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JULY

1940

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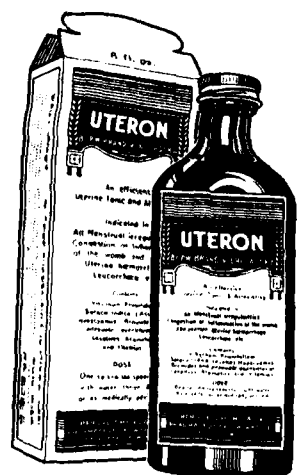
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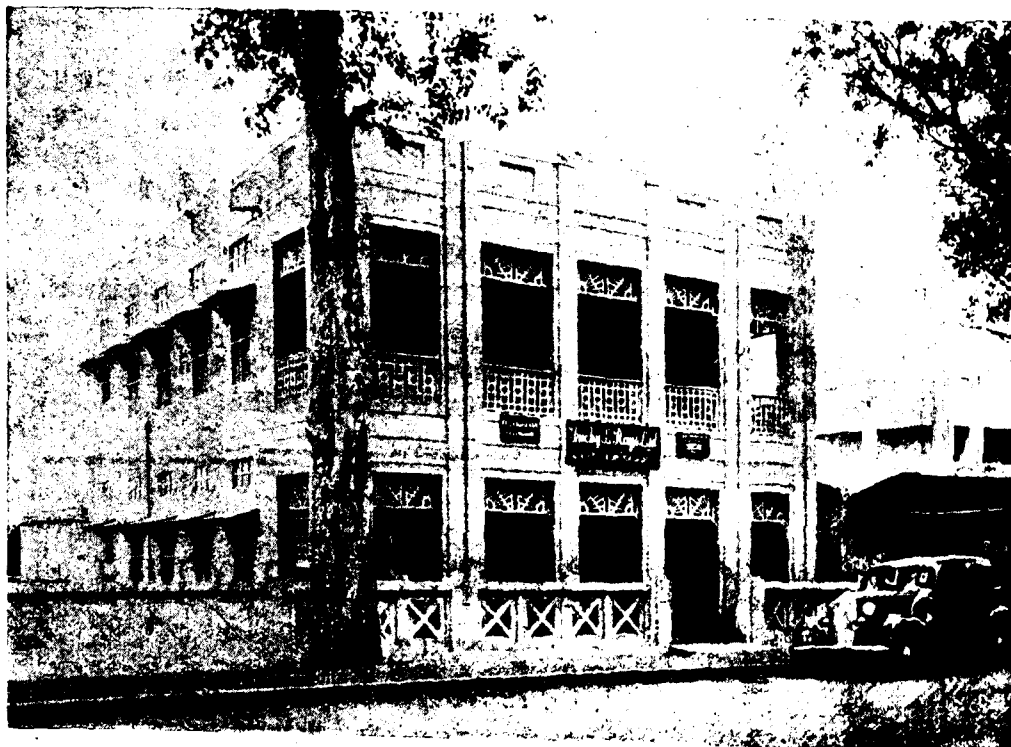
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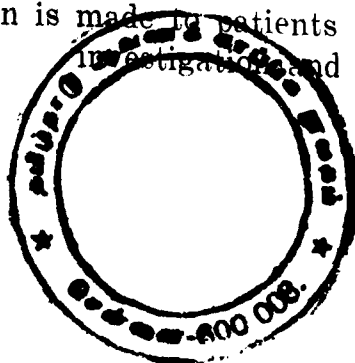
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Vol. VII]

JULY 1940

[No. 7

The Diagnosis and Treatment of Intracranial Tumours

BY

WYLIE McKISSOCK, M. S., F.R.C.S.

AND

J. W. D. BULL, M.B., M.R. C.P.

RADIOGRAPHY

The skull being roughly spherical in shape, in order that one may "see all round it" a number of pictures must be taken. This requires specialized apparatus, and accurate standardization of projection is necessary. Only one apparatus really satisfies these demands (Lysholm-Schonander skull apparatus). Lysholm, who has advanced this branch more than any other worker, takes five standard views of the skull:—
(1) Right lateral. (2) Left lateral. (3) . Postero-anterior. (4) Antero-posterior (half axial). (5) Submento-vertical (axial).

By taking fewer views than these one is running the risk of missing something. The findings may demand extra projections such as special views of the optic foramina, pituitary fossa, internal auditory meatus. The chief features to be looked for are as follows:—

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- (1) *Shape and size of skull.*
- (2) Presence or absence of *bossing*—the so-called beaten copper appearance may indicate increased pressure.
- (3) *Bone texture*—rarefaction or sclerosis, localized or generalized—gives a clue to the lesion.
- (4) Evidence of *fracture* recent or remote. Type of fracture e.g. linear, star-shaped, depressed.
- (5) *State of sutures.* Separation indicates raised intracranial pressure.
- (6) *Erosions.* Particularly of dorsum sellae or anterior clinoid processes. This again indicates raised pressure.
- (7) *Paranasal sinuses.* These should always be inspected. Sinus infection or new growth may lead to cerebral involvement.
- (8) *Vascular markings.* These are modified by such tumours as meningiomas. The vascular foramina may be enlarged by aneurysms or by hypertrophied vessels leading to vascular tumours.
- (9) *Calcifications.* Here it is necessary to differentiate between normal and abnormal calcifications. Normal calcifications may give a clue to the diagnosis for they may be displaced from their normal position. The following list includes those most commonly seen.

Normal	Abnormal
(1) Pineal gland.	(1) (a) Calcified aneurysm.
(2) Choroid plexus	(b) Naevus (Surge-Weber disease).
(3) Falx Cerebri	(2) Granuloma.
(4) Tentorium cerebri.	(a) Tuberculoma
	(b) Gumma
	(3) Tumour
	(a) Oligodendroglioma
	(b) Astrocytoma.
	(c) Some meningiomas.

Thus it is clear that the plain X-ray findings may give considerable information. The information is, however, very seldom sufficient, and often may be completely negative.

The radiological investigation then proceeds along one of two lines:—

(1) Examination of the ventricular system and convexity of the brain with air (pneumo-encephalography).

(2) Examination of the vascular system with a suitable dye opaque to X-rays.

The air examination of the brain will be considered first. This may be performed in one of two ways.

(1) *Ventriculography*:—This is the older method and was first described by Dandy in 1918. It consists in removing a certain quantity of fluid from the lateral ventricles and replacing the fluid with air. As a contrast-material nothing better than air has yet been discovered. Also it has the advantage of being non-toxic, rapidly absorbed, and easy to manipulate about the ventricular system. Two small burrholes are made into the parietal region of the skull (under local anaesthesia) and a cannula is inserted into each ventricle. The fluid is drained off and air replaced. As a general principle as much fluid as possible is removed and an equivalent amount of air replaced.

(2) *Encephalography*:—Encephalography is more simple to perform than ventriculography and has the added advantage of showing up the cerebral sulci and the basal cisterns as well as the ventricular system. Air is best introduced via the suboccipital route (between the foramen magnum and atlas). About 30 c. cm. of air should be introduced, after removing an equivalent amount of fluid. A less satisfactory method is to introduce air by lumbar puncture, but far more fluid has to be removed and therefore much more air needs to be introduced. It is very irksome to the patient, for the air has an irritative effect on the spinal cord. Moreover, a lumbar puncture *per se* tends to produce headache. This applies very much less to cisternal puncture. Suboccipital puncture has fallen somewhat into disrepute in this country, as one or two deaths were recorded in the early days. However, in skilled hands it is undoubtedly a safe operation and workers who perform it

repeatedly prefer it to lumbar puncture, from every point of view. As a general rule encephalography should be regarded as the method of choice in investigating the brain. The chief contra-indication to it is the presence of markedly raised intracranial pressure. But as cranial tumours are gradually being diagnosed earlier, encephalography will be more used.

At this stage the anatomy of the ventricular system must be considered. There are two symmetrical lateral ventricles separated by a thin film of brain substance, the septum lucidum. These ventricles communicate below with the third ventricle by means of two openings—the foramina of Munro. The aqueduct of Sylvius leads backwards and downwards from the third to the fourth ventricle. The fourth ventricle has three exits—two lateral (foramina of Luschka) and one in the midline (foramen of Magendie). The latter conducts fluid into the cisterna magna. In performing a ventriculography or encephalography examination the object is to fill all parts of the ventricular system with air. It is well nigh impossible to do this by injection and in fact undesirable and unnecessary; the same result is obtained by taking a number of projections in different positions. The air, of course, always remains uppermost relative to the fluid. The movements of the air and fluid are comparable to the movements occurring in a carpenter's spirit-level.

In normal cases the ventricular system is symmetrical, but an expanding lesion of any size will dislocate the ventricular system in some way. According to the type of dislocation the position of the lesion can be localized, and not only can it be localized but in many cases its pathology can be determined. This may be deduced from the shape of the deformity, in conjunction with the findings on plain X-ray, and finally by correlating the clinical history physical examination. Encephalography, which provides the pressure of air on the convexity, helps to differentiate intracerebral from extracerebral intracranial lesions. Examination of the ventricular system is quite essential for accurate localization of the process. Space unfortunately does not allow more than a brief sketch of the method and the conclusions.

(From the Practitioner, April 1940.)

Roentgenologically Visible Calcifications of Cardiac Valves

Hoffmann says that there are few records of roentgenologically visible cardiac calcifications. He describes his own observations in two cases. In the first, roentgenoscopy disclosed nothing abnormal on the lungs or the diaphragm. However, a dense shadow the size of an almond was observed in the left half near the center of the heart. This shadow moved up and down and when the patient was turned the shadow could neither be separated from the heart nor even transferred into its periphery. Furthermore, inspiration did not change the position of the shadow. The regularly pulsating movement of the calcium shadow was considerably more extensive than that of the cardiac outline. During lateral exposure the shadow made an almost vertical elliptic rotation. The roentgenogram indicated that the shadow represents a calcification of the mitral valve. The roentgenologic diagnosis of calcification of the mitral valve was supported by the clinical examination, which indicated a mitral stenosis and insufficiency. An endocarditis during childhood is regarded by the author as the cause of the mitral calcification. In the second case a dancing calcium shadow the size of a bean led to a more thorough examination. In view of the position of the shadow and of its dancing movements, the author assumes a calcification of the aortic valve. He thinks that a calcification of the coronary arteries can be ruled out because the movement of the shadow was more extensive than that of the edge of the heart.

