%—50%	50%—75%
IV.	0%—25%	75%—100%

The object of surgical treatment of cancer should be the thorough extirpation of the primary growth, its lymphatic paths and the regional metastases in one continuous mass as in the Breast, or in two stages not necessarily in a continuous mass as in Buccal cancers. In buccal cancers the rigid ideal set for the breast need not be employed as the process of metastasis is more by embolism and the intervening lymphatic channels usually are free.

5. Scope of Pure Surgery in Cancer

Under this heading volumes can be written, but I propose to deal with only certain principles which should govern the surgical management of cancer. Surgery is clearly indicated under the following conditions:—

- (1) Pre-cancerous conditions:—As in leukoplakia, ulcers, fissures, or papillary growths of the tongue, where excision of the buccal lesion is certainly followed by cure; in Kraurosis vulva where vulvectomy is indicated; in chronic mastopathy (cheatle) where the process of cystiphorus desquamative hyperplasia may merge into epithelial proliferation and infiltration, in Paget's disease of the nipple; in long standing cases of gastric ulcers where according to Moynihan and Mayo there is 10% chance of cancerous development; in papilloma of the bladder; in cholelithiasis and nephrolithiasis where the chances are remote but where there are usually other indications for interference, etc.
- (2) Excision of tissue for biopsy to grade the malignancy with a view to appropriate treatment and prognosis.

- (3) In radio-resistant types of carcinoma as in the well-differentiated adult type of adenocarcinoma of the alimentary canal especially the rectum, colon, stomach, breast, body of the uterus, ovary, gall-bladder, etc. In these cases the disease process is slow and the results of early surgical interference are good.
- (4) In tissues or organs where a well-planned surgical operation is expected to remove the whole disease process, without mutilation of the parts and safety to the patient, e.g. early growths of the lip, tongue, breast, larynx, rectum—also in rodent carcinoma of limited extent.
- (5) In cancers of the extremities where a timely amputation combined with dissection of the regional lymph glands may rid the patient of cancer for life.
- (6) In cancer of the penis grown beyond possibilities of cure by radium combined with dissection of both groin glands.
- (7) As a corollary to the clearing of the metastatic areas in cancers of the buccal cavity whatever might have been the mode of treatment of the primary condition, radium or surgery.
- (8) Surgery of access to be followed by diathermy, radium or radon implantation, as in metastatic lymphnodes of the neck, possible sites of metastases as in cancer of the breast, cancer of the maxillary antrum, mediastinal growths, brain tumours, etc.
- (9) In inoperable cases involving the alimentary canal to give relief from pain to the miserable patient by short-circuiting operations such as gastro-enterostomy in pyloric cancer; ileo-colostomy in cancers of the colon; colostomy in cancers of the rectum and gastrostomy in cancers of the oesophagus. Also tracheotomy in cancers of the larynx as a palliative measure.
- (10) As a deliberate measure of post irradiation treatment by radium or X-rays: cancers of the breast, apparently inoperable can be made operable by preliminary radiation.

So there is a wide scope for surgery in the management of malignant disease. In "Butlin's diseases of the tongue" by Spencer and Cade (1931) there is the following suggestive paragraph:—

"The lay public and a number of medical men are still under complete misapprehension as regards the practical

possibilities of radium therapy. Its possibilities are exaggerated, its pitfalls are under-estimated and the medical literature as well as the lay-press, offer constant examples of unreasonable claims and unjustifiable statements. It is however as cruel and misleading to deprecate as to exaggerate the usefulness of this very delicate weapon, which in careful hands, controlled by minds unbiased or unprejudiced "cures" a selected few, relieves a great many and robs no one of the benefits of excisional surgery".

Bloodgood says.—"My experience in radium in early cancer of the tongue is the same as with cancer of the lip: it cannot compete with good surgery".

"Many early operable cases are made inoperable by the use of radium—There can be no question concerning the value of the use of radium in the treatment of malignancy of the tongue under certain conditions but clearly operable cases should not be treated with radium".

6. Properties of Radiation

An atom consists of an equal number of positively charged constituents called protons and negatively charged ones called electrons. But the nucleus of the atom contains more protons than electrons, the balance being made up of the electrons going round the nucleus in definite orbits. Hydrogen atom contains a single proton and a single electron. The diameter of the electron orbit is known as 1 Armstrong Unit, which is $1/100,000,000$ c.m. The diameter of proton is $1/25,000$ A. U. Helium atom consists of 4 protons and 2 electrons in the nucleus minus its two satellite electrons. Beta particles are simple electrons. Both *Alpha* and *Beta* particles are material particles. The *Alpha* particle is projected out with a velocity of 12–18,000 miles per second. The *Beta* particles are projected out with a velocity of 60–18,000 miles per second. A thin sheet of paper will absorb all the *Alpha* rays. The penetrating power of *Beta* rays is greater than *Alpha*. 0.5 m.m. of platinum will absorb all the rays. The *gamma* rays are not material particles. They are high frequency ether vibrations with a velocity of 186,000 miles per second. They are of very short wave-length overlapping the region of the short X-rays (0.05 to 1 A.U.) and extend to shorter wave lengths, some of which are too short to measure. Since in the region of short waves, the penetration increases with decrease of wave length (a ray half as long as another ray penetrates roughly eight times

so far), it is obvious that the *gamma* rays are very penetrating. 1 m.m. of lead will absorb all the *Beta* rays. At least 160 m.m. are required to absorb the most penetrating *gamma*. In their passage through metallic bodies secondary *Beta* radiations of weak intensity are produced which can be absorbed by a thin sheet of paper. Therapeutically only *gamma* rays are used. For superficial lesions, projecting on exposed surfaces, skin and mucous membrane, *Beta* rays may be employed. But they are scarcely superior to other agents as the cautery, diathermy Co_2 snow. Pure *gamma* rays are ensured by interposition of 0.5 m.m. platinum. The disintegration products of radium are shown in the accompanying table:—

SUBSTANCE	HALF LIFE PERIOD.	RADIATION.
Uranium	5,000,000,000 yrs.	<i>Alpha</i>
Radium (226)	1690 yrs.	<i>Alpha Beta</i>
Emanation (Radon)	3.85 days	<i>Alpha</i>
Radium A	3 minutes	<i>Alpha</i>
Radium B	26.8 minutes	<i>Beta</i>
Radium C	19.5 minutes	<i>Alpha Beta gamma</i>
Radium D	16.5 yrs.	<i>Beta (?)</i>
Radium E (polonium)	5 days.	<i>Beta gamma</i>
Radium G (Pb 206)	136 days.	<i>Alpha</i>

Radon is a gas. When radium is placed in a sealed container, emanation gradually accumulates in an increasing amount until a maximum is reached at which point as much emanation is being formed as is being converted into Radium A. Similarly as much Radium A is produced as is being transformed into Radium B and so on throughout the disintegration series. The time taken to reach the peak of activity is 20 days. Radium chloride or radium bromide is dissolved in dilute HCl and placed in one or several flasks. They are connected to a mercury pump. The emanation is pumped off and collected over mercury in a trunk glass test thick tube. Various impurities like H_2 , O_2 , O_3 , N_2 are present. They are first sparkled when H_2 and O combine to form water which is absorbed by caustic soda. The partially purified gas is forced into long and extremely fine capillary glass tube and surrounded with liquid air. The emanation is deposited as a solid whilst the remaining impurities can be removed by a pump. The rate of destruction is about 1/6 per day. When we use radium element we have constant intensity and accuracy of dosage. The advantages of radon are (1) no financial loss from accidents and (2) greater flexibility of technique.

PART III

7. Pathological basis of the action of gamma rays.

THE assumption upon which radio-therapy is based is that the *gamma* rays emitted by radium and X-ray are capable of destroying cells, and further that this destructive action is exerted more readily on cells which are rapidly proliferating. The experimental work at first consisted very largely of irradiating plants, ova and other lower organisms. Cant and Donaldson studied the effects of radium on carcinoma of the cervix uteri. The method was to remove fragments of the growth at different intervals after the insertion of radium and study the changes visible in sections. The immediate effect covering a period of two days after exposure to radium was cessation of mitosis. After this period of quiescence, the third and fourth days are characterized by the return of mitosis in large numbers but in abnormal forms. Numerous cells were observed in metaphase but there were few or no examples of the later stages. The chromosomes were fragmented and the spindle figures sometimes represented only by scattered threads, while droplets appeared in the cytoplasm; the appearances were such that cells might well have been passing through abortive mitosis into actual dissolution. Two other changes were visible at this stage: in area nearest to the radium there was actual necrosis; nuclear staining being completely absent; in more distant areas the cells showed an increase in size, affecting the nucleus as well as the cell itself. Towards the periphery of the irradiated area the frequency of abnormal mitosis was also more marked. It appeared therefore there were three zones: in the innermost, destruction of the growth cells was complete and immediate; in the middle zone there were gross abnormalities of structure suggesting approaching dissolution; in the outer an increase in size and frequent mitosis presenting various abnormal features. After the seventh or eighth day all mitosis ceased. The nuclei were irregular in staining and shape represented by scattered particles of chromatin or actually absent, the cytoplasm was often vacuolated. At this stage invasion by leucocytes began, and, during the ensuing weeks the products of cell disintegration were largely removed. After six to eight weeks no trace of the growth remained, but for "embalmed" areas, concentrically laminated bodies having the general shape of the original islands of growth but without nuclei. These changes were accompanied by progressive fibrosis. Effects of irradiation on tissue cultures and other experiments by cinematograph films have enabled the research workers to come to the following conclusions:—

- (1) The immediate destruction of the cell,
- (2) The inhibition of imminent mitosis, followed by abnormal mitosis and the disruption of the cell, or, if mitosis is completed, of the daughter cells.
- (3) Damage often not immediately demonstrable of cells in the resting stage, resulting in failure to proliferate after one or more subsequent generation.
- (4) The malignant are clearly more susceptible than normal cells.

8. Scope of Radio-therapy in Cancer

(a) To the exclusion of Surgery

There are certain situations in the body and certain types of new growths which can be successfully treated by radium application not necessitating any but the most minor surgery. Implantation of needles by the interstitial method, say, in a cancer of the lip in its early stages, is a very minor procedure. By no stretch of logic can it be called surgery in the real sense. So also the intracavitary application of massive doses of radium in a case of carcinoma of the cervix is a minor procedure. The chief indications for pure radium therapy are as follows:

- (1) *In early cancer of the lip*:—In the majority of instances cancers of the lip are mild and progress very slowly. The object of radium treatment is to get the best cosmetic result. But it is in these early cases that Surgery also can compete equally. Nevertheless the cosmetic results are better with radium than surgery.
- (2) *In rodent carcinomata in all stages except in the very advanced cases*.—Though there is a difference of opinion between the English and American schools as to the mode of origin of the ulcer, the English maintaining it is a basal celled carcinoma of the skin and the Americans holding that it arises from a sebaceous gland or hair follicle, the pathological fact remains that it is less differentiated than a squamous celled carcinoma and so gamma rays should be expected to be lethal to them. Radium does not belie this expectation and radium can be said to hold its own and may be said to be even better than surgery since the cosmetic results are better with radium than with surgery.
- (3) *In cancers of the cervix as opposed to cancers of the body of the uterus, in the early stages and even in advanced cases*. Cancers of the uterus are usually the well

differentiated adenocarcinomata in contra-distinction to the squamous epitheliomata of the cervix uteri. In this sphere it can be said that radium has triumphed over surgery. The Wertheim's operation of pan-hysterectomy combined with excision of major portions of the vaginal wall is a really terrible operation associated with a high mortality even in very experienced hands.

- (4) In cases of cancer of the oesophagus in inaccessible situations, Southar's technique of radon seed implantation with a radon gun through an oesophagoscope is a very welcome palliative technique.
- (5) In inoperable cases of cancers of the Breast, cervix uteri, inoperable metastatic malignant glands, nasopharyngeal fibromata, etc. radium has distinctly triumphed over Surgery. There was a Surgeon in this Hospital under whom I learnt my A. B. C. of Surgery in my student days who would emphasize repeatedly in his teaching that for inoperable carcinoma of the cervix and rectum there was no better treatment than to put gun-powder and blow up the patient for good. The surgeon is living now and I am afraid he will have to revise his judgment on these unfortunate sufferers from inoperable carcinomata.

(b) Combined with Surgery

The indications for Surgery combined with radium therapy are many. In some situations even with the most radical surgery, one cannot be sure that all the cancerous tissues have been extirpated. The chief indications for this procedure are as follows:—

- (1) *Cancers of the tongue*.—Small growths can be excised with the diathermy knife and radium or radon can be implanted at the same time around the area. Since cancers of the tongue metastasize early block dissection should be undertaken. Even after block dissection it would be advantageous to put radon or radium needles into the several regions of the wound or radium collar applied to the neck after the wound has healed. In cancers of the posterior part of the tongue and epiglottis an incision above the hyoid bone can be made and radium implanted in the floor of the mouth.
- (2) In cancers of the lips, cheek, etc. radium treatment by moulds to the primary site combined with block dissection of the regional nodes followed by radium implantation in the wound, radium collar or deep X-ray therapy.

- (3) *Operable cancers of the Breast*:—After a radical operation a few needles implanted about the 2nd, 3rd and 4th intercostal spaces, at about the costo-chondral junction, is a valuable technique strongly approved by Sampson Handley. Keyne's technique of radium implantation without surgical intervention is claimed by some to have given excellent results.
- (4) In tumours of the brain where after exploration it is found that the growth is inoperable. In such cases radon implantation should be the method of choice.
- (5) In carcinoma of the penis in early stages, the primary growth can be successfully treated with radium implantation followed immediately by dissection of both groin glands.

Similar instances can be multiplied indefinitely and since it is not possible to deal with details within the scope of the subject matter of this lecture, I have to content myself with stating only principles. In actual practice each individual condition should be judged on its own merits and a plan of attack should be proposed which is expected to give the best clinical results without jeopardizing the patient's life.

9. The Clinician and the Technician

Medical science has freely given to the other sciences and has freely taken from the other sciences. The history of ancient Hindu chemistry was bound up with Auyurveda. More recently Bio-chemistry as a pure science has profited a good deal from Medicine. The most recent and outstanding contributor to the physiology and pathology of the brain and cerebrospinal fluid circulation, is a master surgeon, Harvey Cushing. Even psychology has profited from medicine.

Under the circumstances to divide Medicine into water-tight compartments is bad. To speak of radium and deep X-ray as the sole monopoly of the physicist and the radiological technician, into whose sanctum the clinical man is forbidden to step his foot, is a condition of administrative pathology. The uncompromising clinician looking with derision on the technical methods and the extremist technician claiming to monopolize all importance to himself and claiming also much more therapeutic benefits to his pet radium or deep X-ray, or the bacteriologist claiming all virtues to his pet vaccine, all these individuals must be placed on the border line. There cannot be anything competitive between

the clinician and the technician. Without the technician the clinician will have to practise the 16th century medicine. If the technician sits in his water-tight compartment assuming superiority over clinician, he will never learn to improve his technique in the practical management of his methods of therapy. In the Mayo Clinica of America, the clinician makes it a point to consult the technician in the interpretation of skiagrams, etc. And the technician in turn calibrates his findings on the altar of the operative findings. Especially in gall-bladder surgery, the Mayo-clinic has made great strides because the clinician and technician form the very warp and woof of the clinico-technical fabric.

It must, however, be conceded, I have tried to be as impartial as possible, that the clinician and the technician alone is responsible to the patient. The specialists and technicians are only important auxiliaries in the same sense as the violinist and the drummer are second only to the vocalist in a music party. The responsibility of a clinician is great and he, in consultation with the pathologist, radiologist, bacteriologist, biochemist etc. must evolve a plan of campaign for the successful management of an individual case. He has got the right to ignore certain findings of his compeers if they are found antagonistic to his clinical sense.

10. Future of Cancer Management

Since the management of cancer is closely bound up with the technicalities of radium and deep X-ray, the technician must have had a preliminary grounding in general medicine and surgery. The clinician must also be familiar with the principles and practice of radiology. Under modern conditions it is next to impossible to combine in one man the pathologist, clinician, radiologist, etc., though that might be the ideal solution. The next best method is certainly the Mayo-Clinic practice of the clinician clearing his doubts at the hands of the radiologist and the radiologist verifying his interpretation of the shadows to the judgment of the knife.

I cannot better conclude these lectures than by quoting an extract from the speech of Dr. Cabot of United States of America. Says he, "A much more far reaching use of grading can be had by the routine use of biopsy as a preliminary to the determination of the methods appropriate to the management of individual cases. This requires that the diagnosis of the neoplasm having been made, a sufficient amount of material shall be obtained to enable an expert to classify the tumour and grade it. This having been done, the appropriate measures may be apportioned between surgery and various types of radiation in a much more logical and apparently in a more successful manner. I think this aspect of

the problem of grading should be fully considered and it will lead logically to the transference of the treatment of cancer from the individual physician, commonly a surgeon, to the group representing the interest the pathologist, the surgeon and the radiologist. This is I believe the essential machinery which must be set up if we were to deal most effectively with cancer in the present state of our knowledge".

Hence, in my opinion, the present position of Surgery and radium in cancer, in military language, is that surgery is a sagacious and resourceful war minister, and radium an uncompromising commander-in-chief to fight the ruthless enemy—the human cancer.

THE COMPLICATIONS OF GONORRHOEA IN THE MALE AND THEIR TREATMENT

BY

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GONOCOCCAL infection may extend to the prostate, vesicles and the epididymis as a result of complication in the genito-urinary tract. Infection of the eye may occur at any time during an attack of Gonorrhœa. Conjunctivitis and an Iritis may arise as a metastatic complication of severe gonococcal infection. The chief metastatic complication of generalised gonococcal infection occurs in the joints. Rarely Gonococcal infection affects the pericardium, the endocardium, the spinal meninges and the central nervous system. Late complications of gonorrhœa in the male are stricture of urethra and sterility.

Statistics of Venereal department, General Hospital, showing the complications of gonorrhœa are given below :—

Year	Total No. of Gonorrhœa cases.	Epididymitis.	Arthritis.	Vesiculitis.	Stricture of Urethra.
1932	906	74	42	15	81
1933	724	81	61	35	65
1934	1346	85	63	15	40
1935	1461	108	48	8	64

Prostatitis occurs as a result of extension of gonococcal

infection to the gland. It is characterised by frequency and urgency of micturition associated with urethral discharge. Urine in both the 1st and 2nd glasses is turbid. There is referred pain in the rectum. On rectal examination the prostate feels enlarged and tender, slightly nodular due to peri-glandular infiltration. In acute prostatitis, there is extreme tenderness and painful enlargement of the prostate. It may go on to subacute or chronic stage. Chronic prostatitis results, due to imperfect local antiseptic treatment of the posterior urethra and the lack of prostatic massage in the acute and sub-acute stages. In chronic prostatitis there may be recurrent attacks of gleet discharge. The urine in the 2nd glass test is clear with threads. There is the usual morning drop. The urine, which is passed after prostatic massage is turbid and contains threads.

Treatment—In acute prostatitis, absolute rest in bed is essential. Bland diet with a large quantity of barley water is given. Hot hip bath twice a day and hot rectal douches alleviate the pain and frequency during micturition. Lot of alkalies are given orally with Sandalwood oil to relieve the spasm and stranguary. Morphia 1/4 gr. and atropine 1/75 gr. suppository is inserted per rectum twice a day to relieve spasm and prevent the onset of vesiculitis and epididymitis. Local urethral irrigation is completely stopped till acute condition subsides. 5 c.c., 7 c.c., 10 c.c. of 10% Calcium chloride is injected intravenously every alternate day up to 6 injections. As the acute condition subsides, gradually urethral lavage with Pot. Permanganate solution 1 in 10,000 is given. There is always a tendency to abscess formation if resolution does not set in.

In chronic prostatitis.—Efficient drainage from the prostatic ducts is established by carefully massaging the prostate, which will vascularise the prostatic tissues, empty the alveoli of their retained products, and create a healthy tone in the diseased tissues. Posterior irrigation will help in clearing up the infection and the warm irrigating fluid will stimulate the blood supply to the posterior urethra and kill any infecting organisms which may be expressed into the urethra during the massage. Bearable warm posterior lavage should be given after prostatic massage. Full-sized curved bougie, as Lister or Clutton, is passed to open up the prostatic ducts and express out the latent infection that lurks there. Prostatic massage should be done twice a week and bougies are passed once a week. In chronic persistent cases, 1 or 2 c.c. of 2% Silver Nitrate solution is instilled into the posterior urethra with an Ultzmann's syringe and prostatic

massage is done after 24 hours to clear up the infection. Silver nitrate sets up irritation in the prostate and all the latent infection comes out after prostatic massage. Prostatic massage and lavage are continued till the urine, after the massage is clear and the prostatic smear is free from pus cells and absolutely free from Gonococci. Injection of graduated doses of polyvalent detoxicated gonococcal vaccine assists in eradicating the infection.

Seminal vesiculitis.—Infection of the vesicles is closely allied to the infection of the prostate. Infection is due to direct extension from the posterior urethra along the common ejaculatory duct and thence by the seminal duct to the vesicle itself. Infection may be acute or subacute. Rarely both vesicles are affected.

Acute vesiculitis is characterised by frequent strainings, severe pain at the end of micturition, followed by terminal hæmaturia, urgency, frequency and stranguary during urination are very marked. There is referred pain in the supra-pubic region and around anus. The signs of vesiculitis are presence of discharge and painful enlargement of vesicle above the prostate as found on rectal examination. A diseased seminal vesicle is always palpable and the palpable one is always diseased.

Chronic vesiculitis is a common complication of posterior urethritis. Rectal discomfort is felt during seminal ejaculation and there is a vague radiating pain from the groin on to the back or down to the perineum. Frequent gleet discharge, and occasional attacks of painful priapism are characteristic. The urine is clear in all 3 glasses and threads are present in the 1st two glasses due to littritis. Thickened indurated vesicles due to peri vesiculitis, are felt on rectal examination. The four glass test will confirm the diagnosis in that the urine in the 4th glass will be turbid with pus cells and a trace of blood if the duct from the vesicle is patent. Examination of the expressed secretion from the prostate and seminal vesicles both microscopically and macroscopically is essential in diagnosing a case of chronic vesiculitis.

Treatment.—*Acute vesiculitis*—Rest in bed, bland diet with plenty of barley water to drink and a good purge are essential. Hot antiseptic hip baths and hot rectal douches relieve the pain and stranguary. Irrigation is contra-indicated in acute conditions. Alkaline diuretics with sandalwood oil are given to relieve the spasm and stranguary. Morphia and Atropine suppository is inserted into the rectum twice a day to allay the pain and stranguary. All local treatment is stopped till the acute symptoms and pain subside completely. Inject 5 c.c., 7 c.c. and 10 c.c. of 10% cal. chloride

intravenously daily or every alternate day till the hæmaturia ceases. Cal. chloride prevents bleeding by increasing the calcium content of the blood. Within 10 to 12 days the acute condition subsides resulting in a condition of sub-acute vesiculitis. As the hæmaturia ceases, start gentle low anterior urethral irrigations and continue the same if it does not give rise to pain or recurrence of the frequency of micturition.

In chronic vesiculitis the chief object in treatment is to establish efficient drainage from the ejaculatory duct and to restore the seminal vesicles to their normal consistency. Instil 1 or 2 c.c. of 2% Silver nitrate solution into the posterior urethra with an Ultzmann's syringe and nozzle to produce a mild inflammatory reaction in the posterior urethra which results in the removal of inflammatory products from the ejaculatory and prostatic ducts. If this is not effective in establishing drainage, pass a fine Geraghty syringe with a blunt pointed needle through the posterior urethroscope and instil the ejaculatory ducts with silver nitrate solution or catheterise the ducts. In resistant cases where the drainage from the vesicles cannot be re-established by the above measures, vasotomy is done.

Epididymitis arises by a direct extension of the gonococcus from the posterior urethra to the ejaculatory duct, and thence by the Vas deferens to the epididymis. Rarely it may occur due to a lymphatic spread from any part of the urethral tract. Predisposing causes are injury of the epididymis, trauma of the urethra from faulty instrumentation or by the too early prostatic and vesicular massage or by giving irrigation at a great height.

Acute epididymitis occurs usually during the 2nd or 3rd week of gonococcus infection. It is characterised by painful, tender swelling of the cord and epididymis, usually Globus Minor is affected. The infection is usually unilateral or may be bilateral. Symptoms of Rt. Epididymitis may stimulate an acute appendicitis. The skin over the affected part of the scrotum is red, inflamed and tender. There may be little urethral discharge and the urine in the 2 glass tests is turbid. In majority of the cases, acute, condition subsides in 4 to 6 days and a sub-acute or chronic stage gradually supervenes. Suppuration is rare.

Chronic epididymitis results due to imperfect treatment with a marked tendency towards the formation of fibrous tissue in and around the Vas deferens and in the epididymis. On palpation the epididymis feels indurated and enlarged and in association with this chronic fibrous thickening, the structures of the spermatic cord are thickened and bound together by fibrous adhesions.

There is usually a degree of vesiculitis and prostatitis. A turbid urine in the 4th glass of the four glass test, while the other 3 test glasses contain clear urine, suggests prostatitis or vesiculitis. Besides this, fibrous thickening of the epididymis resulting from a previous gonococcal infection clinches the diagnosis.

Treatment.—*Acute Epididymitis:* absolute rest in bed and bland diet are imperative. Irrigation is contra-indicated in acute stage. Plenty of alkaline diuretics with Tr. of Belladonna are given orally to prevent an extension of the infection to the other side. Local strapping with Pigmentum Belladonna or Ichtyol and Glycerine 25% very effective, is applied to abort the infection and to give considerable relief to the swollen and painful epididymis. The painful scrotum is kept in a suspender with a T. shaped bandage, which may be renewed every day to keep up the continuous action of the drug. The pain may be alleviated by inserting Morphia and atropine suppository per anus twice a day. Under local treatment the swelling and pain subside. In resistant cases diathermy is applied to painful epididymis. When the pain and swelling of the epididymis subside, local treatment may be started by giving low anterior warm urethral lavage. Inject 5 c.c., 7 c.c. or 10 c.c. of 10% Cal. chloride intravenously every alternate day till the condition subsides completely. As the infected area is not easily accessible to antiseptic therapy, treatment through the blood stream by vaccines or proteins is of considerable value. Polyvalent detoxicated vaccine cuts short the inflammatory process and lessens the tendency to induration. Epididymitis rapidly improves with a course of Gonal injections.

Chronic epididymitis.—Local strapping with Pig. Belladonna is applied. Prostatic and vesicular massage is done twice a week till the urine passed after massage is clear and free from pus cells and gonococci. Examine through the urethroscope for foci of infection in the lower urinary tract and eradicate these foci, if any. Usually pyogenic organisms may keep up the condition. So autogenous vaccine in addition to polyvalent detoxicated gonococcal vaccine is very effective.

Arthritis.—Infection of the joint and tendon sheaths occurs as a metastatic complication of Gonorrhœa. Usually joints are involved about the 3rd week of the disease, or as early as 3rd or 4th day of an acute gonococcal infection. Gonococcal arthritis is frequently mono-articular and occasionally poly-articular. Usually the knee joint is involved first and the ankle, wrist and elbow follow in order of frequency. Suppurative joint destruction

is extremely rare. Clinically it may be acute or sub acute and chronic arthritis.

Acute arthritis occurs frequently in a single large joint which is swollen and is extremely tender and painful. The swelling is due to effusion of synovial fluid or a peri-articular exudate. There is marked limitation of movement and the skin surface is red and hyperæmic. Suppuration may occur if other pyogenic organisms infect the joint. Sometimes acute polyarthritis occurs involving the smaller joints of the hand and foot giving rise to fusiform swellings of the joints. There is active urethral discharge which is positive to gonococcus. The condition does not respond to salicylates as articular rheumatism. There is very slight rise of temperature in gonococcal joint infections. It occurs during the acute or sub-acute gonococcal infection.

Sub-acute and chronic arthritis may occur in 2 forms:

- (1) A hydrops articuli affects a single joint, usually the knee-joint. The affected joint is swollen, tense and slightly painful due to effusion of the synovial fluid. There is slight limitation of movement.
- (2) An osteo-arthritis affects multiple joints, especially the smaller joints. There is a sero-fibrinous exudate into the joint and a marked tendency to the formation of adhesions with subsequent limitation of movement and deformity. There is wasting of muscles which act on the affected joints. This muscle wasting is due to gonococcal myositis and is more marked than in Tuberculous arthritis. Usually occurs in chronic gonococcal infection. Examination of the genito-urinary tract will help in locating the focus of infection. Previous history of gonorrhœa and the presence of any abnormal condition in the prostate or seminal vesicles point to the gonococcus being a likely cause in the case of hydrops articuli and of osteoarthritis. The blood may be examined by the complement Fixation Test which always gives a positive test in gonococcal arthritis. Gonococcus can be cultured from the joint exudate in some of the sub-acute cases, but not in acute conditions. X-ray examination of the joints will help in differentiating between tuberculous, gonococcal or rheumatoid arthritis. Urethroscopic examination reveals evidence of littritis or sub-epithelial infiltration in the urethral tract as the result of previous uncured gonorrhœa.

Treatment consists of:—

- (1) Local treatment.
- (2) Eradication of the original focus of infection, and
- (3) Treatment through the blood stream. Prognosis is good in a majority of cases and there is complete recovery if properly treated at the start.