Roentgenpraxis: Leipzig.

Stricture of Rectum Secondary to Lymphogranuloma Venereum Treatment with Diathermy

HARRY MARTZ, M.D.

MERRILL N. FOOTE, M.D.

In the past few years a voluminous literature has appeared on the subject of stricture of the rectum secondary to lymphogranuloma venereum. Almost without exception, however, the treatment of this condition has been dealt with superficially and briefly. The obvious reason for this has been the inadequacy of all forms of treatment instituted. An utter feeling of despair has arisen in both patient and physician, so that permanent colostomy has been accepted as the procedure of choice. What a high price this is for the young adult afflicted with an otherwise benign condition that can be reached with the finger! And no hope was entertained by these patients of ever having these colostomies closed after any local form of treatment to the strictured areas. Adult in his review of venereal diseases of the rectum states that "No permanent cure of stricture due to lymphogranuloma venereum has been reported to date."

In treating a patient with an almost complete stricture of the rectum, for which a colostomy was performed two years previously one of us (H.M.) came upon a form of treatment which was found quite satisfactory in curing these strictures. While no priority in the use of this form of treatment is claimed, since it was suggested in 1925 by Picard for so-called benign strictures of the rectum, its use is here reported in a small number of cases of stricture secondary to lymphogranuloma venereum with complete cure. This preliminary report is offered in the hope of having this treatment more extensively used, in an effort to save these patients from a permanent colostomy.

A few words regarding the etiology of this condition may lead to a better understanding of its clinical manifestations. Like syphilis, lymphogranuloma venereum has an early primary and a late secondary lesion. The first stage is an evanescent painless lesion, consisting of a herpetiform vesicle lasting a few days. Following this lesion and depending on its location, there

arise the various manifestations of the condition according to the lymphatic drainage from the particular area involved. Should the lesion occur on the external genitalia in either sex, the lymphatic glands of the groin, which drain these areas, become directly involved.

When the primary lesion is implanted on the posterior vaginal wall or on the cervix, the virus permitted to drain not to the inguinal glands, where it would be relatively benign, but to the posterior lymphatics lying in the uterosacral ligaments, which skirt each side of the lateral walls of the rectum, as Nesselrod has shown. Here they anastomose with and invade the rectal lymphatics, where an extensive perirectal fibrosis is produced, which is the underlying factor in the stenosis. By reason of this more common implantation in the female, buboes are relatively rare and stricture of the rectum is more frequent. In the male, however, the primary lesion commonly occurs on the surface of the glands or in the anterior urethra, both areas of which drain to the groin. This accounts for the more frequent occurrence of buboes in the male. There being no connecting lymphatics between the glands in the groin and those about the rectum, stricture in the male could not arise by any such spread. In the male a history is usually obtained of direct implantation of the virus in the rectal mucosa by sodomy and is accompanied with an ulcerative proctitis. Bensaude and Lambling state that a previous history of this was obtained in 80 per cent of seventy cases of stricture in the male. Sodomy was admitted by two of our male patients. Following this proctitis, which is usually associated with a sanguinopulent discharge, there results a stenosing fibrosis, leading eventually to a complete stricture.

There are, however, two other possible explanations for the occurrence of the condition in the male. If the infection should spread from a primary lesion in the anterior urethra to the posterior urethra, drainage to the perirectal lymphatics can occur. The drainage from the posterior urethra is similar to that from the prostate gland, and, since the prostatic utricle is embryologically homologous with a uterus, its lymphatic drainage is the same. The virus is therefore carried from the posterior urethra directly back to the perirectal lymphatics, where it produces

peradenitis and subsequent perirectal fibrosis. Another possible explanation for the production of rectal stricture in either sex is the development of a primary anal lesion with spread of the infection upward to the rectal lymphatics, through the columns of Morgagni.

The great variety of treatments offered for this condition leads one to conclude that there is no one really effective cure. The proctitis, which may precede the stenosis in the male or be associated with the stenosis in both the male and female later in the disease, with secondary fistulas and ulcerations of the mucous membrane, may be remarkably affected by antimony and potassium tartrate, faudin, sulfanilamide or Frei antigen. This we have found to our satisfaction, as have others (Bloom, Bensaude and Lambling and Shropshear). The pain in the rectum disappears, as do the purulent discharge and tenesmus. But in the cure of the stricture the results with these chemotherapeutic agents have been uniformly discouraging. One would hardly expect the dense fibrous stricture to yield to any form of parenteral injection therapy.

As regards surgical intervention, apart from colostomy little hope can be held out for it in the cure of these patients, for in nearly all cases there is a recurrence of the stricture. Colostomy when used for the relief of a complete obstruction, has its place in the care of the emergent symptoms of the far advanced stage. But as a form of treatment, with or without abdominoperineal resection of the rectum it is far from adequate or satisfactory, for it leaves these young victims with the care of a permanent foecal fistula. Even as a preliminary to other forms of treatment for the stricture, with the hope of subsequently closing the colostomy, it is of no avail. Lazzari did this in nine cases and could subsequently close but one.

We suggest a form of treatment which in our hands has been quite successful in the cure of these patients with stricture of the rectum, namely diathermy. This method is here emphasized because of its infrequent use in clinics in this country. Picard whose report appeared in 1925 was apparently the first to apply this form of treatment to fourteen cases of benign stricture of the rectum, with complete cure after a three year follow-up study. In December 1925, Bensaude and Merchand

reported on the use of diathermy with excellent results, after having tried a number of other procedures for these strictures. They, however, did not report its use in any cases in which this treatment the necessity for a colostomy is avoided. In February 1937 however, D'Allaines Hillemand reported the cure of a lymphogranulomatous stricture of the rectum in a patient who had had a colostomy performed for complete intestinal obstruction, by forty applications of diathermy in association with intravenous injections of sodium salicylate. The stricture melted away and the colostomy was subsequently closed. This is the only report of cure with diathermy in this type of case. One of us (H. M.) tried it in three such cases with complete success and subsequent closure of the colostomy.

Many of these patients had had other forms of treatment previously, such as administration of fuadin, antimony and potassium tartrate and Frei antigen, was given. The first patient so treated was given other forms of treatment at the same time, but in view of their known inefficacy it was believed that the diathermy was the effective agent. This, in association with Frei antigen injections, was therefore used in subsequent cases.

The diathermy machine used was of the old long wave type. One pole consisted of a metal plate applied to the lower part of the abdomen, and the other was a metal Hegar dilator which was inserted into the rectum. Increasingly larger sizes of dilators were used as the strictured area increased in caliber and were inserted without pain or any intention of mechanically dilating the stricture. The largest metal dilator that could be comfortably inserted was used. Treatments were given twice a week for twenty minutes each. The patient's tolerance to the diathermy was gradually increased by first using 900 milliamperes of current and then gradually increasing to a maximum of 1,800 milliamperes. Once a week during the period of treatment 0.1 c.c. of Lederle mouse brain Frei antigen was injected subcutaneously. It was found that this combined therapy of Frei antigen plus diathermy produced a more rapid dissolution of the stricture than the diathermy alone.

Jour. A. M. A., Mar. 23, 1940.

Clinical Application of X-Ray and Electrical Treatments in Modern Medicine

BY

G. GOSH, M.B., B.S., D.T.M.,

The Rontgen Clinic, Allahabad.

INTRODUCTION:—The importance of the application of Electricity in modern medicine and surgery is becoming greater and greater year by year, not only in relation to the actual diagnosis of disease, but also in respect of the cure of alleviation of various diseases. The control of electric current has opened up, for modern medicine and surgery, a wealth of diagnostic and therapeutic possibilities, which a generation ago were practically unthinkable or considered impossible.

In its most varied forms, applied directly as electrical energy, or converted into heat, light or movement, the electric current is a willing helper, whenever help or healing is required. As electrical energy we use galvanic, faradic and undulatory or sinusoidal current for the most varied medical purposes. The usefulness of ultra-violet light therapy is now an established fact. Every medical man knows that the rays have a profound effect on those nutritional disorders which are a result of a deficiency of vitamins in the diet, e. g. rickets in children and osteomalacia in adults. Many skin diseases derive much benefit from ultra-violet radiation.

The use of X-ray is one of the most important applications of electricity to medicine and surgery. During the last forty years, since the discovery of X-ray, a new therapeutic science has grown up and become firmly established as an essential procedure in the treatment of human ills. At the present time, X-ray therapy has fully justified its status as an efficient modality of treatment on a par with other therapeutic agents. An attempt has been made in this article to enumerate the conditions for which this form of therapy is of value.

Of recent years, a rational use of electricity is that of the employment of high frequency currents, for medical and surgical diathermy. More recently, great interest has been aroused in the uses of short waves in the treatment of various diseases. This constitutes one of the most important chapters of progress in medical electricity and opens up vistas of still greater possibilities for the future.

The following pages have been written for the guidance of the general practitioners in selecting their cases for the electro-medical treatment. It is necessary, however, at the outset to state definitely that electro-therapy is not a panacea for all ills.

The diseases which have been considered are those for which electrical treatment can be prescribed. In many of them, cure or relief can be expected in the major number of cases. The results that may be anticipated are mentioned under the headings of the various diseases. In stating these results, the various competent authorities under whose guidance these results have been achieved, have been quoted.

CLINICAL APPLICATION OF X-RAY THERAPY:—Owing to the limited amount of space in an article like this, it is not possible to describe in detail all the conditions amenable to X-ray therapy. The description must, therefore, be limited to a brief outline of its use in connection with the treatment of the more important and more common diseases, which the radio-therapist is called upon to combat. There are many other conditions which respond favourably to X-ray therapy. But it may be pointed out that X-ray must not be regarded in the light of a panacea or cure-all. In many cases it does not cure at all, but merely inhibits the pathological cells, allowing the normal body forces to perform their normal functions, and sometimes merely affording relief. In some conditions, X-ray alone will effect a cure.