Local treatment consists of complete rest to the affected joint by strapping it with Fig. Belladonna. In gonococcal rheumatism, early passive and voluntary movement of the affected joint is necessary to prevent the formation of adhesions. It is dangerous to immobilise the joint rather too long than it is absolutely necessary since adhesion will be formed which will result in limitation of movement and subsequent deformity. In cases of Hydrops, the affected joint is strapped with Scott's ointment to help in the absorption of fluid. Diathermy gives excellent results in some cases. Operative measures are not necessary save in severe cases of deformity. If there is much tension in the joint the fluid is aspirated under the maximum aseptic conditions and strapped in elastic bandage to exercise even pressure over it. Massage considerably reduces the amount of inflammatory exudate in the joint.

Treatment of the original focus of infection.—In the male eradicate the focus of infection—which may occur either in Littre's gland ducts, the prostate and the seminal vesicles.

Prostatic massage twice a week and passing of full sized bougies once a week should be done in the male to clear the focus of infection.

Treatment through the blood stream.—The metastatic complication of gonorrhoea as arthritis is effectively treated through the blood stream, as the original focus and the seat of disease can be scarcely reached by antiseptics. Detoxicated vaccine acts like a charm in gonococcal arthritis. The vaccine therapy supplements the local treatment of the joint and that of the original focus. 10 c. c. of 20% of Sodium Iodide is injected intravenously every alternate day in gonococcal arthritis. The joint condition subsides rapidly with 2 or 3 injections. To enhance the effect of the vaccine therapy in resistant cases, non-specific protein therapy as 5 or 10 c.c. of sterile milk is injected intramuscularly in between the vaccine injections.

In chronic arthritis which resists the usual treatment, vasotomy is done and 15 to 20 c.c. of 10 % Argyrol is injected into the vesicles through the vas deferens to clear the focus of infection that lurks in the seminal vesicles. Such cases rapidly

improve and the joint condition subsides quickly within 3 or 4 days after seminal vesiculotomy.

Gonococcal conjunctivitis.—Infection of the eye may occur at any time during an attack of Gonorrhoea. There is always the possibility of any one who is suffering from a gonococcal urethritis or vulvo-vaginitis infecting their eyes by towels, handkerchiefs or by the hands. The patient is to be warned of this danger. The conjunctival surface becomes red, angry looking and inflamed and there is swelling of the eye-lids, photophobia and pain. It progresses rapidly and a purulent discharge oozes from the edges of the swollen eyelids. Bacteriological examination of the discharge shows gonococci. If the condition is not treated immediately, iritis, ulceration of the cornea, keratitis and penophthalmitis follow. Inflammation of the eye which occurs in adults is a metastatic or toxic condition.

Treatment.—The eye-lids and the surrounding skin surface are cleansed with any mild antiseptic. The eye-lids are separated and washed with a gentle stream of warm saline or boric lotion. Then few drops of 1% Nitrate of Silver solution are instilled into the eye. In acute conjunctivitis, the conjunctival sac should be washed every 4 hours to prevent any accumulation of pus in the sac and then prevent corneal ulceration. Silver Nitrate solution is instilled 3 or 4 times a day in acute cases and lessened gradually in frequency as the symptoms subside. Under treatment the inflammation subsides in 2 or 3 days in most cases. In the subsiding stage, astringent healing solution as zinc sulphocarbolate 1/2000 may be used. Smear preparations are examined at intervals for the absence of gram negative intracellular diplococci. It is better to treat the case for at least 6 weeks after an apparent clinical and bacteriological cure. If there is slight involvement of cornea, atropine solution $\frac{1}{2}$ to 1% is instilled into the eye immediately once or twice a day. General health of the patient should be attended to. If one eye only is affected it is important to prevent the spread of infection to the other eye by sealing up the sound eye with a Buller's shield. The eye is examined from day to day to make sure that it is not infected. Local treatment is given if there is active urethral discharge. Graduated doses of polyvalent detoxicated vaccine are given to cut short the prolonged course and convalescence. Gonococcal conjunctivitis in adults is seldom severe, though the inflammatory reaction may be more marked in the ocular region than it is in children.

Stricture of the urethra.—From the early stages of the infection and throughout the course of the disease, the gonococcus

tends to produce fibrous tissue. There is an inflammatory small celled infiltration of sub-epithelial tissues in the initial stages. In course of time the soft infiltrate becomes the hard infiltrate, consisting of fibrous tissue alone. Stricture occurs in places where soft infiltration of the urethra is common, such as the opening of Littre's gland ducts in the penile, bulbous and membranous urethra. Infiltration or stricture is very common at the junction of the bulbous and membranous urethra. The onset of a urethral stricture is always gradual and the condition may exist for several years before it gives rise to definite signs and symptoms. The signs and symptoms are a gradual lessening in the size of the stream of urine, difficulty in starting the act of micturition and dribbling of urine after the urination is over. In addition there may be temporary attacks of retention of urine following exposure to cold or a chill or following an alcoholic excess.

Treatment.—1. Early diagnosis and the prevention of the development of soft infiltrates during the course of acute or sub acute Gonorrhœa. (2) Examine the urethra with a urethroscope to make sure that the urethra has been restored to its normal calibre, dilatibility and lustre, subsequent to the clearing up of the infective process.

(3) Treatment of the established stricture in which the fibrous tissue changes have taken place.

Early diagnosis of infiltrates.—As the gonococcal infection subsides and the urine in the 2 glass test is clear and free from turbidity, it is advisable to pass straight bougie to find whether Littre's gland ducts are affected. Pass full sized straight sound and palpate the corpus spongiosum urethra over it. This enables to detect the presence of infiltrates in the anterior urethra, at the same time it smoothens the roughened surfaces of the healing urethra and tends to promote vascularisation which results in the absorption of newly formed fibrous tissue. Urethroscopy is used to locate exactly the infected follicles and the localised or generalised infiltrate. Until the urethral surface has regained its normal lustre, its regular strictions and its power of dilating and collapsing rapidly, we cannot be sure that all infiltrates are absorbed. Passage of straight and curved sounds as Lister or Clutton is done as a routine in the resolving stages of Gonorrhœa, as a test of cure and to prevent stricture formation.

Urethroscopic examination is done to make certain that all infiltrates are cleared up and that the treatment has achieved its object in restoring the urethral canal to its normal calibre, lustre and dilatibility before the patient is discharged cured.

Fibrous stricture—In early cases the prognosis is good. The site and nature of the stricture varies in individual cases, as crescentric or bridge stricture, annular or tunnel stricture. Treatment depends on the clinical condition. In acute retention, give hot hip bath for 20 to 30 minutes and the patient should attempt to pass urine. If the hip bath fails, soap and water enema is given to empty the bowel. If the bladder is distended and these measures fail to afford relief, the patient is relieved by passing a catheter observing scrupulously antiseptic precautions. The patient is put on restricted bland diet and lot of barley water. Hot hip baths are given every 4 hours.

First locate exactly the site and nature of stricture by passing a large straight sound along the urethra until there is obstruction. Gradually bigger sizes of bougies are passed once a week till the biggest size is passed. In cases of stricture at the bulb, a curved sound, as Clutton or Lister is passed in increasing sizes till the biggest one is reached. To relieve the pain or spasm, instil about 8 to 10 c.c. of 2% Novacaine into the urethra and then begin the gradual dilatation with straight and curved sounds.

In impassable strictures, external urethrotomy is the operation of choice. Strictures in the penile urethra dilate more easily than those in the membranous urethra and can be dilated more rapidly. After passing bougies, urethral lavage with Pot. Permang. solution 1 in 10000 is given to prevent cystitis and Mist. Quinine Cum opio is administered by mouth to avoid catheter fever. Once a week gradual dilatation is done till 30 straight sound and 28/32 Clutton is passed successfully. If the biggest sound is passed, further contraction of the strictured area rarely occurs. If maximum dilatation is done, the stricture may not readily contract again. The overdilatation leads to the formation of new blood vessels which vascularise the previously fibrosed area, restore its elasticity and make for recovery of function.

If there is stricture at the meatus, as a narrow meatus, meatotomy is done to enlarge the urethral orifice.

Sterility may occur as a result of occlusion of the epididymis, the vas efferentia and vas deferens. The obstruction in the vas is tested by performing vasotomy on either side at different sittings and normal saline is injected to note that the lumen is patent throughout. If there is any obstruction along the passage, the fluid may stop there.

My thanks are due to Dr. R. V. Rajam, M.S., M.R.C.P., Venereal Specialist, General Hospital, Madras for kindly permitting me

and gives rise to symptoms of acute toxæmia. The exact nature of the toxin has not yet been determined, but most probably it is a product of protein disintegration occurring under the action of excessive heat and it is said to consist chemically of primary and secondary proteoses. There is some evidence to show that the toxins are carried by the red blood corpuscles themselves and have produced lesions of the liver, kidneys and spleen similar to those seen in typhoid fever and diphtheria.

The third stage, stage of septic or secondary toxæmia.—This arises from ordinary septic infection of the burnt areas. Some degree of infection is present in all cases where the skin is involved. Signs of septic infection appear about the 5th day. The subsequent course depends on the virulence of the infection and on the treatment employed. A few cases of infection with the tetanus bacillus have been recorded.

Treatment

The principles of treatment as indicated by the pathological condition in each stage will now be considered.

First stage.—In shock, the main lines of treatment are to avoid undue exposure to cold and restore normal body temperature, to administer fluids and to relieve pain. Pain is frequently severe and drugs of the morphine group should be given to adults. The depressant effects of morphine or heroin in young children must be borne in mind. Treatment of the injury by local measures is begun at the earliest possible opportunity which is frequently during the first stage and involves cleansing and dressing of the affected area. The value of a general anæsthetic cannot be over-estimated.

Second stage.—Here the primary indication of treatment is to prevent the absorption into the circulation of the toxin which is produced in the burnt area. There is no anti-toxin available. The absorption of the toxin is best prevented by inducing coagulation of the damaged tissue, thus rendering the toxin non-soluble. For this purpose, a local application of tannic acid is the best. To Davidson of Detroit belongs the credit of having introduced the tannic acid treatment in 1925. Tannic acid minimises the acute toxæmia or prevents it entirely.

The third stage is that of a septic wound and *the fourth* is the healing stage.

Details of Management

The patient is put to bed at once. From the commencement the burnt area is exposed to air. No dressings are applied and

and the bed clothes are supported on a suitable cradle fitted with electric lamp bulbs. If the shock is severe, subcutaneous saline is administered. Morphine or Heroin is given for the relief of pain.

Cleansing.—Under gas and oxygen or ether, the area is cleansed. Blisters are opened up and evacuated and all the epithelium over the blister is removed, so that the tannic acid may come into contact with the damaged tissue underneath. It is here that the toxin is formed and gets absorbed. The whole area is cleansed with ether which exerts a drying and purifying effect and especially if any oily substance has been applied, it helps to dissolve it away, so that the watery solution comes into proper contact with the tissues.

Application of tannic acid.—The solution that is used is a 2½% aqueous solution in warm water. This should be prepared freshly for each application since tannic acid in solution is rapidly changed to gallic acid which has no power to precipitate or coagulate protein. The solution is sprayed with an atomizer and the parts are dried by the bulbs inside the cage. This is carried out at frequent intervals of half an hour as a rule, until all the burnt area is covered by a thin layer of brown coagulated tissue. The coagulation may occur more rapidly in some areas than in others. The areas coagulated are protected from fresh sprayings. In about 8 to 12 hours the coagulum is formed as a rule. If more deeply involved, it requires further sprayings.

Special circumstances.—In burns of the face, the eyes, nostrils and the external auditory meatus are protected during sprayings by pledgets of moist wool. It is not necessary to dry it artificially if the temperature is above 101°. In any case drying of the parts by artificial heat is both unnecessary and inadvisable when the temperature is high. If the front and back of the trunk are involved, the more affected area is sprayed and tannic compresses are applied to the less affected area. The compresses consist of sterile gauze swabs soaked in the tannic acid solution. These are applied at intervals of 8 to 12 hours and the dressings are removed after the coagulum is formed. The areas which are not coagulated are dressed further and the parts that have become coagulated are protected by dry gauze and cotton wool.

Local effects.—The immediate effects of the tannic acid are that after the first one or two applications, the pain is relieved and rapidly disappears. The entire area becomes covered by a thin brown or brownish black leathery coagulum, which is quite insensitive. This also acts as a splint, being rigid in character.

Care of the burnt area.—From the time the coagulum is

formed till it comes off completely, no special local treatment is necessary. The bed clothes are supported and the areas exposed directly to air. If blisters are formed they are snipped open and the raw areas left are sprayed again. If fluid collects under the coagulum, it is evacuated through an aperture cut with scissors. If the perineum is involved, the bowels are regulated by enemata and the soiling of area with urine is to be prevented.

Treatment of Sepsis in the third stage is the most difficult problem in the tannic acid method. Signs of a mild degree of infection as evidenced by a discharge of a little purulent fluid from the edges and some reddening of the surrounding skin are occasionally seen at different parts of the area. In this case, no active treatment is necessary. Gross infection is rare and is associated only with the formation of sloughs in the very deeply burnt areas. In such a case the collection of pus may float the coagulum and the coagulum is stripped off or softened by vaseline and then removed. It is very important to note that in no circumstance whatsoever should wet dressings be applied for the coagulum. The presence of moisture is associated with some signs and symptoms of acute toxæmia. The toxins gain access to the blood stream. Only when all coagulum is removed may wet dressings be employed in the treatment of sepsis.

In uncomplicated cases, healing under cover of the coagulum proceeds. In the second and 3rd degrees, the epithelium covers up the area in from 8 to 16 days. In the deeper ones, the coagulum is adherent till granulations develop. The coagulum is left alone till it can easily be peeled off. Sterile vaseline is applied after the coagulum comes off.

The tannic acid method can be applied even as late as 72 hours, whether or not other methods have been used. After this period the toxæmic danger is passed and in untreated cases frank sepsis generally occurs. At this stage it is to be treated as an infected wound.

General treatment.—As mentioned before, morphia has to be given in these cases. It is most important that the patient should have abundant fluids. If the patient can take the fluids by the mouth, it is sufficient; otherwise, the rectal and intravenous methods will have to be resorted to. If the pulse is rapid and feeble, brandy and glucose can be administered. If vomiting occurs, sodium bicarbonate 15 grains in 2 drams of water every hour has to be given for 5 or 6 hours. If sepsis is found, food of high calorific value should be given. In the severest cases, where a considerable amount of toxin enters the blood stream before

coagulation occurs, the method of *ex-sanguination-transfusion* has to be adopted.

This is a valuable accessory method for dealing with the toxic state. The quantity of toxic blood is removed and is replaced by an equally or slightly greater amount of blood from a suitable donor. The amount of blood varies from, say, 120 c.c. for an infant to 250 to 300 c.c. for a child of 3 years old. In an infant, puncture of the superior longitudinal sinus through the fontanelle with a special needle is the best method.

The temperature is carefully watched, especially in children. If 106 or higher, tepid sponging is indicated. Artificial cooling is very important in these cases. High temperature is very rare after the tannic acid treatment.

Clinical course.—The mortality is very low now after the adoption of the tannic acid treatment. The outlook is not grave even if 40 per cent of the body surface is affected.

Tannic acid should form part of the armamentarium of the village practitioner. In factories and other large establishments it should find a place in the first-aid equipment, and its application by the compress method included in first-aid training. Where facilities do not exist for proper treatment, patients should be sent at once to the hospital immediately after the burns. Contractures must be prevented by adequate movements if near a joint and by suitable splints. It may be necessary to skin-graft the raw areas left behind.

Alternative methods of treatment

Paraffin 7.—The wound is dressed with wool soaked in this mixture which consists of paraffin, vaseline, olive oil and B naphthol. The paraffin and the wool cover it in layers. This is a very satisfactory method.

Picric acid method.—This method has been given up now. Another method is to dress the burns with a saturated solution of sodium bicarbonate. This is applicable for the first and 2nd degree of burns only.

URETERAL CALCULI AND THEIR TREATMENT

BY

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MOST of these are formed in the kidneys and are, either temporarily or for a longer period, held up in the ureter. The ureter is made of three spindles separated by definite slight constrictions. These are called the abdominal, the pelvic and the vesical or intramural spindles. There are also two bends, the first where the ureter crosses the iliac vessels and the second just before it enters the bladder. The mucous membrane of ureter is normally smooth and small smooth stones as of urates, uric acid and cystine are passed down with transitory and mild symptoms or silently. The sites of impactions according to Jeanbrau are (1) Lumbar ureter 22% (2) Iliac ureter 7% (3) Pelvic ureter 51% (4) Intramural part 17%, 70% of impactions occur below the brim of true pelvis. In addition to this there may be congenital or acquired strictures of ureter proximal to which impaction may occur.

In children calculi are chiefly of urates and uric acid and these being smooth pass down silently or with mild symptoms, except in the presence of congenital strictures. Ureteral calculi are rare before twenty and after sixty. About 70% of impacted stones occur between the ages of 20 to 50. They are twice as common in men as women. Unilateral impaction is usual occurring with equal frequency on either side. Apart from calculus anuria, bilateral impacted stones are uncommon.

Composition.—50% of stones passed naturally are of uric acid. Uric acid and urate stones being smooth are not held up for long. Calcium oxalate stones being rough are irritating to the mucosa and the resulting spasm grips the calculus. In the absence of infection calcium oxalate stones predominate. B. Coli infection may occur with calcium oxalate stones, urine being still acid. In the presence of pyococcal infection, phosphatic stones are usual. These may have a nucleus of calcium oxalate or uric acid or be phosphatic throughout, depending on whether infection was secondary or primary to the stone. In the majority of cases, stones in the ureter are single but if infection be present there may be more, especially where stricture is also present.

Changes: Stone.—A stone when impacted for some time grows against the urinary stream by deposit of urinary colloids and salts. If infection is present the deposit is greater and growth more rapid. In alkaline urine of pyococcal infections heavy deposits of phosphates and albuminous matter occur.

Ureter.—The stone forms a niche for itself and the ureter round it becomes fibrosed. Fibrosis of peri-ureteral areolar tissue also occurs, binding the ureter to the peritoneum and the posterior abdominal wall. In long standing cases a small pouch or diverticulum results. Such may ulcerate resulting in an abscess which may burst externally or into the intestines and discharge the pus and stone leaving a fistula behind.

Kidneys.—As there is some obstruction to passage of urine the kidney above undergoes changes. The calyces, pelvis and ureter become dilated to a greater or less extent. The kidney undergoes fibrosis and parenchyma is steadily destroyed. If infection is present, pyelitis and pyelo-nephritis occur with more rapid destruction of kidney. The dilatation of proximal part of ureter is slight in non-infected cases and more marked in infected cases. It is greatest in cases of ureteral strictures. In the last type the stone acts as a ball valve resulting in large hydro nephrosis or pyonephrosis. The stone also takes the shape of an almond being broad at the upper end.

In sudden complete obstructions by impaction of stone, the kidney ceases to secrete and is liable to atrophy if the obstruction is not relieved in a couple of weeks.

The opposite kidney shows compensatory hypertrophy where one kidney is so destroyed. But this occurs only to a slight extent if infection is present in the primary kidney. A pyonephrosis of one kidney is always a danger to the opposite kidney which may suffer from toxic nephritis and even get infected through the blood.

Symptoms and signs.—These may be classified into those due to:

- (1) A rapidly migrating stone,
- (2) Those due to a slowly migrating stone,
- (3) Those due to renal back pressure,
- (4) Those due to infection.

1. **A rapidly Migrating Stone.**—Smooth small stones may give rise to mild transitory symptoms often overlooked as in children and young people.

Rough stones as of calcium oxalate give rise to severe renal colic with typical radiating pains into the groin, genitals or inner side of thigh. There is a frequent desire to pass urine but little is passed out and this may show some blood. There is severe nausea, vomiting and abdominal distension. These bouts of renal colic may repeat at intervals of a few hours for couple of days till the

stone drops into the bladder. The urine is visibly coloured with blood or presence of blood is observed only with the microscope. The urine clears in a few days.

2. *A slowly Migrating Stone*.—It gives rise to intermittent attacks of renal colic which may recur once a day, once in couple of days, weeks or at longer intervals depending on the rate of its migration. The attacks are milder and of shorter duration. In this type there is a maximum point of pain and tenderness that gradually shifts with the site of impaction. At first it is in the renal angle, then shifts to a point half an inch below and medial to the tip of 9th costal cartilage, then along the outer border of the rectus muscle to the external abdominal ring. This point is usually a little above the site of impaction. When impacted in the abdominal spindle, abdominal symptoms as nausea, vomiting, distension and constipation are more marked. When impacted in the pelvic spindle bladder symptoms with pain referred to the testicle are present. Pain on coitus, blood stained semen, night emissions and pain on defaecation are complained of when the stone is impacted just above the intra-mural part, owing to inflammation extending to seminal vesicles. When impacted in the intra-mural part frequency of micturition and tenesmus with pain referred to the frenum when the stone is at the mouth of ureter, are present.

Changes in the urine.—Haematuria. This may be microscopic or macroscopic varying from smoky urine to that of port wine colour. The rougher the stone the greater the amount of blood. Guyon has pointed out that persistence of haematuria for more than a few days after the cessation of renal colic strongly suggested impaction of stone. The presence of white blood cells in a greater proportion than red blood cells indicates impaction of stone. In infected cases the deposit is greater due chiefly to pus cells, epithelial cells from renal pelvis and ureter and red blood cells are few or absent. Hyaline casts may also be present. Presence of blood casts is indicative of pyelo-nephritis.

Symptoms of back pressure.—Persistent dull pain in the back and tenderness to pressure in the renal angle are significant of back pressure. The kidney may or may not be palpable depending on the distension and tenseness of renal pelvis. Large hydro-nephrosis are not common and even these are flaccid.

Infection.—Pyelitis and pyelo-nephritis give rise to intermittent or remittent types of temperature with shivering or rigors. There is increased pain and a tender palpable swelling may be felt. Other signs of chronic sapraemia are also present.

Examination

A stone in the ureter can rarely be palpated except when it is in the lower end where it may be felt per vaginum or rectum.

X-Ray Examination.—Radiograms may show shadows of stones in about 80%, pure urate, uric acid and cystine stones throw no shadows. An intravenous pyelogram may show the condition of kidneys, dilatation of renal pelvis or ureter and the relationship of shadows to the urinary tract.

Cystoscopy.—Changes in the ureteral openings, as oedema, congestion, haemorrhages etc., may be seen, when the stone is in the intramural part. In acute cases of impaction the orifice is seen to contract violently and either no efflux is seen or it is small in amount and often blood stained. When the stone is actually at the orifice it can be seen projecting, surrounded by bullous oedema and congestion.

Next an opaque catheter is passed up the suspected ureter and radiogram is done. Then sodium iodide solution is injected and another picture is taken. Then the fluid is allowed to run out and a third picture is taken. With this technique failure to show the shadow of a stone is only about 5%.

Calculus Anuria

This is the most important emergency in renal lithiasis, due to obstruction of ureters by stones. The obstruction may be:

- (1) Of both ureters simultaneously or consecutively with a few days interval.
- (2) Obstruction of the only functioning kidney, its fellow being destroyed by disease, by obstruction or absent.
- (3) Obstruction of one ureter, the opposite kidney, though healthy, not functioning owing to nerve reflexes.

Oliguria may occur in cases where opposite kidney is damaged by disease. Complete obstruction lasting over a fortnight is usually fatal to the kidney above. In the majority the obstruction lies in the upper portion of ureter and the stone is usually small not larger than a pea.

In fatal cases either both ureters become blocked or the ureter of the only functioning kidney is blocked. If one kidney is blocked and the other is healthy, there may be temporary anuria for 24 to 48 hours, after which it usually starts secreting. But one cannot be certain of this condition in such an emergency.

Signs and symptoms.—In many no prodromal symptoms may be evident. Often a previous history of renal colic and passage of stones may be obtained. Some may complain of backache and

polyuria preceding the onset of anuria. The painless type is serious as it indicates degeneration of both kidneys. In the painful type if anuria persists after pain has subsided, it indicates that the opposite kidney is functionless.

Clinical course.—*Stage of tolerance.*—During the first five days patient feels well enough to carry on his work but passes little or no urine. His blood urea rises steadily to about 100 mgms. per cent. on the third day, 150 mgms. on the fourth and is usually 200 mgms. before toxic symptoms appear. Anuria is rarely absolute, a few ccs. of blood-stained urine being passed daily.

Stage of intoxication.—He complains of headache, thirst, craves for water and has an aversion for solid food. Tongue is dry and coated. Bowels are constipated and abdomen distended and tympanitic. Nausea, vomiting and hiccough appear. If kidneys are diseased the symptoms appear earlier.

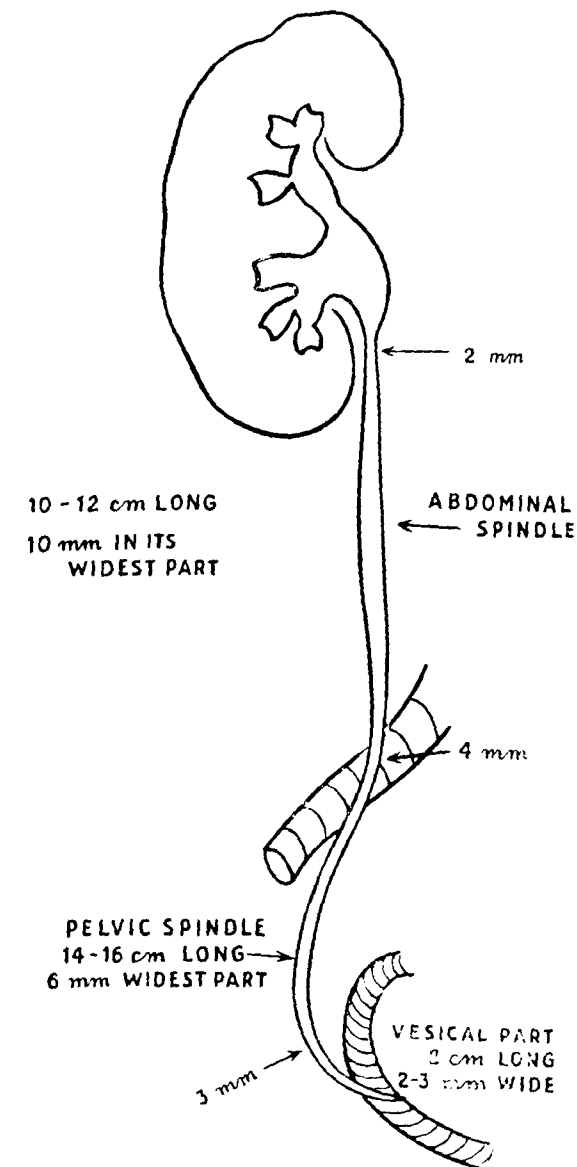
Stage of Coma.—Gradually drowsiness and mental confusion appear. Patient lies listless and apathetic. Finally coma and death occur.

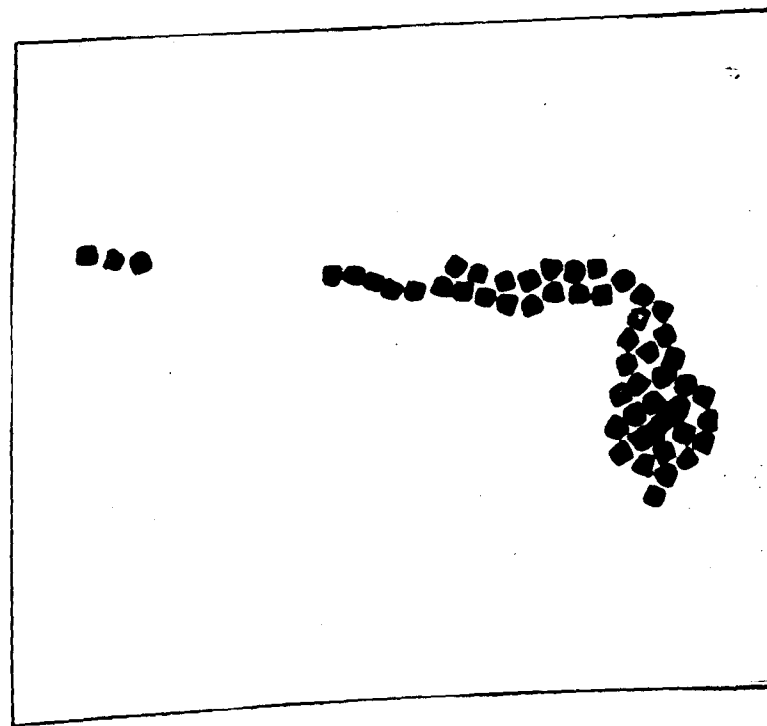
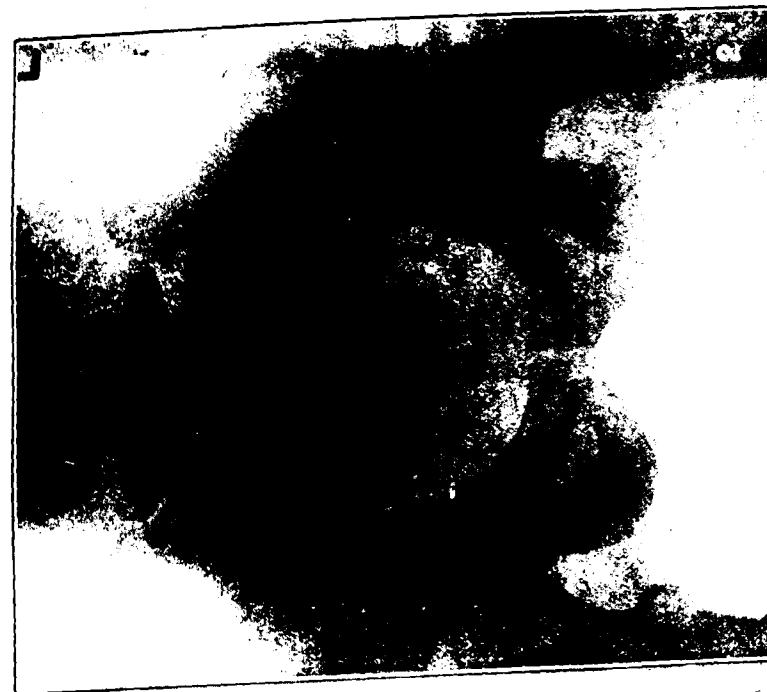
Pulse at first slow and hard, becomes soft, rapid and finally thready. Respiration is slow, deep and noisy. Temperature is normal at first, later it becomes subnormal. Blood urea may vary between 200 to 400 mgms. per cent.