Generally speaking, X-ray has an unlimited field of usefulness in medicine and is one of the most valuable therapeutic agents which modern science has to offer. Its scope of usefulness is constantly increasing, and, with a better understanding of its value and closer professional co-operation, it presents unlimited possibilities for the future.

I. DISEASES OF THE SKIN:—In dermatology, X-ray has long been a routine measure, and it was in this branch of medicine that it had its first principal application. In some instances, it is curative where other methods have failed. In others it is a valuable adjunct to medication. The advantage of its cleanliness, convenience, and absence of pain, and the elimination of the use of irritating and offensive ointments, usually commend it to the patient.

1. *Eczema*:—Probably in no dermatological condition has X-ray a wider therapeutic range or greater value than in eczema, both in acute and chronic types. The response of eczema to the ray is usually very prompt, frequently being manifest after the first or second exposure. Among the early symptoms to be relieved is the intense pruritus.

2. *Psoriasis*:—The majority of cases of psoriasis will clear up under X-ray treatment.

3. *Pruritus*:—X-ray forms one of the most valuable weapons in the treatment of pruritus. The commonest sites of this condition are the perineum and the anal region.

4. *Acne vulgaris*:—To-day, the use of X-ray is the counsel of perfection in the treatment of acne vulgaris, and is one of the most reliable servants of the dermatologist in this disease.

5. *Erysipelas*:—X-ray treatment is stated by several authorities to be of great value if administered in the early stages of this disease.

6. *Chronic ulcers*:—Oriental sore or Delhi boil and Lupus vulgaris (vegetating forms) yield quickly to this form of treatment.

7. *Tinea Tonsurans* (Ringworm of the Scalp) and sycosis (Barber's itch)—In these diseases, it is the treatment "par excellence."

8. *Cheloid and Warts* respond well to X-ray treatment.

9. *Malignant conditions* of the skin, e.g., rodent ulcers and epithelioma—Radium is the treatment of choice if available. When radium is not available, they may be treated by X-rays.

II. DISEASES OF THE BLOOD:—There are various blood conditions e.g., splenic anaemia, myeloid and lymphatic leukaemias in which X-ray treatment is, in many cases, the only therapeutic weapon capable of giving a measure of relief. The object of treatment is to reduce the number of abnormal cells, circulating in the blood to approximately a normal level. The general condition of the patient is thus improved and in some types, life appears to be definitely prolonged by this treatment.

III. DISEASE OF THE LYMPH GLANDS:—The treatment of lymph glands forms an important section of X-ray therapy. In Hodgkin's disease, the glandular enlargement can be considerably reduced by X-ray treatment. Simple inflammations of the lymph glands respond well to small doses of X-ray treatment. Where suppuration has not occurred X-ray treatment may prove very successful in dealing with tuberculous glands.

IV. TUMOURS:—Many kinds of tumours—both benign and malignant—of various parts of the body have been treated with benefit by X-ray. For fibro-myoma of the uterus, X-ray therapy is the treatment of choice, because it avoids operation with its attendant hospitalisation, disability and possible mortality which, though small, can hardly be called negligible. Uterine fibroids can confidently be expected to disappear or markedly diminish in size under X-ray treatment. The menorrhagia usually accompanying a fibroid is as a rule controlled after the first treatment.

Perhaps the greatest field for X-ray therapy is tumours and certainly the one that at present is holding the most widespread attention, is that of carcinoma. Many cases of carcinoma have been clinically cured by X-ray. In inoperable conditions, the use of the ray offers positive relief of the symptoms, probable prolongation of life, and perhaps regression and clinical cure.

V. MISCELLANEOUS DISEASES:—There are many other conditions where X-rays are recorded on good authority to have produced beneficial results. Thus many forms of acute and chronic inflammations are eminently amenable to X-ray therapy.

If treated at the proper stage, irradiation may either cause the process to abate at once or shorten the course of the disease by hastening the formation and absorption or spontaneous drainage of pus. These diseases may be considered under the following heads:—

1. *Inflammatory conditions*:—Among those which appear amenable to X-ray treatment are furuncle, carbuncle, cellulitis, erysipelas, phlegmon or abscess of the soft tissues, adenitis, onychia and paronychia, orchitis, epididymitis, mastitis and frontal and maxillary sinusitis. Cases of unresolved pneumonia have been treated with success. Parotitis yields readily to early exposure to Rontgen rays.

2. *Tubercular adenitis* responds well to X-ray treatment. Disappearance, or marked diminution in size, and subsequent calcification of the glands, can confidently be expected in this disease. In tubercular peritonitis also, X-ray irradiation, every three or four weeks, supplemented by daily exposure of the whole body to increasing doses of ultra-violet rays, is the most satisfactory method of treatment.

3. *Enlarged tonsils* of the infected type are benefited by X-ray treatment, their size being reduced to normal, the hypertrophied lymphoid tissue being destroyed, and the pus evacuated from all the cysts. The systemic diseases produced by infection from the diseased tonsils are greatly improved or cured. The reduction in size of the tonsils becomes apparent after the fourth to the sixth treatment. The shrinking continues after treatment has been completed, and it is not until after six months that they reach their ultimate size.

4. *Hyperthyroidism* (primary thyrotoxicosis):—The value of X-rays in this disease has been proved beyond doubt. The first improvement noted is a decrease in nervousness, reduction of pulse rate, and diminution of tremor. The patient begins to sleep better and there is less sweating. A gain in weight is usually noted early. The goitre is usually, but not always, reduced in size, sometimes disappearing altogether.

5. *Osteo-arthritis*:—Certain cases of osteo-arthritis respond to X-ray treatment when all other remedies have failed. The

knee joints appear to respond better than hips. Treatment of the spines also gives good results.

6. *Neurological conditions*:—Having observed that pain was relieved when cancer was treated with X-ray, the early workers conceived the idea of utilising this analgesic effect in the treatment of neurological conditions. Neuralgias are frequently markedly relieved by X-ray treatment. Obstinate cases of sciatica may sometimes be relieved by irradiation of the nerve roots in the lumbar area.

A number of tumours of the nervous system are also radio-sensitive. A certain number of cases of pituitary tumours have been very successfully treated, but a great majority respond little, although in the majority of cases an improvement in the diabetic syndrome associated with the condition takes place.

7. *Diseases of the urogenital system*:—In no other field of gynaecology is irradiation more helpful and promising than in the treatment of functional disturbances of the ovary and in sterility. X-ray therapy is also used with benefit in a large number of conditions where pathological changes have taken place in the pelvic organs of the female. The main indications for its use are:—

- (a) The production of an artificial menopause.
- (b) The control of excessive uterine haemorrhage.
- (c) Uterine fibro-myomata (fibroids).
- (d) Malignant disease of pelvic organs.

In the males prostatic hypertrophy requires consideration from the point of view of X-ray therapy. The early relief from the frequency of urination, afforded by the use of X-rays recommends its use, especially in those cases which are poor surgical risks.

CLINICAL APPLICATION OF ELECTRICAL TREATMENTS—
Abdominal diseases:—Experience in this field though not plentiful, is still very promising. Thus, according to SCHLIEPHAKE, chronic appendicitis appears a very suitable indication for short wave therapy.

RECHOU has reported equally favourable results. In chronic peritoneal adhesions, short wave seems to work favourably. Pains which had persisted for years were cured in a few sittings. Cases of gastritis react excellently. Cholecystitis is generally relieved in a few sittings.

Various diseases of the liver appear to afford a suitable field for short wave. RECHOU reports very good results in the early cases of cirrhosis of the liver.

Acne Vulgaris.—Electrical treatment is frequently successful in cases where antiseptic lotions and ointments have failed (CUMBERBATCH). Ultra-violet radiation gives very good results in all forms of acne. (AUSTIN FURNISS). FINSEN stated in the earliest results which he published, that he had cured thirteen out of 25 cases which had resisted ordinary measures.

CUMBERBATCH recommends diathermy and Salicylic iontophoresis.

SCHLIEPHAKE has treated Acne Juvenilis with short wave, with rapid disappearance of this long-standing trouble.

This disease has also been treated with great success by X-rays.

Alopecia.—More particularly Alopecia Areata is a condition in which the use of ultra-violet rays is specially indicated. (F. Howard Humphris).

Amenorrhea.—In cases where amenorrhoea is not due to pregnancy or structural disease of the reproductive organs the normal menstrual periods can be made to return by diathermy (CUMBERBATCH).

Angina Pectoris.—In this disease, excellent results have been obtained by treatment with diathermy by NAGELSCHMIDT, HAY and DYSON. Cases have been recorded in which the patient remained free from further attacks for one, two or more years after a course of cardiac diathermy.

Arthritis.—Milder cases of joint affection can often be successfully treated by diathermy but short wave therapy appears to be much superior. This appears from the publication of

PITZEN and others. Numerous cases of arthritis have also been treated with short wave by PFLOMM, RAAB and DAUSSET with good results throughout.

The results have been very favourable with gonorrhoeal arthritis which were often cured in a few days. (SCHLIEPHAKE.)

Both Graf and NAGELL report equally good results.

The sensitiveness to the pain often abates after two or three sittings, which in this extremely painful disease means a great advance.

Asthma.—Considerable improvements have been obtained with short wave therapy even in severe cases which have resisted all the known remedies. (SCHLIEPHAKE).

The application of diathermy to the chest is successful in some cases of bronchial asthma by X-ray in reducing the frequency and severity of the paroxysms.

GILBERT SCOTT has treated asthma by X-ray irradiation with encouraging results. Out of 121 cases, he obtained good results in 89, slight recurrence in 10, slight improvement in 7 and no improvement in 15.

Backache.—Patients complaining of chronic pain in the lower portion of the back should be examined in order to ascertain whether cervicitis is present. Treatment of cervicitis by diathermy will bring the inflammation to an end and then the backache will also disappear.

Boils and Carbuncles.—See also skin conditions. Various sizes of carbuncles were repeatedly subjected to short wave treatment by SCHLIEPHAKE with good results in all cases.

Climacteric.—CUMBERBATCH has noted considerable improvement in patients suffering from symptoms such as flushing, headache, depression and even mental aberration by general pelvic diathermy. The haemorrhage which is an occasional accompaniment of the climacteric should be treated by the same method and in all cases the bleeding has stopped by this treatment.