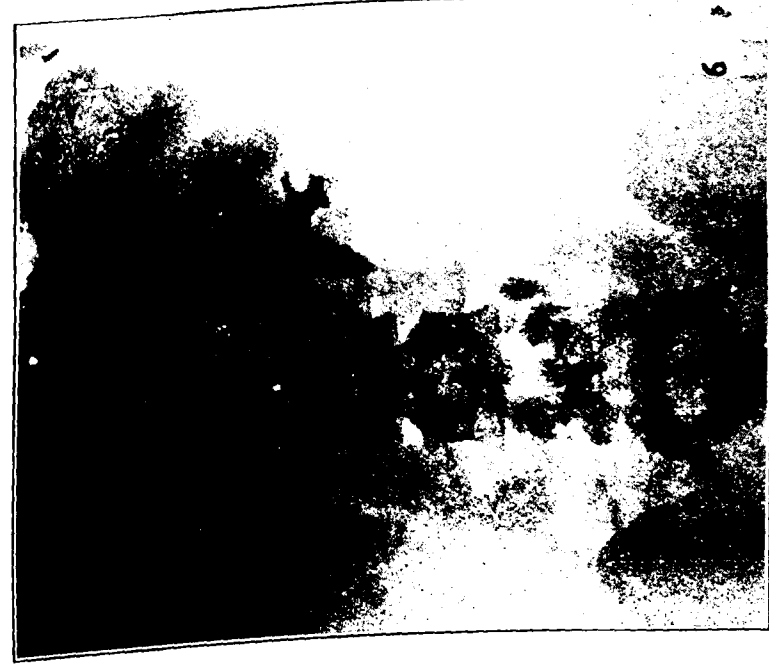
Treatment.—In the absence of uraemia, the first consideration is to establish urinary excretion by catheterising the ureters. Under local anaesthesia and aseptic precautions a cystoscope is passed in, ureteral openings are identified and examined. Next a No. 4 or 5 catheter (Charrier size) is manipulated and passed up the suspected side. If successful in passing it beyond the obstruction, a gush of blood-stained cloudy urine escapes from the catheter. Next a catheter is similarly passed up the opposite side. The catheters are left in for 48 hours, the catheters and penis being wrapped round with sterile gauze and the ends of catheters left in a sterile bottle with a known quantity of some antiseptic. The patient is placed in Fowler's position and plenty of fluids are given. 5% dextrose solution intravenously encourages urinary excretion. Solutions of sodium chloride (N. saline) should be avoided as it throws more work on the kidneys. Drugs as Caffein citras, theocin, sodium acetate etc., encourage urinary excretion. The polyuria, thus set up, brings down the blood urea fairly rapidly. The renal pelvis should be lavaged with silver nitrate solution 1/10,000 daily.

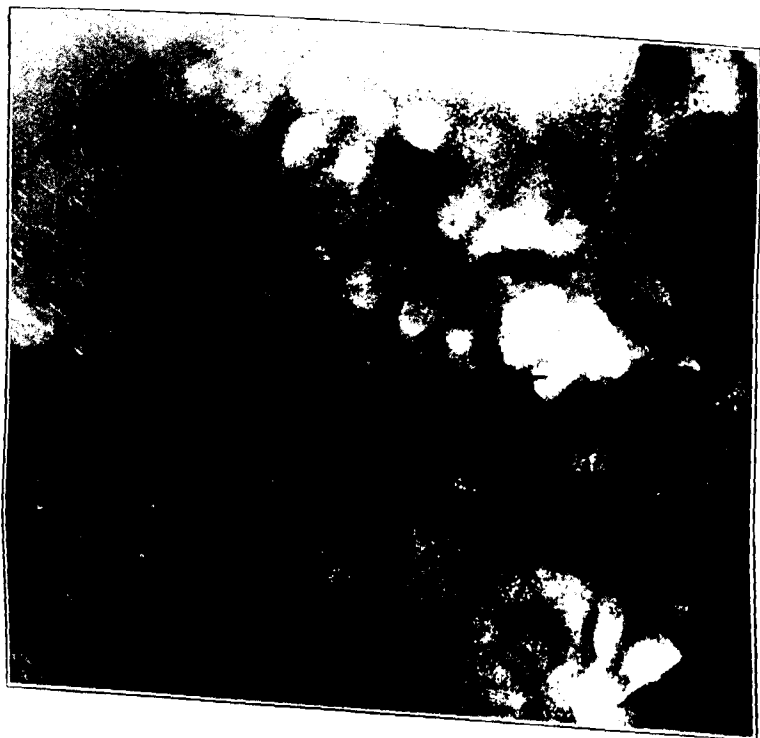
Catheters should be removed after 48 hours.

Open operations of pyelotomy or nephrostomy are indicated











REFERENCE TO RADIOGRAMS.

- (a) Showing the normal Constrictions of the ureter.
- (b) Multiple stones in the ureter.
 1. Same stones after removal.
 2. Stone left ureter is "nested" in the pelvic part.
 3. Stone with an opaque catheter passed up the left ureter by the side of the stone.
 4. Intravenous pyelogram. Shadow of an almond shaped stone in the line of left ureter.
 5. Same stone pushed up by two opaque catheters passed up the left ureter.
 6. Retrograde Pyelogram showing slight dilatation of Renal pelvis and calyx; stone seen in line of ureter.
 7. Retrograde pyelogram showing the opaque fluid surrounding the stone.
 8. Pelvis of Kidney is not dilated.
 9. An opaque shadow opposite the IV lumbar vertebra was proved to be a stone in the left ureter by a ureterogram. Renal pelvis is dilated.
 10. Radiogram showing one stone in the bladder and the other in the left ureter.
 11. Bladder stone removed by lithotripsy and two catheters passed up the left ureter and injection of papaverin.

in (1) Where one fails to pass up ureteral catheters. (2) Where anuria recurs. (3) Where uraemia is manifest.

It should be done under local anaesthesia with the addition of gas and oxygen where necessary. After bringing the kidney out, the renal pelvis is exposed on its posterior aspect and incised in its long axis and a drainage tube with its end cut obliquely, is fixed into renal pelvis by couple of catgut sutures. The tube becomes loose in 8-10 days. Some prefer a nephrostomy into lower calyx followed by insertion of a drainage tube into it.

If the exposed kidney is found disorganised or contains a large giant stone, the opposite kidney should be exposed and its pelvis drained.

A kidney with acute obstruction of ureter is found to be swollen, congested and plum coloured and its pelvis is distended with cloudy blood-stained urine.

Polyuria after these operations is a good sign, but oliguria is a bad sign. Blood urea estimations are carried out daily. A falling blood-urea is a good sign. Mortality is practically nil if operation is done within 48 hours of onset, but rises steadily to 25% on the third day, 30% on the 4th day, 42% on the fifth day and so on.

Treatment of Impacted Stones in the Ureter:

This consists in aiding the patient to pass the stones with the least damage to his urinary organs.

Medical treatment is indicated in cases of gravel or calculi not more than 1 cm. in diameter. In cases of renal colic a hypodermic injection of atropine with papaverine and Tr. Ammi Visnag, 3 ccs well diluted, by mouth is advised. This is combined with ingestion of large amounts of fluid.

The contraindications for medical treatment are:

- (1) Where signs of renal back pressure are present.
- (2) Presence of chronic parenchymatous nephritis, as fluid cannot be forced in these.
- (3) Evidence of obstruction in the lower urinary passage as enlarged prostate, urethral strictures etc.
- (4) Chronic hyperpiesis. Here fluids should not be forced in.
- (5) If urine shows presence of infection.

Cystoscopic methods are very successful in recently impacted stones of 5-10 mms. diameter.

If stone shows no signs of moving after 4-6 weeks of medical treatment cystoscopic manipulations should be tried. Ureteral

catheter size 4 Charrier is passed in and attempts made to slip it up past the stone. If held up, a couple of ccs of 0.2% pantocain with two drops of adrenalin are injected. This reduces local spasm and congestion. After a few minutes interval further attempts may succeed and catheter slip upwards. This is shown by a free flow of urine. Another catheter is now passed along the first one. Both are left in for 24 to 48 hours. Renal pelvis is daily lavaged with silver nitrate solution 1/10000. Before their removal two ccs of 2% papaverine solution is injected. This is followed by forcing in fluids by mouth. While removing, the catheters should be twisted several times. This may cause the stone to move down while catheters are slowly pulled out. But for stones in the abdominal portion of ureter, with a transverse diameter of 1 cm. and a vertical one of 2 cms, a *uopen* operation is advisable. Such stones can only be passed after much suffering and damage to ureteral mucosa and the kidney, as most of them are of calcium oxalate. Phosphatic stones are the result of infection and cystoscopic methods should not be attempted for fear of setting up pyelonephritis. A long cylindrical stone is usually "nested" and has to be removed by open operation.

Stones in pelvic ureter:—Stones in the intramural part of ureter should be dealt with by cystoscopic methods as slitting the ureteral meatus with diathermy electrode or cutting instruments.

Stones above the intramural part of ureter:—The ureteral meatus is first slit up with diathermy electrode and the ureter above is gradually dilated, followed by injection of papaverine solution, by glycerine etc. The stone moves down into the bladder in a few days.

Indications for open operations:—

- (1) Stones in the abdominal ureter, 1 cm. in diameter or more.
- (2) All stones over 1.5 cms. in diameter.
- (3) Where nesting of stone and peri-ureteritis are present.
- (4) Where kidneys show hydro or pyo-nephrosis.
- (5) Where cystoscopic manipulations have failed.
- (6) Where cystoscopy is badly tolerated, or ureteral manipulations cause severe reactions.

Operative treatment:—Where the kidney above is disorganised by hydro or pyo-nephrosis or contains a giant stone and the opposite kidney is adequate to carry on the urinary excretion, nephrectomy is indicated. The removal of stone is done at the

same sitting if easily accessible or deferred to a subsequent operation depending on the condition of the patient.

Where the renal function is good on the affected side, though containing stones, the ureteral stone is removed first and then the stones in the kidney either at the same sitting or at a subsequent date.

Uretero-lithotomy.—The abdominal spindle is exposed by a lumbar incision prolonged downwards parallel to inguinal ligament. The pelvic portion is exposed best by a sub-umbilical median incision. The stone is palpated and fixed by the thumb and index finger of left hand and an incision is made directly over the stone and extended upwards for one centimeter. After removing the stone the ureter below is dilated by bougies. The incision in the ureter is closed by Lambert stitches of fine catgut and wound closed with drainage.

I am obliged to the Barnard Institute of Radiology for the radiograms.

VISUALISATION OF THE URINARY TRACT FOR DIAGNOSIS

BY

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It is necessary to visualise the urinary tract to clinch the diagnosis. This may be done by direct methods with the help of a special instrument as the urethroscope and cystoscope or by indirect methods with the help of X-rays.

For this purpose the urinary tract may be divided into two parts, the upper and the lower, the upper one consisting of kidneys and ureter and the lower consisting of the bladder and urethra.

The upper part has to be visualised only by indirect methods in which the co-operation of an expert roentgenologist is necessary. Occasionally it may become necessary to examine the kidneys by direct vision after exposing the organ.

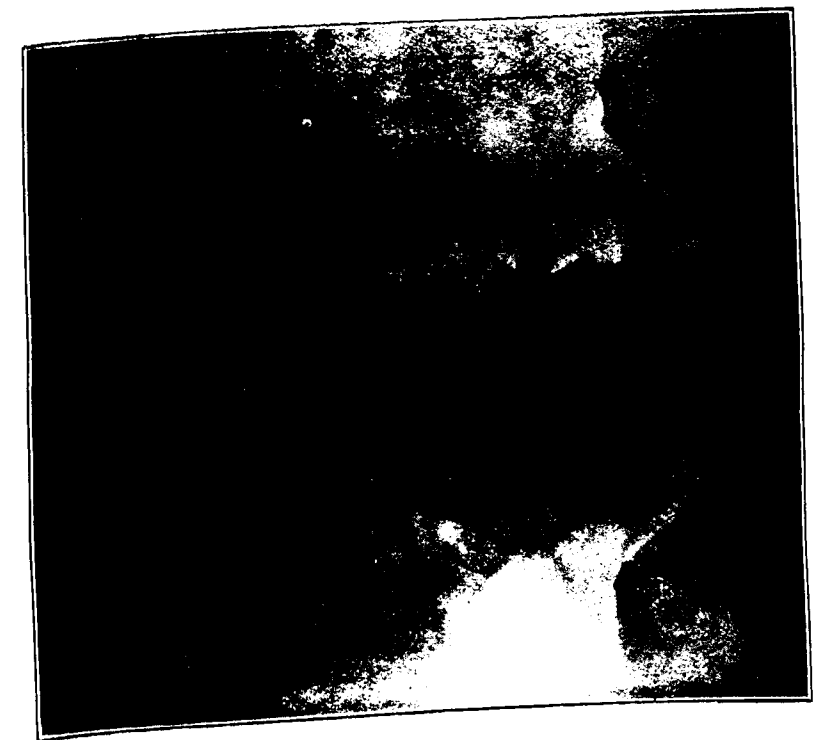
Prior to the advances made in roentgenology, diagnosis of diseases of this part of the tract was very poor. It is now possible to make a fairly correct diagnosis of surgical lesions of upper urinary tract. The introduction of organic iodine compounds,

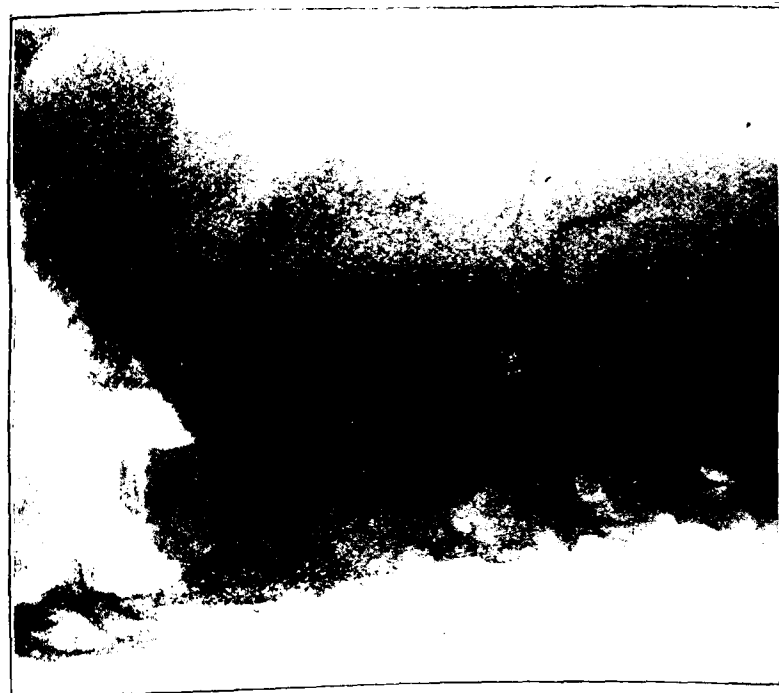
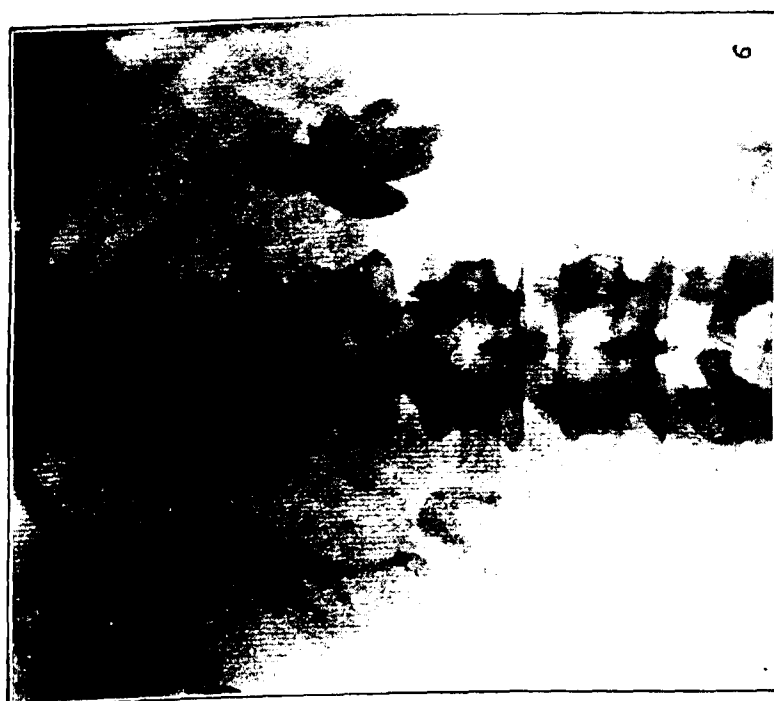
with a selective affinity for the kidneys without causing any damage to the body organism or the urinary tract, has been of the greatest advantage to the Urologist in his diagnosis.

For taking radiograms it is essential that the intestinal tract should be emptied of foreign material and gas. It is advisable to give the patient a good laxative two days prior to the examination and place him on a non-gas forming soft diet on the previous day. Fluid in-take should be restricted for 12 hours prior to intravenous pyelography. The colon should be emptied of gas on the previous evening and on next morning by enemata and pitressin.

First thing to do is to take a plain antero-posterior radiogram of abdomen and examine it. If it shows too much gas in the intestines, further enemata should be ordered to render the field clear. This plain radiogram may show distinct opacities due to renal, ureteric or gall stones, or calcified glands etc. Radiograms taken in two directions often help in diagnosis. Urinary calculi are seen in the line of the pelvis and ureter in an antero-posterior radiogram and these shadows are seen just anterior to or superimposed on that of the vertebral column in a lateral view, while shadows of gall stones lie nearer the anterior abdominal wall. The shape of these shadows and their density are often a guide. A pyramidal shadow denser in the centre with its pointed end directed downwards and slightly inwards opposite the transverse process of 2nd lumbar vertebra is more likely to be a stone in the renal pelvis than anything else. A dense fusiform or date-stone shadow in the line of the ureter is more likely to be a ureteral stone. Shadows of calcified tubercular glands are usually crenated and irregular. Diagnosis may be made more certain by excretion pyelography, by passing opaque ureteral catheters and by retrograde pyelography. There are certain calculi as of pure urates, uric acid and cystine which give no shadows, but their presence can be ascertained by the above methods where they may appear as negative shadows and filling defects.

Excretion Pyelography.—There are two well known organic iodine compounds. Perabrodil and Uroselectan B, are used for this purpose. Both have about 50% of iodine content. Both are now put up in ampoules ready for intravenous injection on the roentgenological table. The syringe to be used should be boiled in distilled water and the ampoule warmed to body temperature by being placed in warm water. The tourniquet used for injection if left on till the injection is over and then removed, helps in a higher concentration of the drug reaching the kidneys and hence better pictures result. The injection itself takes about













REFERENCE TO RADIOGRAMS.

1. Showing one large pyramidal stone with pelvis of left kidney and a number of small stones in the lower calyx.
2. Giant stone in right kidney. Nephrectomy was done for calculus pyonephrosis.
3. Giant stone in the left kidney. Small stone in the right kidney.
4. Lateral view of stones in the pelvis of right kidney. These removed by pyelotomy.
5. Lateral view of gall stones. Note the distance of opacities from the vertebral column as compared to No. 4 above.
6. Intravenous pyelogram—shows right kidney excreting normally. Left kidney occupied by a giant stone is not excreting the dye. Nephrectomy was done.
7. A pear shaped opaque body, an inch lateral to an opaque catheter in the left ureter.
8. Same case with sodium iodide injected into left renal pelvis. The solution surrounds the opaque body. Diagnosis is stone in the lower calyx of left kidney.
9. An opaque round shadow showing rings in left renal region.
10. Same patient, after uroselectan. Right kidney excretes the dye, the left does not. The left renal pelvis contains a large stone. This was removed by pyelotomy.
11. Intravenous pyelogram. Left renal pelvis and ureter are dilated. Early case of hydro-ureter and hydronephrosis.
12. Same case—retrograde pyelogram.
13. Retrograde pyelogram shows left ureter and left renal pelvis dilated. The ureter is pushed outwards by a mass of malignant lumbar glands.
14. Retrograde pyelogram—shows right kidney pushed downwards and inwards, by a malignant teratoma in the right lumbar region.
15. Intravenous pyelogram in a case of right hydronephrosis. Left kidney is normal.
16. Another case of right hydronephrosis. Left kidney is functioning normally. Both were treated by nephrectomy of right hydronephrotic kidney.
16. Left hydro-ureter and hydronephrosis visualized by intravenous pyelogram. There was a stricture of ureteral meatus, which was dilated through a cystoscope.
17. Retrograde pyelogram. Left ureter dilated. The opacities outside the line of ureter are calcified glands. Case of renal tuberculosis of left side.
18. Retrograde pyelogram showing a low placed right kidney with deformed pelvis suggestive of malignant growth in the kidney.
19. Retrograde pyelogram showing pyonephrosis of right kidney.
20. Retrograde pyelogram. Note the elongated minor calyces, suggesting polycystic condition of both kidneys.
21. Retrograde pyelogram. Note the dilated condition of right upper calyx ulceration probably tubercular.

30—40 seconds. The drug can be used in children and infants, the doses being proportionately smaller.

The advantages of excretion pyelography are obvious. Easy visualisation of upper urinary tract without the necessity of urethral instrumentation which is either difficult or impossible in children and often contra-indicated in some cases in adults, *e. g.*, in acute and chronic sepsis of lower urinary tract, tuberculous nephritis, severe haemorrhages from urinary tract, where ureters have been transplanted into the colon, in ureteral obstructions, in bifurcated ureters, where the urea clearance is low and where instrumentation is likely to be followed by severe reaction. In addition to this excretion urography gives a fair indication of the functional capacities of each kidney and both sides being visualised simultaneously can be easily compared. In conditions of hydronephrosis, there is no risk of rupture but delayed pictures of 1 to 2 hours should be taken. Relationship of intra-abdominal tumours to the urinary tract can be visualised with advantage in diagnosis and operative treatment. The contra-indications are only few, *e. g.*, severe disease of liver, acute infections of urinary tract, acute and chronic uraemia as shown by a high blood urea and low urea clearance. Iodine idiosyncrasy is rare with this drug. If possible screening should be done and pictures taken when the urinary tract is well visualised. Usually two small spots are seen at first in the renal region. These gradually increase in size and outline the calyces and pelvis. Next the image of renal pelvis becomes continuous with that of ureter. This is the period of maximum elimination and a picture should be taken now. This ends the diastole of renal pelvis. With the onset of its systole the ureters become visible and the bladder slowly fills out. Both sides should be compared carefully to determine the normal from the abnormal. There is often an alternating activity in the kidneys, when one is in systole, the other may be in diastole. Pictures are best taken at 8 to 10 minutes, 20 min. and 45 minutes with a picture of the bladder between the first and second pictures. The bladder should be emptied before the second and third pictures, so as not to obscure the lower ends of ureters. Ureteral compressions, before the second and third pictures, is one of the best methods for improving images as it increases concentration by stasis. But the compression should be applied simultaneously to both ureters, should be equal and at the same levels. This is best done by an inflated rubber bag being pressed over the supra pubic region. However this is not indicated in every case but only where an early lesion is suspected or where

an intensity of the image is desired. Compression may show dilatations in the ureters which otherwise would not be noticed.

The interpretations should be done jointly with the Radiologist guided by the clinical signs and symptoms of the case. A good image indicates a well functioning kidney and a poor image means a poorly functioning kidney. Absence of an image in all pictures may mean the absence or destruction by atrophy or anuria of the kidney. If only the calyces and pelvis are seen but not the ureter and the former appear dilated, it would indicate a block at pelvi-ureteral junction by stone, growths, pressure by artery, pressure by growths outside or kinks in the ureter etc. If the affected side can still be visualised even after the healthy side shows no shadows, it may mean a partial block repairable by a plastic operation.

Hydronephrosis.—The minor calyces become convex towards the renal paranchyma and appear as knobs. A flattening of the curved inferior border of pelvis with inward bulge of pelvi-ureteral junction becomes evident. Finally the pelvis and calyces become enlarged and rounded.

New growths.—In the early stages some minor calyces are blotted out especially the upper ones and the outline of pelvis becomes distorted.

Tumours of renal pelvis are shown by filling defects or a complete obliteration of pelvis in the presence of some dilatation of minor calyces.

Calculi in ureters of uric acid and cystine may appear as filling defects or negative shadows or as ringed shadows when the pelvis has emptied.

Megalo-ureter with hydronephrosis.—It is the result of prolonged partial obstruction low down in the ureter when unilateral. When bilateral with a dilated bladder the obstruction is in the neck of bladder or prostatic urethra but with a contracted bladder it is due to tumours in the pelvis causing compression of both ureters.

Sometimes shadows extraneous to urinary tract may get super-imposed on that of the urinary tract and cause a doubt. Hence we advise that a preliminary plain radiogram should always be done.

The picture of the bladder may show presence of diverticula etc. The shape of bladder often gives some information. In the absence of obstruction to lower urinary passage a strong bladder picture indicates a good condition of the kidneys and a weak bladder picture shows a poor condition of the kidneys.

A single diseased kidney may be met with occasionally. It is in such cases that intravenous pyelogram is a good guide of the danger of any surgical intervention including urethral instrumentation.

One is able also to make out congenital deformities and defects of urinary tract such as horse-shoe kidney, fused kidney, misplaced kidney etc.

Ascending pyelo-ureterography

This has to be done by a Urologist as it can be done only with the help of a cystoscope.

It should be undertaken only for confirming a diagnosis as in the case of tumours of kidneys, tumours of renal pelvis, polycystic kidney or other abdominal tumours. The contra-indications for this procedure are:—

- (1) Cases of renal inefficiency as shown by high blood urea and low urea clearance as in bilateral renal disease.
- (2) Acute inflammation of lower urinary tract.
- (3) In severe chronic urinary sepsis as cystitis, pyelo-nephritis etc.
- (4) Very old people and young children.

It should never be attempted where diagnosis by other means can be definitely made. It should be used as an accessory method to excretion pyelography where diagnosis is uncertain. Retrograde pyelography is not advisable in tuberculous nephritis. In advanced cases of diseases of kidneys a retrograde pyelogram if indicated should be done only on the diseased side. If the healthy side is irritated by the sodium iodide, there is a liability for the blood urea to rise. The trauma caused by the introduction of ureteral catheter is liable to set up a temporary congestive obstruction in the ureter of the only healthy kidney.

The patient is given a hypnotic as bromide grs. 20-30, luminal etc., two hours prior to cystoscopy. Local anaesthesia with pentocain or a small low spinal anaesthetic is given and the cystoscope is passed under aseptic precautions. After a survey of the bladder etc., opaque ureteral catheters are passed and urine collected for bio-chemical and bacteriological examinations. Then a plain picture is taken showing up the ureters by the presence of opaque catheters and their relation to other shadows. Next 5 to 10 ccs. of opaque medium are injected by gravity method. The pain or ache elicited in the patient by distension of renal pelvis is the warning to stop further injection. If small sized catheters are used overdistension is avoided as the fluid can run

the prostate. The ducts of the middle lobe open above the verumontanum.

The normal colour of mucosa here is a little deeper than that of the bladder. Congestion of verumontanum due to inflammation or sexual mal-practices may be noticed. Granulations at the mouth of utricle, ulcers in the floor, polypi and papilloma that give rise to frequency of micturition, etc., may be seen and treated. Sinuses leading to lateral lobes of prostate may be seen on the lateral walls. Openings of false passages and fistulae may also be seen. Fine opaque catheters should be passed up these and sodium iodide solution injected for fully visualising the tracts by a roentgenogram. Congenital valves are best seen by this instrument. Diathermy fulguration of polypi, papillomata, granulations and topical application of drugs could be carried out under direct vision.

Indirect Visualisation.—A plain roentgenogram may show prostatic stones or stones impacted in prostatic urethra. Fistulous tracts opening in the prostatic urethra have to be visualised by passing fine catheters into them through a urethroscope and injecting sodium iodide solution.

Bladder.—Direct visualisation is the best and is done by cystoscopy. A retrograde viewing telescope in addition to the ordinary one is of great advantage. With the former, one can visualise the vesical aspect of the sphincter for an enlarged middle lobe, etc. Of this type a Swift Jolly is the best. With a cysto-urethroscope both the bladder and posterior urethra can be examined. In males the irrigating cystoscope is introduced and bladder is lavaged till return flow is clear. Where bleeding is present the bladder after emptying is slowly filled with half a drachm of adrenalin 1/1000 diluted with one pint of water. If the field is still dim, it should be emptied and filled with sterile liquid paraffin. As this does not mix with urine or blood one can make out the source of bleeding. In women it is better to lavage the bladder and fill it before introducing the cystoscope. Bladder should be distended with 8 ounces of fluid in males and 10 ounces in females. Where bladder is irritable from chronic cystitis gradual distension should be done. A spinal or caudal anaesthesia is the best. Where blood clots are present, it is better to evacuate them by Bigelow evacuator before any examination is undertaken. Cyanide of mercury lotion 1 in 8000 is quite clear and also a good antiseptic and non-irritating. A regular examination of the whole of bladder should be done and charted out. Most pathological conditions are found round the ureteral openings, trigone and

neck of bladder. A general survey of lateral walls and superior wall is done. Then the *Bas Fond* and ureteral openings are carefully examined and compared with each other. Next the trigone and neck of bladder are examined. After this ureteral catheters are passed up the ureter for visualising ureters and renal pelvis. If openings of diverticula are seen an opaque catheter should be laid into them and roentgenogram done.