Colitis:—By means of the pelvic diathermy applied by the rectal route, CUMBERBATCH has been able to obtain apparent cures in cases of mucous colitis. The frequency of defaecation was progressively lowered until the normal was resumed.

In ulcerative colitis, Zinc Ionisation has more recently been used with success.

Deafness and Tinnitus aurium:—(noises in the ear), have been treated by Ionization by DYSON with great success.

CUMBERBATCH advocates the use of diathermy for defective hearing due to catarrh of the middle ear.

Deficient hearing due to oto-sclerosis does not appear to improve much under electrical treatment.

Dysmenorrhoea:—In cases of congestive dysmenorrhoea, the results are very satisfactory with diathermy, relief always being obtained (CUMBERBATCH).

Endocervitis:—Diathermy is of value in the treatment of this disease. When the infection agent is the gonococcus, diathermy can always be relied on to bring the infection to an end, either in acute or chronic cases. In non-gonococcal endocervitis, diathermy is of equal value.

Epididymitis:—Gonococcal epididymitis with or without orchitis, responds in a uniformly satisfactory manner to diathermy. (CUMBERBATCH). Short wave treatment has been tried in this disease by SCHLIEPHAKE with equal success.

Fibrositis:—Is the inflammation of the white fibrous tissues of the body. This may be situated in the muscles, (muscular fibrositis e.g. lumbago), in the joints, (arthritis), or in the nerves, (neuritis). According to DYSON, in the acute stage of fibrositis, ionization is the most successful method of relieving the condition and is usually rapid in its action. In the chronic stage, even the most severe and persistent cases are frequently seen to respond to this method, when all other forms of treatment have failed to produce any improvement.

According to CUMBERBATCH's experience, diathermy treatment is very satisfactory for this condition.

Gonorrhoea and Gonococcal infection:—Diathermy is of great value in the treatment of infection due to gonococcus, (CUMBERBATCH). GUMPERT cites surprisingly favourable results with short wave.

Haemorrhoids:—Diathermy is of much value in relieving pain and spasm when present in cases of internal haemorrhoids. Internal haemorrhoids can be destroyed by diathermic coagulation or by electro desiccation.

Myelitis:—The weakness of the lower limbs rectum and bladder that is left after an attack of myelitis can be considerably benefited by galvanic and sinusoidal currents.

Nervous system:—Diseases of the nervous system have been treated by various German, French and American workers with short wave. Cases of general paralysis of the insane have been treated with success. Tabetic troubles are also very favourably influenced by this treatment. Good results have been described in fresh cases of poliomyelitis, especially by RECHOU. In apoplectic lesions, rapid resolution is attained as long as the damage is not too severe.

Peripheral facial paralysis is often cured by short wave 5 to 6 radiations being sometimes enough.

Of diseases of the peripheral nervous system, neuritis is the most important. The pain of neuritis may be relieved by various methods of electrical treatment e.g. short wave, diathermy, iontophoresis and sinusoidal currents.

Nocturnal incontinence:—In cases of incontinence resulting from weakness of the sphincter, electrical treatment is usually successful. The surging sinusoidal or faradic current is used.

Osteomyelitis:—SCHLIEPHAKE treated a number of cases of osteomyelitis by short wave under the supervision of the surgical department of the Virchow Hospital, Berlin, and the results were very satisfactory. In early cases, there was complete remission of symptoms (fever, pain, swelling). In late cases, demarcation and sequestration were favoured.

Otitis media:—Chronic suppurative otitis media can be rapidly brought to an end by introducing zinc ions into the infected mucous membrane of the middle ear by means of the Galvanic current (CUMBERBATCH).

Acute cases of otitis media with initial suppuration of the mastoid have been treated by short wave with very gratifying results by DR. TREU.

Respiratory tract:—In many diseases of the respiratory tract, the effects of the short wave and diathermy are unique.

1. Pneumonia (lobar)—The use of diathermy in the treatment of lobar pneumonia has been widely practised in the United States. Dr. H. E. STEWART has obtained remarkably uniform and good results.

In almost every case, the temperature began to fall by lysis directly after the first application of diathermy to the affected lobe, cyanosis disappeared and respiration became easy.

2. Empyema of the nasal sinuses—Very good results have been claimed to have been attained by short wave in the treatment of empyema of the antrum of Highmore, the ethmoidal and frontal sinuses. Cases have been reported in which complete relief was given to patients who had suffered from empyema of these sinuses for many years.
3. Catarrhs of the upper air passages, e.g. colds, laryngitis, tonsillitis and bronchitis etc., have been successfully treated by short wave (SCHLIEPHAKE and RECHOU).
4. In pleural empyema, pleural effusion and pulmonary abscesses, SCHLIEPHAKE has obtained very impressive results, as has been demonstrated by X-ray photographs.

Rickets:—The improvement of sickly rickety babies, under the ultra-violet treatment, is little short of marvellous. There are a number of other diseases of bone where general irradiation with ultra-violet rays is helpful, namely, osteitis deformans, fractures with delayed union and osteomalacia. This last

disease is very common in India owing to Purdah system and poverty of the masses.

Prostate:—Enlargement—When the increase in size of the prostate is due to adenoma, there is no other form of electrical treatment that will reduce the new growth of the glandular tissue except x-rays.

However, in the congestive type of enlargement, good results can be obtained by subjecting the prostate to diathermy.

Prostatitis:—Infective prostatitis should be treated by diathermy. The best results are obtained when the infecting agent is the gonococcus. Prostatitis due to infection by Coliform bacilli also responds well to diathermy (CUMBERBATCH)

Pruritis:—This is a disease which, of all others, calls insistently and urgently for team work. Ultra-violet radiation will ease the hyperæsthesia and allay irritation (HOWARD HUMPHRIS). X-Rays form one of the most valuable weapons in the treatment of pruritis.

Puerperal fever:—Remarkably successful results have been obtained by Dr. C. A. ROBINSON at the West Middlesex Hospital, in the treatment of puerperal fever by general pelvic diathermy

Salpingitis:—due to gonococci or other organisms, has been successfully treated by diathermy in the Electrical Department of St. Bartholomew's Hospital. Cures have been obtained both in chronic and subacute cases. The same result can be obtained with short wave therapy.

Skin Conditions:—1. Furuncles, Carbuncles, Hidradenitis (Abscesses of the sweat glands in the axillae), whitlows and paronychia. The success of treatment by short wave therapy in these cases of acute inflammations of the skin is unchallenged. The same applies even to extensive phlegmonous processes, erysipelas and purulent infiltrations in the subcutaneous tissue, including that of numerous cases of erysipelas...always with good results.

2. Chronic ulcers, herpes, impetigo, eczema, psoriasis and warts. Many of these cases which have defied ordinary methods

of treatment by ointments and lotions, can be successfully treated by ultra-violet rays.

Sexual disorders:—Impotence in male subjects, if unaccompanied by constitutional or local organic disease, may be treated by subjecting the prostate gland and the testes to diathermy.

Tennis elbow can be treated by diathermy with benefit. In some cases, it yields more readily to negative galvanism.

Tonsillitis:—As an alternative to its removal by the guillotine or by dissection, the chronically inflamed and infected tonsils can be removed by coagulations by means of diathermic current. In this method of treatment, tonsil and the organisms that infect it are killed. At the same time, its blood vessels and lymphatics are sealed. The operation is done under local anaesthesia, and confinement in a hospital or nursing home is unnecessary.

During the last four years, the author has removed tonsils by this method in more than forty cases with very gratifying results.

Ulcers:—Iontophoresis (ionization) with the introduction of therapeutic ions is an effective method of treating various kinds of ulcers e.g. corneal ulcer, indolent ulcer, varicose ulcer, etc.

Warts can be easily and quickly removed by electro-desiccation. They can also be successfully treated by ultra-violet rays and X-rays.

(*The Antiseptic*, Vol. 37, No. 7.)

Role of X-Ray Screening in Detecting Pulmonary Tuberculosis

BY

K. EISENSTAEDT, M.D., T.D.D.,

and

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Regarding the various branches of the anti-tuberculosis campaigns carried on in recent times, such as treatment, prevention, after-care, etc., we have to bear in mind that the diagnosis is of primary importance. It goes without saying that best results depend on early detection. For this purpose it becomes more evident that in mass examination, clinical methods, sputum analysis, and tuberculin test cannot compete with x-ray screening in rapidity and reliability.

According to a Swiss report, the average result of such mass screenings of apparently healthy young persons is the discovery of 0.5 to 1 per cent active lung tuberculosis is not recognized at all, even by the affected persons themselves.

A report from Denmark gives the following findings:—out of 1,180 students, 12 were suffering from pulmonary tuberculosis of which 7 had positive sputum.

An American report shows that mass screening gives a discovery rate of 2.9 per cent.

The latest experience in tuberculosis clinics in Europe has proved that clinical examination alone, especially in early and even sometimes in more-or-less advanced cases, is not reliable without X-ray examination.

Percussion and auscultation are of no avail in cases of early infiltration, diffuse small nodular infiltration, miliary tuberculosis, etc. In many cases of roentgenologically-visible

cavities also, the classical clinical symptoms fail us. Even in patients with big cavities, auscultation signs may be absent and the negative findings of so-called 'silent cavities', is a fact well known to all specialists.

We have to admit the fact definitely that the time has gone when the doctor can rely on clinical examination only in diagnosing lung affections. Even in cases with evident dullness and catarrhal signs, the general practitioner cannot give a better diagnosis than a probable one. There are no reliable distinguishing clinical signs between tuberculous and other lung affections, e. g., bronchiectasis, bronchitis, asthma, carcinoma, pneumoconiosis, etc.

Again, examination of sputum is impracticable in mass detecting work, as it is complicated and takes up too much time and fails even in so-called 'virtually open' cases.

A merely probable diagnosis of lung tuberculosis is of little help in deciding to take preventive or curative measures.

The extent of the lesions, on the one hand, and the allergic-clinical character on the other hand, may produce so great a variety of appearances that their diagnosis depends largely on roentgenological examination, and further every step in therapeutic measures depends on the X-ray diagnosis, because various appearances require various measures.

How far a private practitioner can do his share in detecting work depends on local conditions. Whatever these conditions may be, there is no doubt that the co-operation of physicians is of extraordinary importance within the framework of anti-tuberculosis campaigns. This fact was stressed recently by Plunkett (1939). He says: 'More cases of tuberculosis are discovered by the examination of patients referred by family physicians for diagnosis than by any other generally practised method of case-finding. It is important that no stone should be left unturned to secure the co-operation of the practising physicians in obtaining the examination of all adults, who present symptoms which might even remotely be referred to the chest'.

Detection work can be carried out on the same lines as in some countries in Europe by mass screening of select groups of the population, e.g., hospital admissions, military, police, educational institutions, state employees, and even private concerns such as mills, mines, banks, etc. It rests with the medical department to set an example by screening once all cases admitted into the State hospitals. According to the experience of Plunkett (*loc. cit.*) this selected group reveals the greatest number of cases, viz., 1.2 per cent. 'Of special significance is the study being made of admissions to 14 general hospitals throughout New York, which not only shows the highest yield, but also shows that a surprisingly large number of cases of tuberculosis are admitted to hospitals without being recognized. No children are included, nor any persons in whom there was a previously-known tuberculosis lesion. Of the 47 new active cases already discovered, 19 had evidence in the hospital charts which might have led the attending physician to diagnose the case before discharge. However, 28 or 0.7 per cent of adult admissions were found to have active tuberculosis, although there was no evidence in the hospital records, which indicated that tuberculosis was suspected at the time of admission. If the same conditions prevailed throughout the United States, about 45,000 unrecognized cases of tuberculosis, were admitted in general hospitals during 1937.

A case with distinct clinical signs is revealed on x-ray examination generally to be in a fairly advanced condition. Unfortunately the patient does not become aware of his disease till then, and so it is too late for any medical treatment that can stop the progress of the disease. Very few people ask for medical advice for the minor affection; and most of the general practitioners also look upon these as minor troubles and neglect the x-ray control. It is incumbent on every medical practitioner to direct such patients to the proper centre of x-ray examination. The following points will be a guide to him under which circumstances a patient ought to be suspected of lung tuberculosis.

X-ray examination should be undertaken for

(1) everybody who applies for examination because suspected of or exposed to lung tuberculosis.

- (2) everybody who is under medical treatment for more than 3 months on account of any disease of the respiratory tract,
- (3) everybody who has chronic or periodic febrile conditions,
- (4) everybody who has sought for, during the last years, repeated medical advice for 'colds', bronchitis or similar diseases,
- (5) everybody who is suffering from an 'atypical' influenza, pneumonia or other diseases of the respiratory tract,
- (6) everybody who is suffering from a dry pleurisy or pleurisy with effusion (these patients should be observed for several years and be examined by X-rays at regular intervals),
- (7) everybody who spits blood,
- (8) everybody who is suffering from any extra-pulmonary tuberculosis, erythema nodosum, anal fistula or abscess, cervical adenitis, diabetes or any other obstinate and obscure disease of the digestive tract, chronic otitis media of uncertain origin, and
- (9) everybody who wants a certificate of health and has symptoms which may be caused by tuberculosis.

Looking at the above statistics in western countries, it is our emphatic suggestion that every centre of the anti-tuberculosis campaign should be equipped with an x-ray plant fit for serial screening and should be conducted by an experienced specialist who, by the support of public and private co-operation, would be able to carry out detection work to the utmost advantage.

(From I. M. G., April, 1940.)

X-Rays in Pulmonary Tuberculosis

A TALK BY DR. P. A. S. RAGHAVAN OF TRICHINOPOLY

at the monthly meeting of the Medical Association at Perundurai on 20-7-1940.

"More cases of pulmonary tuberculosis are referred to X-Ray than in other diseases. X-Ray mindedness is more prevalent amongst laymen than even amongst medical men. In the western countries, where civilization has developed more than here, most of the population is examined annually either under the medical inspection programme or the workmen's compensation act and along with the health card goes the skiagram of the chest."

"It is a fallacy to think that submitting the patient for the X-Ray examination will give the whole diagnosis and treatment of all chest diseases. X-Ray machines, like clinical laboratories are not *penny in the slot* which machines give all directions to the medical men. But an X-Ray examination is one of the essential routines in the diagnosis of a case, as important as the clinical and laboratory findings, for after all the skiagram is only the shadowgraph and has to be valued along with the other findings; but it is one of the cardinal factors in determining early infections and a means to correlate other clinical findings. It is also to be used to contradict suspicious cases. It is a well-known fact that physical signs and symptoms vary considerably to the extent of the disease, and it is not uncommon to find far advanced cases of pulmonary tuberculosis, which exhibit little or no signs and symptoms. Another great aid, which X-rays give, is to watch the progress of treatment. It is well nigh impossible to carry on physical treatment as by artificial pneumothorax, phrenic evulsion or Thorocoplasty without having the aid of X-rays. Pitfalls in X-ray diagnosis of lungs are conditions simulating tuberculosis such as bronchitis, metastasis in the lungs and luetic infections. These have to be distinguished from pulmonary tuberculosis both by location of the lesions and the other signs and symptoms." "X-rays are of essential necessity in carrying on Anti-Tuberculosis work

and in cases of mass examination it is quicker and more reliable especially by screening than the other tests. In very early cases, percussion and auscultation may not indicate the disease. It is already stated sometimes even in advance cases physical science may be wanting, whereas X-rays will reveal the underlying condition. A physical examination alone is not possible to distinguish tuberculosis from bronchitis, asthma, carcinoma and pneumoconiosis. When physical findings are defined probably the case is too far advanced for treatment."

He then demonstrated a number of skiagrams of pulmonary tuberculosis in various stages and at different stages of treatment. He also demonstrated a few skiagrams of bronchitis and metastitis.

Trichinopoly Municipality

Details of Public Health Activities during June 1940

I. Vital Statistics :

Number of births registered	...	...	...	408
Number of deaths registered	...	...	...	352
Number of deaths from fever	...	...	...	5
Number of deaths from respiratory disease	...	...	...	94
Number of deaths under one year	...	...	...	75
Estimated birth rate	...	...	...	34.3
Estimated death rate per mille	...	...	...	29.6
Number of deaths from child birth	...	...	...	5
Number of deaths from Alimentary disease	...	...	...	48
Infant Mortality rate	...	...	...	183.8

II. Infectious diseases :

	Attack.	Death.		Attack.	Death.
Cholera	Nil	Nil	Measles	Nil.	Nil
Small-pox	5	2	Tuberculosis	Not known	31
Chickenpox	3	Nil	Pneumonia	Do.	49
Typhoid	1	1	Diphtheria	Do.	Nil
No. of anti-cholera inoculation done	...	...	...	...	Nil
No. of anti-typhoid inoculation done	...	...	...	...	353

No. of vaccination done :

Primary Vaccination	...	...	...	785
Re-vaccination	...	...	...	3732
			Total	4898

III. Maternity and Child Welfare

(1) No. of cases visited by Woman Medical Officer.		(2) No. of houses visited by Health Visitor.	
(a) Labour	Nil.	(a) Infants	... Nil.
(b) Ante-natal	Nil.	(b) Pre-school	... Nil.
(c) Post-natal	7	(c) Ante-natal	... 16
		(d) Post-natal	... 79
(3) No. of labour cases conducted by Midwives	...		91

IV. Propaganda :

No. of lectures with magic lantern demonstration	...	48
No. of lectures without magic lantern demonstration	...	7

V. Food adulteration :

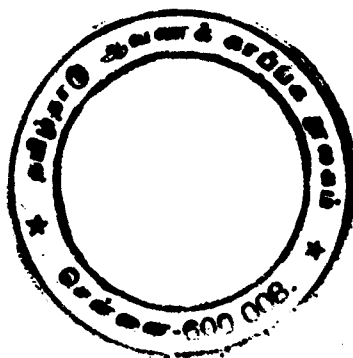
No. of samples taken	...	...	...	21
No. prosecuted	...	...	...	10
Amount of fine imposed	...	...	...	Rs. 126
No. of samples reported adulterated	...	...	...	10
Number Convicted.	...	...	...	8

VI. Meat Inspection :

	No. passed	No. condemned
(1) Sheep	4725	71
(2) Goats	5558	22
(3) Cows and heifers	360	6
(4) Bulls and Bullocks	100	4
(5) Buffaloes	41	2
(6) No. of dogs caught	2	
(7) No. of dogs destroyed	1	
(8) No. of dogs released	Nil.	

VII. General Remarks : Nil.

K. P. THOMAS,
Health Officer.



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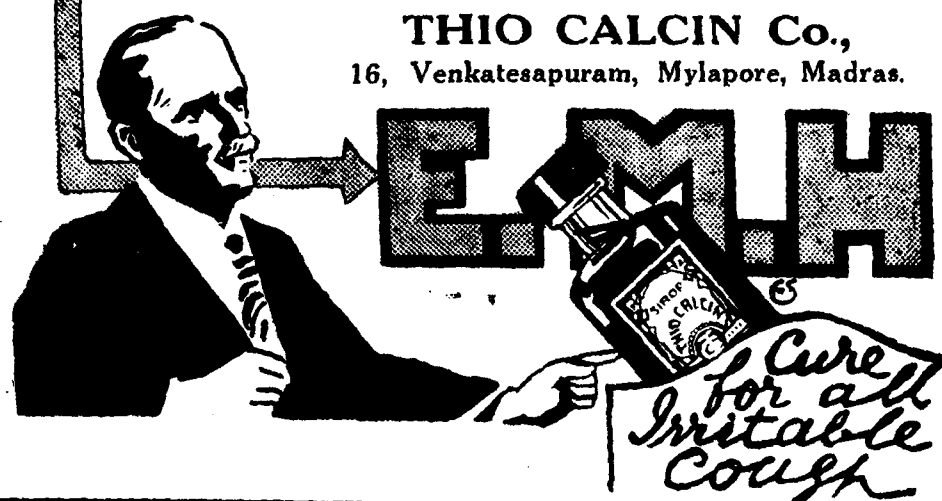
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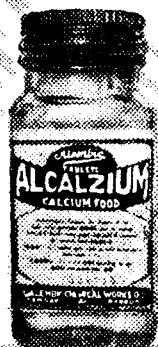
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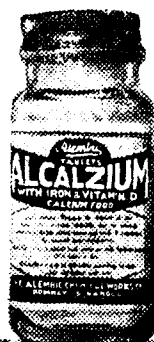
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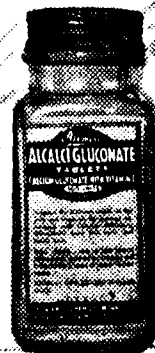
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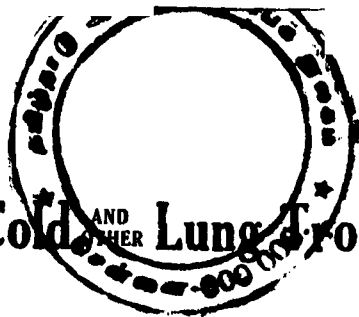
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AUGUST 1940

[No. 8

Cardiac Failure

BY

RONALD ELLIS, M.A., M.D., M.R.C.P.