1. *Indirect visualisation.*—A plain radiogram would show presence of stones in the bladder or lower end of ureter and sometimes the contour of bladder as well in alkaline cystitis owing to deposit of calcium phosphates on the wall.

2. *Cystograms.*—The bladder is filled with 200 to 300 ccs. of a 10% sodium iodide solution and radiograms in different planes are taken. These would show filling defects by growths and presence of diverticula.

3. *Pneumo-cystograms.*—After completely emptying the bladder 200 to 300 ccs. of air are injected through a fine catheter and radiograms taken. Complete filling is necessary, stopping when patient complains of discomfort or the piston of syringe is pushed out by contraction of bladder. In taking radiograms an angle of 15° to 25° is given so that the lower margin of bladder is seen 4" or more above the symphysis pubis. A posterior film is taken with the central ray directed upwards and forwards so as to project the coccyx and sacrum above the field. A low kilo-voltage tube of 40 to 50 K. V. is used. This brings out in relief enlargement of prostate, bars, diverticula and even fasciculation of bladder. Foreign bodies that were not visible are rendered visible by contrast. If a sodium iodide cystogram was previously done growths stained by that solution are distinctly brought out in relief.

1. A normal bladder gives an ovoid pneumogram of 300 ccs. capacity, and its base is seen parallel to the upper border of symphysis.

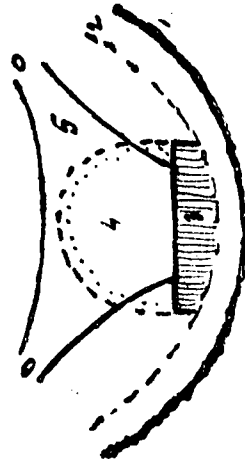
2. A simple mid-lobe hypertrophy is seen as a smooth edged ovoid projection into the bladder going well above the symphysis pubis. Lateral projections are seen in hypertrophy of lateral lobes.

3. Irregular projections from bladder base line are usually those of malignant growths. Such ulcerating growths are brought out well if previously stained by sodium iodide solution.

4. Calculi in the prostate, bladder and lower part of ureter are made more clear.

5. Growths as papillomata are seen as shadows lateral to the trigone.

Diagram to interpret Pneumo-cystogram.



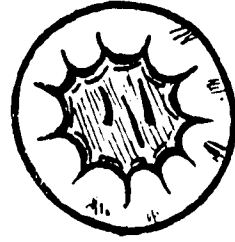
1. Outline of symphysis and bony brim.
2. Outline of air distended bladder.
3. Shadow of bar.
4. Outline of shadow of enlarged middle lobe.
5. Outline of trigone when hypertrophied.



1. Outline of bony brim.
2. Outline of air distended bladder.
- 3-4. Malignant growths.
- 4-4. Non-malignant growths as papilloma.



1. Floor of posterior urethra with upper part of Verumontanum and verumontanum.



2. Normal view of vesical outlet from urethral aspect.

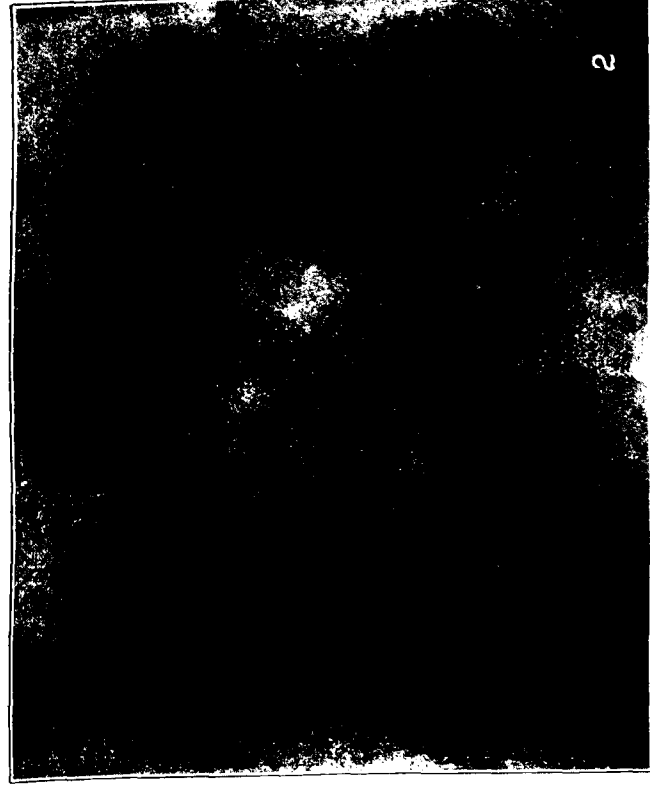


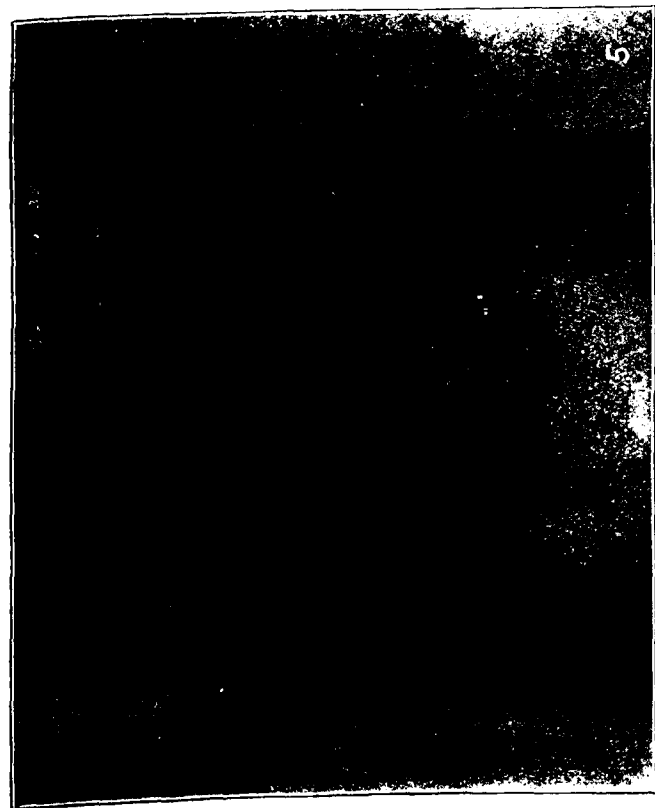
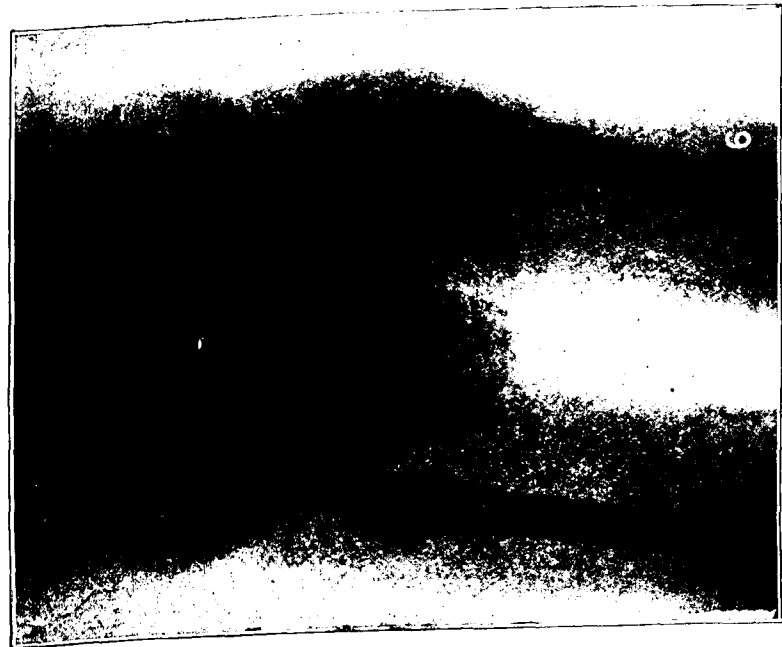
3. Enlarged prostatic lobes and upper part of verumontanum.

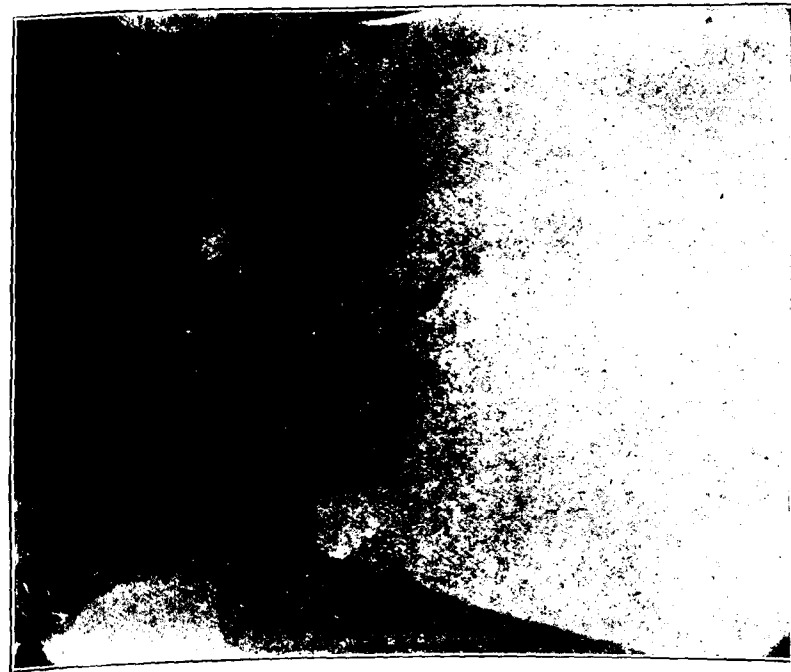
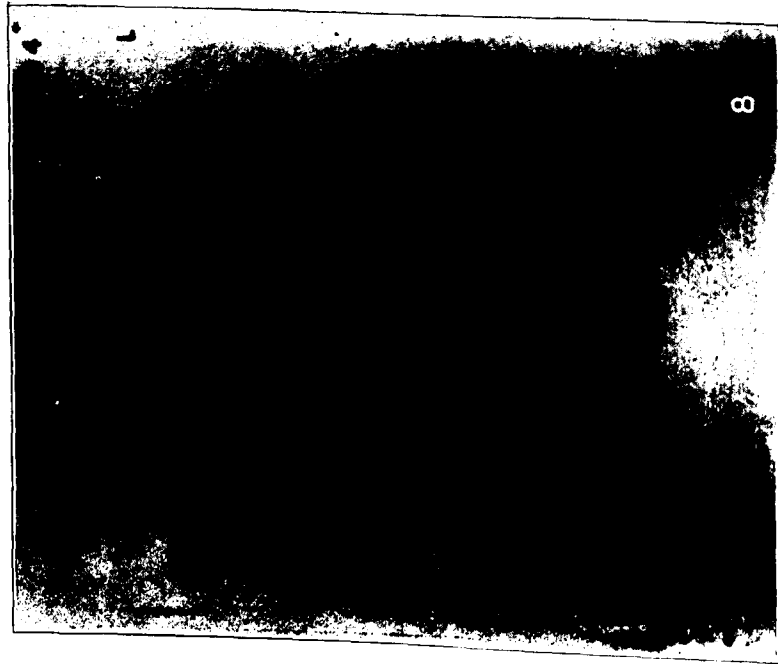


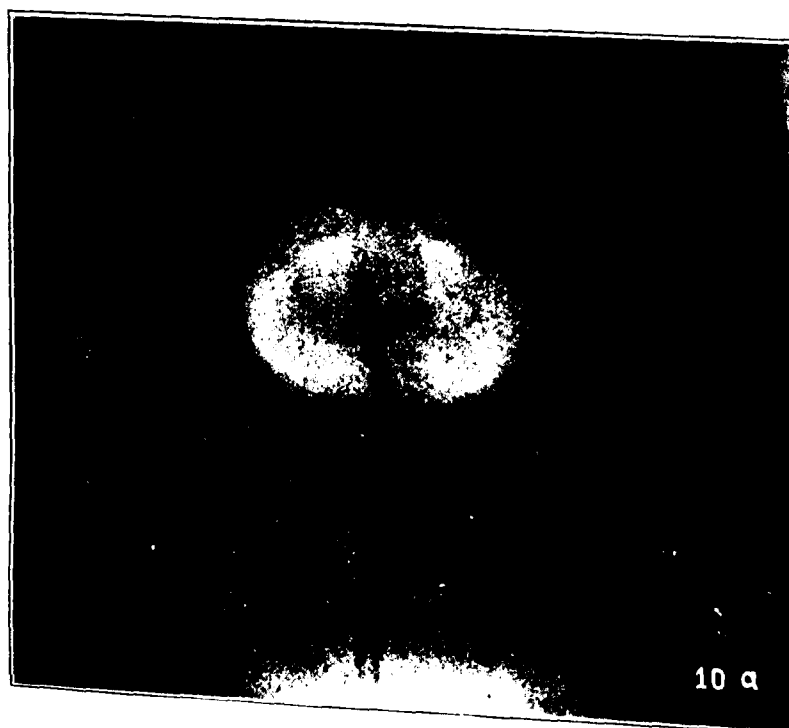
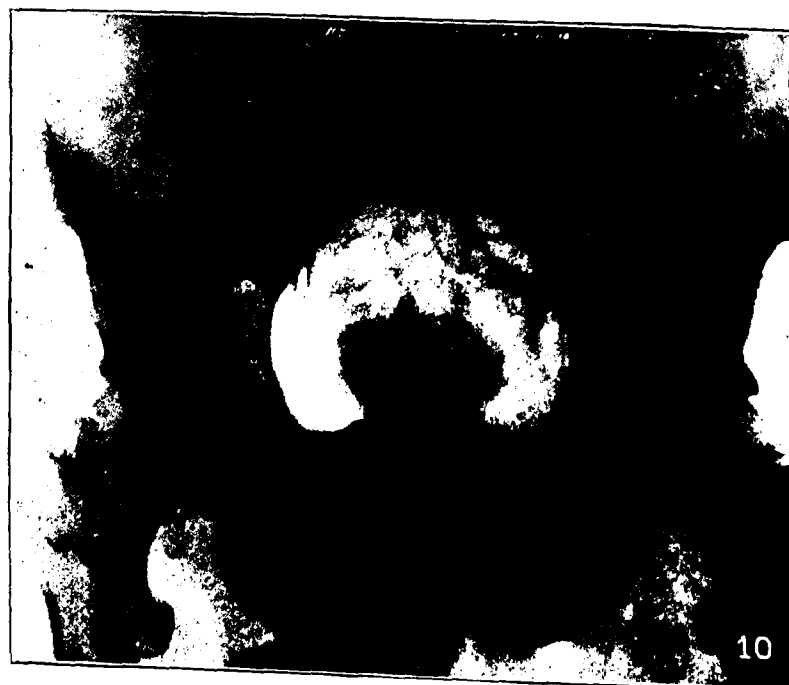
4. Enlarged prostatic lobes with a middle lobe.