(Honorary Assistant Physician, Liverpool United Hospitals)

My object in this short paper is to summarize modern views of the mechanism of cardiac failure, or more accurately of circulatory failure. We are not concerned with the production of heart disease *per se*, but with mechanism of heart failure. The problem of great perplexity, but enormous importance, is the immediate causation of failure of the circulation. It is probably true to say that only in recent years has it been realized that in the majority of cases of heart failure we do not know why the heart becomes unable to cope with the needs of circulation.

Most of us will end our days from chronic heart failure, the failure of a heart severely taxed and ultimately exhausted by a devitalizing disease of some other organ or organs. But in some of us the primary cause of death will be failure of the circulatory mechanism itself, and death will be truly due to a primary deficiency of the circulation. Now it is the precise understanding of this latter primary failure which still, with a few exceptions, eludes us. Why, for example, does the individual who has had aortic regurgitation for many years without symptoms, suddenly or gradually develop the syndrome

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of cardiac failure? The clue will seldom be provided by the necropsy, the latter generally suggesting that the valvular lesion has undergone no change for many years. Why does such a heart without obvious anatomical change alter so drastically from the functional point of view? It is still not possible to provide a certain answer.

We do, however, know that in certain instances gross postmortem findings are adequate to explain cardiac insufficiency. Such is true, for example, in the case of a massive coronary infarct, or in the myocardium poisoned by the toxins of diphtheria. But those cases are the exceptions rather than the rule. Examine a heart removed from a body; subject it to the ordinary pathological examinations. In many cases you will not be able to say whether or no the owner in life suffered from the symptoms of failure; you will have to look in other organs for the subsidiary evidence of passive congestion etc. Dilatation of the chambers of the heart, gross coronary artery disease, or even a severe valvular defect, cannot be taken as evidence that failure symptoms occurred during life. And the contrary picture we know equally: symptoms in life, and post mortem so little to account for them.

As gross lesions of the myocardium are not responsible evidently for most causes for heart failure, it is natural to turn to the microscopic findings in the tissues of the heart, and to attempt to find there the causes of the failure. Many investigators have searched high and low in the heart muscle and some find evidence of a granular, fatty, or other degenerative change in the muscle-fibres, accompanied by interstitial cellular infiltrations. But other workers, repeating such investigations in greater detail, came to the conclusion that histologically demonstrable lesions of the myocardium are entirely inadequate to account for the heart failure.

"Fatty degeneration" and a "fatty heart" have long been oft encountered diagnosis, being possessed of the necessary vagueness to make them invaluable in the exigencies of a coroner's court. But it has been realized recently that the amount of lipid material contained in or around the muscle-fibres has little or no bearings on the function of the heart

muscle. We cannot be satisfied, therefore, with the diagnosis of "fatty heart" as a cause of sudden death: we should admit that our post-mortem examination has not explained the cause of death. The fat found in and around the heart is much more probably due to the cardiac failure, as occurs in passive congestion in other organs.

In rare instances, nevertheless, widespread necrosis of the heart muscle is found associated with various infections, of which a classical example is diphtheria. Histologically the nuclei are seen to be destroyed and the muscle fibres disintegrated. Apart from diphtheria such necrosis is rarely diffuse enough to be blamed for the cardiac defeat; but diphtheria can be regarded as the classical example of a condition in which findings in the myocardium are sufficiently definite to be the cause of heart failure.

The most important and common form of myocarditis is, of course, that occurring in rheumatic fever, characterized histologically by the Aschoff body. But Aschoff and his fellows pointed out 30 years ago that rheumatic myocarditis is primarily interstitial and perivascular, and rarely involves enough of the myocardium to convince one that it is the essential cause of heart failure. Repeated attacks of rheumatic fever may leave in the healing process numerous scars, but the proportion of the heart muscle that suffers is usually quite small; there is practically no diffuse degenerative change in the muscle fibres. We are, therefore, driven to conclude that cardiac failure in rheumatic diseases is rarely explained by the anatomical findings in the myocardium—the conclusion reached by Aschoff and Tanara 30 years ago. As Fishberg points out, the rare exceptions are fulminating cases of rheumatic fever, usually in children, with high fever, and who succumb rapidly to failure.

A word must be said about the significance of the interstitial fibrosis found associated with the cardiac hypertrophy of essential hypertension. This fibrosis was formerly thought to be of the nature of a replacement fibrosis, consequent on degeneration of elongated muscle fibres. But there is really no evidence that myocardial strain in itself produces fibrosis.

It is much more probable that the condition is consequent on coronary artery disease, or more especially on *eschæmia* produced by the hypertrophied heart outstripping, so to speak, its blood supply. But what part the fibrosis plays in the production of heart failure is not obvious.

A remarkable form of generalized heart failure occurs in myxœdema and beri-beri. These conditions are of course rare, but they have an important bearing on the subject. In myxœdema all the bodily functions are sluggish, and the cardiac action and blood-flow are no exceptions. The body, of course, does not require a powerfully acting heart, but there is evidence that in severe hypothyroid states true circulatory failure may develop. Evans has recently described two cases of congestive failure with enormous cardiac dilatation which rapidly responded to thyroid gland administration. The precise pathology is still unknown, but one must assume some reversible change, some temporary weakening of the muscle fibres allowing for dilatation.

The changes in the beri-beri heart are very similar to those of myxœdema. The same type of generalized dilatation occurs, with evidence of right heart failure in the form of engorgement of the systemic veins, enlarged liver and œdema. The cardiac œdema must be differentiated, of course, from the œdema characteristic of beri-beri. Various hypotheses regarding the mechanism of beri-beri heart failure have been advanced, and the most likely one is Wenckebach's that deficiency of vitamin B entails water retention in the muscle-fibres, with consequent impairment of efficiency.

Now, from the foregoing, the only deduction to be made, to quote Fishberg, is that the known morphological changes in the myocardium do not suffice to explain the majority of instances of cardiac failure. We are left with the theory of recent investigators—that heart failure is most often due to a change in the metabolic state of the heart muscle, analogous to what is known as fatigue in skeletal muscle. As Fishberg says, this altered metabolic state results in a diminution in the amount of energy production, and hence of mechanical work. The type of failure which we have found difficult to explain

on pathological grounds usually follows on a protracted period of heart strain. Before the heart finally allows the burdens of the circulatory demands to master it, it has generally performed increased work for a considerable time—increased work due, say, to a high blood-pressure, valvular defects, etc. In many instances we may feel satisfied that neither the burden of work nor the state of the heart muscle has altered for some considerable time before the transition from compensation to that of failure. The only acceptable explanation of this is that the failure is due to fatigue of an overworked myocardium. One might quote much data to support this view, but it must suffice to mention the enormous value of rest in the treatment of failure—it is, of course, the basis of all treatment.

Intimate details of the nature of muscle fatigue are lacking. Much experiment has been performed, but much remains to be learned. It has, for example, been shown in experiments with the excised animal heart that fatigue can be accelerated by deficiency of blood-supply, oxygen, various lipoids, etc. But the relation of these findings to human failure remains to be elucidated. Investigations on the surviving mammalian heart have shown that as the heart fails, it consumes more oxygen for the performance of the same amount of work—that is to say, the mechanical efficiency is decreased. Starling found that the increase in oxygen consumption in the heart-lung preparation as the heart fails is proportional to the dilatation. A further interesting observation was that digitalis increases the mechanical efficiency of the heart.

We cannot leave this discussion of the *ætiology* of central failure without some mention of the mechanism of heart failure in rheumatic carditis. It has been shown by Coombs and others that the proportion of rheumatic cardiacs who still have active carditis at the time of the final failure varies with the age at which the latter occurs. In the first two decades, death is associated with active carditis in 100 per cent. of cases. The failure of the rheumatic heart is frequently associated with an exacerbation of active carditis, but not always so. In later life there are many cases of rheumatic heart failure without active carditis. However, even in the hearts showing active

infection, in which it is possible to demonstrate Aschoff bodies and other changes in the connective tissue, the heart muscle reveals comparatively little demonstrable change. We are driven to the theory, that rheumatic infection damages the heart muscle, lowering its functional capacity in some way not yet reflected in histological changes. The myocardial changes do occur in acute rheumatism is revealed also by the electrocardiogram, almost any variant from the normal having been demonstrated, including the Parde curve. The point of interest is, that these changes are reversible; only occasionally is the change of a permanent one, due doubtless to the location of a scar at some vulnerable site.

But what of cardiac failure in those examples of long-standing valvular defects where there is no evidence whatever of active rheumatism or any signs to suggest active infection? A severe mechanical burden has been imposed on these hearts by the valvular obstruction or inadequacy. They invariably show hypertrophy, and have obviously had much increased work to perform for years. The cause of failure is probably the same as discussed above—ultimate muscle fatigue and failure consequent on some myocardial metabolic inadequacy in a heart which has outgrown its blood-supply.

This brief summary of the mechanism of cardiac failure which I have attempted would be more incomplete than it is without reference to the condition known as peripheral circulatory failure. We have dealt so far only with the cause of failure of the central pump but an equally common or even commoner cause of circulatory collapse resides in the peripheral portions of the circulation itself. Peripheral circulatory failure is a comprehensive term for the circulatory disturbances characterized by diminution in the venous return to the heart. Now it is important to realize that the clinical entity which we know as shock is the symptom-complex resulting from peripheral circulatory failure. It is characterized, as is well known, by cold extremities, a pallid and searing skin, feeble or imperceptible pulse, and collapsed superficial veins. The symptoms occur under a great variety of circumstances; following trauma, operation or haemorrhage, rupture of an

abdominal or thoracic viscus, coronary infarction, intractable vomiting and diarrhoea, and many other conditions. It is a mistake to confine the word "shock," as was formerly done, to the collapse symptoms which followed trauma operative or otherwise—so called surgical shock. We may with as much justification talk of medical shock. Whatever the circumstances under which shock develops, the fundamental feature common to all varieties is a diminution in the venous return to the heart. This common form of circulatory failure is extracardiac in origin. In the central failure there is a diminution in venous return to the heart, but this is consequent on the decrease in cardiac output, whilst in peripheral failure the converse holds: blood fails to be returned in adequate volume from the dilated vessels of the splanchnic area. I hope I have made it clear that the circulatory failure of shock is not due to cardiac insufficiency. Cannon observed that in soldiers succumbing to wound shock the heart continues to beat after respiration has ceased and the blood-pressure has fallen practically to zero. There are no symptoms whatever of central failure. Of course the problem of the causation of shock is the problem of the causation of the peripheral vascular disturbance.

Circulatory failure is common in the acute infections, such as pneumonia, typhoid fever and diphtheria. For many years it was assumed, and still it is so by many, that such failure is due to damage of the myocardium by the toxins produced by the invading organisms. That myocardial damage does occur is proved by electro-cardiograph, but apart from the outstanding exception of rheumatic fever and diphtheria, the circulatory failure much more often peripheral than central—the patient dies after medical shock. In young people with healthy hearts this is probably always the case, with the exception of the two diseases just mentioned. Of course, in the elderly arteriosclerotic patient with an enfeebled myocardium, central failure may rapidly dominate the clinical picture, but we can say, with Fishberg, that the healthy heart rarely gives way during an acute infectious disease, other than rheumatic fever of diphtheria.

(From Clinical Journal May 1940)

The Modern Treatment of Gonorrhoea

BY

WILFRED BARBER, M.A., F.R.C.S.

(Capt. R.A.M.C., formerly Surgical Registrar, Middlesex Hospital.)

The application of chemotherapy to gonorrhoea during the last two years has changed so rapidly the time-honoured technique of treatment still described in recent editions of surgical text-books that no excuse is needed for presenting a short account of the chief methods in which the sulphonamides are to-day used in the disease. Prior to the introduction of this group of drugs in the treatment of gonorrhoea, the measures adopted had been chiefly mechanical, in that they had aimed at adequate urethral drainage, or else they were adapted to encourage the natural cure, which it was known would occur in a small proportion of untreated cases. To-day these methods still have a place, but they are looked upon as adjuvant to chemotherapy, and it seems probable that in uncomplicated cases they will eventually be dispensed with completely.

Choice of Preparation

As far as gonorrhoea is concerned the vast amount of literature now accumulating strongly suggests that the choice of drug rests between sulphanilamide and sulphapyridine (M and B 693). The majority of English workers have been unable to repeat the high percentage of cures claimed in Germany for uletron. A series of cases collected in this hospital showed only 43 per cent. of cures after one or more courses of this drug. Although a great improvement on the previous methods, this does not approach the results obtained here and elsewhere with sulphanilamide or sulphapyridine. Between these two preparations a choice has not yet been made, and it seems probable that, failing the advent of a yet more potent compound, they will both continue to have their place, particularly in resistant cases, where a change of preparation may

frequently produce a cure. On the whole, the evidence at present seems to be more in favour of M and B 693 as the drug of choice, but clinical experience suggests that it is the more toxic of the two, especially if given over a period of weeks. In addition, American workers have discovered great individual variations in the degree and rate of absorption of the drug. Until these factors are more clearly understood no dogmatic choice can be made.

Technique of Administration

Generally speaking, three methods of giving these drugs are now employed.

Immediate therapy.—The patient is given sulphonamide in doses of 1 gm. three times a day for three weeks, as soon as the diagnosis has been made.

Delayed therapy. Some workers have suggested that the sulphonamides are bacteriostatic and not bacteriocidal, and have argued from this that the patient's own resistance to the infection should be allowed to develop before commencing chemotherapy. Those who hold this view suggest that the exhibition of the drug in the early stage of infection may lead to relapses, due to "dormant" organisms becoming active again when treatment is discontinued. An optimum period of ten days from the start of the disease is therefore suggested for commencing therapy, and this is carried out for three weeks as above.

Intensive therapy.—The 4—2—1 gm. technique: There seems to be general agreement on the greater toxicity of M and B 693 when given over a prolonged period; in an effort to circumvent this, other methods have been evolved. Such a one is the so-called 4—2—1 gm. technique. Here an attempt is made to bring the patient under the influence of the drug and to continue treatment for three or four days only. Results by this method to date are as good as, or better than, any so far obtained, but the number of recorded cases is small. The technique produces a higher percentage of early, but not serious, toxic effects, which in the majority of cases subside after twenty-four hours in spite of the continuation of the treatment.

The patient is made to swallow 4 grm. (eight tablets) on the spot. He is instructed to take 2 grm. four hours later, and thereafter 1 grm. four-hourly during waking hours, for the next three days. The actual amount taken will vary in individual cases, but the total dose to be aimed at is 16-20 grm. in three to four days. Certain advantages, theoretical and practical, in favour of this method may be quoted: "It is reasonable to assume that an abrupt intensive attack will always mean a more swiftly deleterious effect upon the gonococcus, by which attack the infection may be eradicated more quickly and efficiently, and by which may be avoided the development of what may yet become known as M. & B. 693 resistance. Further, as has already been suggested, the avoidance of serious toxic results may possibly be effected more by short rigorous treatment than by prolonged, though milder, methods. Finally, it is a point worth knowing that if necessity arises, a man may be cured of gonorrhoea by treatment lasting only three days, or even less."

Adjuvant Treatment

In the male irrigations are employed whilst the discharge is copious. In practice this usually means that acute cases require irrigation until they have had chemotherapy for about five days. It has yet to be shown that any better results are to be obtained by use, but there is some evidence that the discharge will clear up a day or two earlier if they are employed. Probably, the greatest benefit is psychological: the patient is encouraged to attend regularly, and the suggestion that further irrigations may be necessary late in treatment discourages in him the belief that he is suffering from a minor complaint which clears up rapidly after swallowing a few tablets. Potassium permanganate 1:8000 is the solution commonly employed, using a douche-can at a height of 3 ft. above the urethra. Prolonged irrigation, too high a pressure, or too strong a solution are all likely to cause a urethritis in themselves.

In the female the disease has in the past been notoriously more difficult to diagnose, for the early symptoms are less marked and may pass unnoticed until the disease has entered on a chronic phase where complications develop, and even then

gonococci may be found only with difficulty in the cervix. In spite of this, however, it would appear that intensive local treatment no longer has a place in any but the most chronic or resistant cases. Certainly instrumentation and cauterization of the cervix should be reserved for this type of cases alone; nothing further than the daily douche, followed by the insertion of a glycerine tampon, is necessary in recent cases, and could probably be dispensed with more often than not were it not useful as a means of making the patient attend regularly.

Veccine therapy is still employed, particularly in the delayed type of sulphonamide treatment, where it is commenced as soon as the diagnosis is made. It is extremely difficult to prove its value in early cases, but the majority of venereologists still use it, more particularly for resistant infections. Injections are given twice weekly for three weeks, working up from 5 million of mixed gonococcus vaccine to 100 million. In chronic cases this final dose may be repeated for two or three further weeks.

Subsequent Treatment and Tests for Cure

The rapid improvement and disappearance of symptoms which occur in most cases within a few days of the onset of chemotherapy may give clinician and patient a false feeling of satisfaction at the result of what is apparently such a simple treatment. Great emphasis must therefore be laid on the necessity of keeping the patient under observation for a minimum period of six to eight weeks after the cessation of all treatment, and of carrying out routine tests of cure during this time. Not until these have all proved continuously negative over the prescribed period can the patient be safely discharged, for late relapses are not uncommon.

In the first place the urine should be consistently clear and free from threads or pus, and there should be no evidence of urethral discharge. Urethroscopy is probably unnecessary as a routine. Almost as clear an idea of the condition of the urethra can be obtained by the "two-glass" method of examining the urine.

Both during and at the end of a course of chemotherapy a watch is kept on the progress of the disease by the bacterio

logical examination of smears. In the male these are obtained from the anterior urethra after massage over a sound, and from the prostate after the digital massage.

In the female frequent swabs are taken from the cervix and urethra, particularly after menstruation, when cervical smears are most likely to show gonococci.

If at the end of a course of chemotherapy no gonococci are found, all treatment is suspended for three weeks, during which time the patient is kept under observation and further smears taken. If the smears continue to show no gonococci, and the cells present contain not more than 5 per cent. of pus cells, an attempt is made to flare up the disease. The prostate is massaged firmly, a provocative dose of vaccine injected (1000 million), and the patient told to drink a liberal quantity of alcohol, if he has been in the habit of taking it. The patient, if a man, is instructed to watch for a discharge, which most frequently occurs between the second and fourth days after the vaccine, and if anything is seen, a smear is made for examination. Women require daily swabs taking for a few days.

Should these results be negative, i.e. no discharge, obtained or nothing significant found in the discharge, the patient is watched for three weeks more, when a further effort to provoke the disease is made. If smears and urine remain clear after this the patient is discharged.

Treatment of Complications

It is not the purpose of this article to give an account of the measures which it is necessary to adopt should any of the well-known complications of gonorrhoea develop. Let it suffice that the advent of chemotherapy has reduced their incidence remarkably, and that when they do occur, they tend to pursue a mild course. Recent work has suggested that the delayed type of therapy allows the development of a greater number of complications. If this be true, it must form a strong argument for instituting chemotherapy from the outset. The patients in whom complications have occurred should be treated exactly as recent cases, with the addition of those further measures, indi-

cated in any particular case, which held before the introduction of the sulphonamides.

Chronic cases may call for a combination of chemotherapy with more active treatment directed against the resistant area, e.g., the prostate may require massage and diathermy, or the cervix may need cauterizing.