DIAGRAMATIC









REFERENCE TO RADIOGRAMS.

1. } Plain Radiograms showing stones in Bladder.
2. }
3. }
4. Radiogram after filling bladder with air. This has brought out shadow of stone very clearly.
5. Stone in bladder prior to lithotrity.
6. Broken bits of stone seen after lithotrity.
7. Large stone, phosphatic coating.
8. Calcium oxalate stone in a boy. Note irregularity of surface.
- 9-a. Cystogram with sodium iodide. Filling defect on left.
- 9-b. Pneumocystogram. Growth causing filling defect in previous picture is brought out distinctly in this, being stained by sodium Iodide.
- 10-a. Pneumocystogram normal showing clean edges parallel to brim of Pelvis.
- 10-b. Pneumo-cystogram showing an enlarged middle lobe projection above base of bladder.
11. Sodium Iodide cystogram showing diverticulæ.

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MARCH '36] FILARIAL INFECTIONS—SUNDARAVADANAM

6. Bars at the neck of bladder are shown as transverse shadows just above the symphysis pubis.

7. Foreign bodies, small stones not clearly visible in an ordinary radiogram become distinct and clearer.

8. Diverticula are brought out clearly.

9. Defects caused by tumours and cysts outside the bladder are clearly seen.

In cases with more than 12 ounces of residual urine gradual emptying of bladder should be done by withdrawing 3 to 4 ounces every hour. If well distended the first withdrawal may be 12 ounces but subsequently 3 ounces every hour should be withdrawn. A stiff No. 5 catheter should be used under usual aseptic precautions for filling bladder with air.

I am obliged to the Barnard Institute of Radiology for the roentgenograms of the cases in my wards.

SURGICAL TREATMENT OF FILARIAL INFECTIONS

BY

DR. B. M. SUNDARAVADANAM, F.R.C.S., (ENG.),

Hony. Surgeon, Govt. General Hospital, Madras.

THE importance of filariasis is centred in the pathological conditions produced by the infection of *microfilaria bancrofti*. The surgical pathology of this condition will be dealt with shortly.

Infection is carried to the human host by the mosquito chiefly by the *Culex fatigans*. The larvae enter through the puncture caused by the mosquito bite. Manson-Bahr however has proved experimentally that the larvae can even enter through the intact pores of the skin from polluted water in the same manner as the *Ankylostoma duodenale*.

The mosquito sucks up the sheathed embryo from a filaria-infected person. These drop off their sheaths while in the mosquito and thus become free, undergo metamorphosis and develop into larvae. These larvae are injected into human beings where the females get fertilized and the embryos are let loose. The adult filaria *bancrofti* lives in the retroperitoneal tissues, the females lay their embryos in the lymph stream which eventually enter the blood stream thus appearing in the peripheral blood.

Regarding the age incidence, it is very rare to see any

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THE importance of filariasis is centred in the pathological conditions produced by the infection of *microfilaria bancrofti*. The surgical pathology of this condition will be dealt with shortly.

Infection is carried to the human host by the mosquito chiefly by the *Culex fatigans*. The larvae enter through the puncture caused by the mosquito bite. Manson-Bahr however has proved experimentally that the larvae can even enter through the intact pores of the skin from polluted water in the same manner as the *Ankylostoma duodenale*.

The mosquito sucks up the sheathed embryo from a filaria-infected person. These drop off their sheaths while in the mosquito and thus become free, undergo metamorphosis and develop into larvae. These larvae are injected into human beings where the females get fertilized and the embryos are let loose. The adult filaria *bancrofti* lives in the retroperitoneal tissues, the females lay their embryos in the lymph stream which eventually enter the blood stream thus appearing in the peripheral blood.

Regarding the age incidence, it is very rare to see any

surgical condition produced by filaria before 10 years of age though many boys living in endemic areas harbour the organism. As a rule these conditions are most common during the second and third decades of life and are rare after 50.

The obstruction of the lymphatic vessels is followed by inflammatory affections of filarial origin. The inflammatory attacks called filarial lymphangitis or filarial fever occur periodically. These inflammatory attacks are presumably the result of toxins which are liberated either by the dying or dead filariae or they may be due to toxins produced by secondary infective organisms. As a matter of fact streptococci have often been cultured from the fluids obtained from the tissues.

Lymphatic obstruction is caused in two ways chiefly:—

- (1) *By the death of the parasite.*—In the course of the absorption of the remains of the parasite, there is a tissue response. Proliferation of eosinophil cells and the fixed connective tissue cells occurs giving rise to fibrosis and cicatrization in the lymph glands and the peri-lymphatic areas. This is a very slow process and generally takes many years.
- (2) *By inflammation due to secondary organisms.*—The organisms that are commonly found are chiefly: streptococci, rarely staphylococci and the B. Coli. The streptococci vary much in their virulence. The milder strains give rise to acute lymphangitic or filarial fever while the severe forms cause acute streptococcal funiculitis, and septicaemia. The staphylococci give rise to localized suppurations in different parts of the body, most commonly in the extremities and the spermatic cord. The B. coli are specially found in cases of intra-abdominal suppuration generally in the iliac fossa in relation to the iliac glands.

Once the lymphatic obstruction is brought about, dilatation of the lymphatics of the skin follows, with consequent lymph stasis and formation of minute lymph cysts. The continued stagnation and irritation cause hypertrophy of the skin which ultimately undergoes hyperkeratosis.

The pathological conditions produced by filaria bancrofti alone or in combination with secondary infective organisms may be divided into the following groups:—

- (1) *Inflammatory conditions.*—These include lymphangitis with the associated fever, lymph-adenitis and peri-lymph adenitis, phlebitis, thrombosis, funiculitis, orchitis and

epididymo-orchitis, acute filarial hydrocele, filarial abscess, even filarial salpingitis and oophoritis.

- (2) *Conditions arising from dilatation, tortuosity and pouching of the lymphatics.*—These include lymphatic varix of the vessels of the spermatic cord and of the scrotum giving rise to lymph scrotum.
- (3) *These include conditions due to obstruction of the lymphatics and subsequent changes that arise in the tissues as a result of this continued obstruction.* These are elephantiasis of the scrotum and the penis, of the vulva, of the mammae, of the extremities and other parts of the body.
- (4) *Conditions due to rupture of filarial lymph vessels giving rise to chyluria, chylous hydrocele and chylous ascites.*
- (5) *The fifth group, filarial arthritis, myositis, synovitis, etc.*

In Lymphangitis, the patient gets repeated attacks of temperature preceded by rigors. There is inflammation of the surface lymphatics of the skin, and at the same time there is enlargement of the lymph glands. Inflammation of the spermatic cords also occurs and the scrotum becomes red, very suggestive of an acute suppurative process within it. There is a well-marked periodicity in these attacks.

The treatment of this condition consists in rest in bed, hot fomentations and keeping the affected part elevated. Local applications of Icthyol in glycerine with injections of sulpharsenol are advocated.

Filarial abscesses as mentioned above may form in several situations. Suppuration in the elephantiasic tissues may occur in any part of the body. The treatment is the same as that for an ordinary staphylococcal abscess.

Filarial funiculitis and orchitis.—The cord becomes very much thickened while the testis and epididymis are considerably enlarged. At operation, flakes of lymph are found adhering to the testis and epididymis, to the parietal surface of the tunica vaginalis. All the structures of the cord are also involved. Secondary pyogenic infection often occurs and there is suppuration in these parts. It is very common to cultivate streptococci from cultures from these parts. Signs of profound toxæmia accompany these inflammations.

The treatment consists of injections of anti-streptococcus serum and cardiac stimulants, and the local treatment for lymphangitis should be adopted. Surgical treatment is required only when there are signs of suppuration.

A hydrocele is very commonly found associated with various degrees of elephantiasis of the scrotum. In chronic hydroceles, the parietal layer becomes very much thickened and often calcified. The surgical treatment is the same as for a radical cure. If the sac is very much thickened, it must be excised.

Lymphangiectasis of the spermatic cord.—The Lymphatic vessels of the spermatic cord become dilated and varicose and cystic dilatations may be found along their course. Examination of the fluid from the cysts may disclose dead or living bacteria. This condition has to be diagnosed from other inguino-scrotal swellings. The treatment consists in excision of the dilated lymphatics.

Lymph scrotum.—When the lymphatics in the scrotum become varicose, they give rise to the above named condition. There is a history of periodic attacks of fever with inflammation, and enlargement of the scrotum may be present. Vesicles containing clear or slightly cloudy fluid are to be found scattered all over the scrotum. When some of these vesicles rupture, there is profuse lymphorrhea. Filariae are sometimes demonstrated in this fluid. The continuous discharge of this fluid over the surface of the scrotal skin causes a chronic eczematous condition. Secondary infection of the nature of erysipelatous inflammation may occur, or even actual suppuration. In advanced cases fibrosis occurs and the scrotum may become elephantiasic.

Treatment:—The skin of the scrotum should be kept clean to avoid secondary infection and to relieve the irritation and reduce the lymphorrhea. A lotion of zinc and lead acetate is very helpful. The scrotum is to be excised as for elephantiasis if there are recurrent attacks of fever and continuous lymphorrhea.

Elephantiasis:—This is the commonest manifestation of filarial infection that is seen here. It is endemic in certain parts of this presidency. The parts of the body generally affected are the scrotum and the lower extremities, less commonly the upper extremities, the vulva and the mammae; rarely are the other parts of the body involved.

There is a definite sequence of events before elephantiasis finally develops. The patient gives a history of attacks of filarial fever with signs of local inflammation limited to a particular part of the body. After the attack is over, the skin over the part is left rather hard and thick temporarily only at first, but after a few such attacks the thickness becomes permanent. This thickening extends to the deeper layers of the skin and the subcutaneous

tissues resulting in elephantiasis. The pathological conditions produced are the result of lymphatic obstruction, stasis and irritation. There is an exudation of lymph and hyperplasia, giving rise to the formation of fibrous tissue. The several changes are not distributed uniformly throughout the elephantiasic tissue. On making a transverse cut into the elephantiasic tissue, two definite layers can be made out. The superficial layer corresponding to the skin is very much hypertrophied and firm and hard. It looks homogeneous and consists mainly of fibrous tissue, oedematous connective tissue, lymphocytes, etc. The deeper layer consisting mainly of the subcutaneous tissue is soft and blubbery in character especially in the scrotum. On cutting into this layer, fluid escapes easily. The connective tissue in this region has undergone hyperplasia. It is important to note that in elephantiasis, the lesions are limited only to the skin and subcutaneous tissues and they do not extend deeper to the deep fascia.

Due to contraction of the underlying fibrous tissue the surface of the skin becomes uneven and even warty. The affected part enlarges slowly and steadily and if neglected may attain enormous proportions. The skin of the penis also may show a similar change. Occasionally the penis becomes elephantiasic without the scrotum being involved.

Treatment is operative. This consists in a complete excision of the tumour. Pre-operative treatment consists in getting the skin of the scrotum free from infections such as eczema, dermatitis, etc. This is treated with suitable antiseptics. The injection of polyvalent anti-streptococcal serum is beneficial before operation. Calcium chloride is to be given for 3 days prior to operation.

The Operation:—Through a median incision from a point about the middle of the pubis to the mouth of the prepuce along the middle line, the dorsum of the penis is exposed. The organ is dissected out, taking care not to injure the urethra. Next the spermatic cord and the testis along with it are freed from the mass of the scrotum and then by a curved incision, the whole mass is removed. If any hydrocele is present, eversion of the sac is performed. In the majority of advanced cases, the scrotum is completely involved. So in this case, it is advisable to bury the testis in pockets made at the upper part of the inner aspects of the thigh and the skin edges are sutured. A drainage tube is inserted at the lower end. The penis is skin-grafted from the thighs.

Elephantiasis of the limbs: Pre-operative treatment.—The skin is to be rendered clean before any operation is attempted on

these parts and especially the lower extremities. Various operations have been devised with the object of draining away the lymph from the lymph-logged areas. By Sampson Handley's silk lymphangioplasty method an attempt has been made to drain the affected area by means of silk threads. Handley performed this operation by leading silk threads subcutaneously from the distal to the proximal parts of the limb by means of special probes devised by him. Favourable results have not yet been obtained in filariasis by this method.

Several methods aim at forming a communication between the lymphatic channels to the subcutaneous tissues and the deep muscular, periosteal and medullary lymph channels through holes made through the fascia lata and passing flaps of it through the muscles and periosteum into the medulla by means of trephine holes made in the femur. Flaps of fascia lata have been tucked in deeply between the muscles in cases of elephantiasis of the latter.

Kondoleon's operation consists of free incision of the fascia lata and excision of large pieces of the aponeurosis of the thigh and leg with the object of forming new anastomotic channels between the lymph spaces above and below the site of the excised aponeurosis. The more radical methods consist in excision of the whole elephantiasic mass down to the fascia over the muscles and then covering the raw surface by Thiersch grafts. This is fairly satisfactory in some cases.

Amputation of the limb is the last resort. An artificial limb is very useful to them.

Elephantiasis of the Mammæ.—This is a rare condition sometimes difficult to diagnose from diffuse hypertrophy. The thickening generally commences in the lower-most parts gradually fading above. Chiefly the lower two quadrants are affected.

Treatment consists in wedge excision of the elephantiasic tissue in a radiating fashion and uniting the margins by deep sutures. Complete excision should be performed if these measures fail or if there is diffuse elephantiasis.

Chyluria and lymphuria.—Chyluria is due to a varicosity of the lymphatics of the urinary tract caused by filarial obstruction either in the main lymph vessels or in the smaller lymphatics draining the tract. The vessels, particularly those of the bladder, rupture, due to over-distension and their contents escape. There is marked periodicity in chyluria. Chyluria itself is not dangerous to life if treated early.

Treatment consists in rest in bed, a low diet free from fats, plenty of fluids. Urinary antiseptics may be administered. Treatment on the whole is unsatisfactory.

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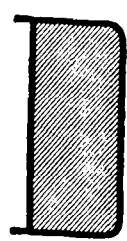
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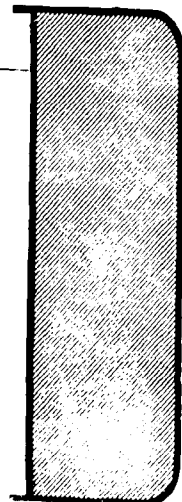
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