Cases which relapse after one course of chemotherapy should be started on another after an interval of three weeks, and it is well to remember that better results are to be hoped for if the type of drug is changed, for as Whitby (1938) has suggested, resistant or insensitive individuals may be developed in cases where the first course has not been successful.

(*Clinical Journal*, Feb. 1940).

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Eruption due to Insulin

Allergic reactions following injections of crystalline insulin have seldom been recorded. Ulrich and others report the case of an undernourished non-diabetic man, aged 53, who had several years previously been treated with insulin for the purpose of gaining weight, and wished to repeat the treatment. On July 2, 1938, he began taking 5 units of standard insulin twice daily. After 9 days large erythematous itching patches of urticaria appeared on the flexor surfaces of the arms and wrists, and the injections were stopped. Next day the lesions had extended over the whole body, then they gradually faded in a few days. The insulin had been made from pork pancreas. An injection of 5 units of insulin made from beef was tried and produced a severe chill, a temperature of 101°, recurrence of the eruption, and a sensation of severe substernal pressure and pain which required injection of morphine.

The treatment was temporarily abandoned, but about 4 months later it was decided to try crystalline zinc-insulin made from beef. Ten minutes after injection of 5 units he had a burning sensation of the eyes, the eyelids began to swell and looked inflamed, a severe pain and a sense of constriction were felt in the chest, there was a feeling of fulness in the throat, erythematous urticarial wheals appeared all over the body, a chill followed and the blood-pressure fell as before. The reaction was in every way similar to the others, although slightly less severe.

Endermal tests with solution of zinc-insulin produced an irregular wheal measuring 23 by 33 mm., and surrounded by an erythematous area measuring 65 by 80 mm. In addition to the local reaction there were general symptoms similar to but much less severe than those observed after the injection of the therapeutic amounts.

Rapid desensitization was accomplished by injecting small amounts, beginning with 0.01 c. c. (0.4 units) intracutaneously, and produced minor local reactions; later subcutaneous injections

did not. The amounts were increased rapidly to 8 units in 14 hours. After that he took 5 units thrice daily without untoward manifestations until about a month later, when allergic symptoms recurred and indicate redevelopment of sensitivity. No further treatment was attempted.

Although the tests indicate hypersensitivity to insulin itself, it was difficult to believe that he could become hypersensitive to a material produced in his own body. But the possibility of molecular differences between animal and human insulins may be an explanation, although crystalline insulins derived from different sources appear to be identical. Since the exact composition of crystalline is not known, it is possible that commercial crystalline insulin contains something else besides the hormone itself. This explanation receives support from Hansen and Eyer, who found that twice-crystallized insulin gave much weaker reactions than crude crystalline insulin. Moreover in this case and in others the reactions to crystalline insulin were less severe than those to standard insulin.

(Clinical Journal, Feb. 1940)

Sulphapyridine in Pneumococcal Infections

The position of sulphapyridine (M and B. 693) therapy in pneumococcal infections is summarized by Dr. H. L. Marriott. The reduction in mortality is such that three patients out of four who would formerly have died may now live. Sulphapyridine is particularly valuable in severe cases with bacteraemia. It is as effective in the elderly as in the young. In persons of 50 and upwards gross mortality in the past has usually been accepted as approaching in percentage figures the figures of the subjects' ages. The average mortality of all patients aged 50 or more treated with sulphapyridine is 16.6 per cent. Sulphapyridine appears to be very effective against all types of pneumococci.

Within 24 to 36 hours of beginning sulphapyridine, irrespective of the day of the disease, the temperature falls by rapid lysis and there is usually remarkable improvement in the general condition. Uneventful recovery in most cases ensues, but the lung condition does not seem to undergo any faster resolution.

The incidence of empyema appears lessened, but clear pleural effusions are commoner. Evans and Gaisford regard the latter as empyemata aborted by sulphapyridine, since the total of empyemata plus clear effusions is the same as used to obtain for empyema alone.

The excellent results in lobar pneumonia are paralleled in the less clearly defined pneumococcal chest infections. Results in bronchitis, bronchopneumonia and post-operative pneumonia are good.

Pneumococcal meningitis has been generally considered to be invariably fatal. Sulphapyridine permits revision of the hopeless prognosis, though the condition is still to be regarded as very serious. A number of cures and a number of failures have been reported. In meningococcal meningitis sulphapyridine, is extraordinarily successful. Not infrequently in meningitis

the exact bacteriological diagnosis is not immediately obtainable. In all such cases where the infecting organism is in doubt, sulphapyridine should be given because not only it is the best agent against the pneumococcus, but it is as good as or better than sulphanilamide, against meningococcal, streptococcal and staphylococcal infections. The prognosis in pneumococcal peritonitis is also likely to be much better.

Dangerous toxic effects in therapeutic doses are rare. Nausea or vomiting occurs in about half of all cases. Many patients feel depressed and languid and may have headache. These effects are unpleasant, but not of serious significance. Cyanosis is less often seen with sulphanilamide. According to Campbell and Morgan the cyanosis due to sulphapyridine is from methaemoglobinæmia and not from sulphæmoglobinæmia, as with sulphanilamide. Methaemoglobinæmia does not persist as long as sulphamoglobinæmia. If considered to be dangerous, because affecting already anoxic patients, it may be quickly abolished by the administration of methylene-blue, but this should very seldom be necessary.

Not strictly a toxic effect, but an effect consequent upon its insolubility, is the formation in the urine of jagged crystals or small calculi of acetylated sulphapyridine. The subject has been studied in laboratory animals. In patients receiving sulphapyridine red cells are found in the urine in a small proportion of cases. Rarely, gross hæmaturia, ureteric or bladder pain and anuria may occur.

When sulphapyridine is given beyond five days, which should not as a rule be necessary, drug fever and rashes become unpleasant and not infrequent features. The rarer but dangerous manifestation of granulocytopenia may also occur. With drug fever the temperature may rise as high as 104°. The rashes usually resemble the rashes of measles or German measles; occasionally they are urticarial or scarlatiniform. Differential diagnosis from these specific fevers may be difficult.

In pneumonia the aim should be to secure and maintain a blood concentration of sulphapyridine of not less than 4 mgm. per 100 c. c. In adults this level is usually achieved by 2 gm.,

followed in four hours by 2 gm., followed by 1 gm. four-hourly. What sulphapyridine does it does quickly, but too early discontinuance may lead to relapse from spread of infection. Hence, after a total of 18 gm. on the above scheme (that is, after $2\frac{1}{2}$ days), the dose should be reduced to 0.5 gm. 4-hourly for 24 hours and then to 0.5 gm. 8-hourly for 32 hours—a total of 23 gm. administered on a decreasing scale during 5 days.

For the children the dosage should be in proportion to the body-weight, but it should be increased relative to that of adults by 50 per cent. to secure adequate blood concentration. Wilson and his collaborators advise doses equivalent to twice those equally given to adults.

In all cases the ordinary measures of medical and surgical treatment should be carried out. An adequate intake of fluid is of greatest importance, so as to avoid urinary crystallization. Five pints per 24 hours should be taken by an adult. The urine must be measured, and an output of less than 50 oz. regarded as unsatisfactory. The urine should be examined daily for blood. Liberal administration of glucose is desirable not only because of its nutritional value but because it helps to prevent nausea and vomiting. In anoxic cases oxygen administration should not be delayed; Carter suggests that it may abolish nausea and vomiting.

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Ultraviolet Irradiation in Grip.

Vitebskiy reports the effects of ultraviolet irradiation in 625 cases of grip observed during the epidemic of 1935-1936. The treatment was begun on the first day of sickness in 308 cases, on the second in 170, on the third in 112 and on the fourth in thirty-five. It consisted of a daily suberythematous dose of ultraviolet rays to the anterior and the posterior surfaces of the thorax. The minimal-number of exposures was three and the maximal six. The temperature fell to normal after the first exposure in 55 per cent of the first group, after two exposures in 33 per cent and after three exposures 12 per cent. In cases in which the treatment was begun on the second day of illness, the temperature came down to normal after one exposure in 51 per cent. after two exposures in 30 per cent. and after three exposures 19 per cent. In cases in which the treatment was begun on the third and the fourth day, the temperature came down to normal after the first exposure in 17 per cent, after the second in 30 per cent and after the third and fourth in 53 per cent. It is thus apparent that the earlier the treatment was begun the quicker was the return of the temperature to normal. Along with the lowering of the temperature there was noted improvement in the subjective and the objective symptoms. The number of sick days in instances in which the treatment was begun on the first or second day amounted to three, which is from one and a half to two times less than in cases in which irradiation was not given. A favourable effect was likewise noted on diffuse post-gripal bronchitis in a group of forty cases in which the treatment was begun on the third or the fourth day. The treatment here was extended to from six to ten exposures. There was not a single instance of bronchopneumonia or any other complication.

VRACHEBNOE DELO, KHARKOV,

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The Little Finger and Clavicle Signs of Congenital Syphilis

In 1926 du Bois drew attention to dystrophy in congenital syphilis of the second phalanx of the little finger, which was shortened by several millimetres. This condition may exist only on one side or on both sides, and the deformity becomes evident on comparing the palmar folds of the little finger with those of the ring finger. It is of course, most easily detected when unilateral, for then comparison of the two hands promptly reveals it. Du Bois demonstrated this sign in 80 per cent. of his cases of congenital syphilis, and Mikulowsky subsequently confirmed his findings. At the Skin Hospital of the University of Leipzig M. Grafe investigated the association of this sign with congenital syphilis as well as Higoumenakis' clavicle sign—thickening of the sternal end of the clavicle due to osteoperiostitis—also supposed to be indicative of congenital syphilis. There is a mechanical factor in the genesis of this sign, for it is always demonstrable on that side of the body on which most work is thrown.

To ascertain with what frequency these signs occur in the presence or absence of congenital syphilis, Grafe examined 100 cases of serologically positive and quite definite congenital syphilis and found the little finger sign in 55. In another series of 120 cases in which the presence of congenital syphilis was only probable, he found 60 cases of the sign. He then made a search for it in a great number of his polyclinic patients and found it in 138. Of these 60 definitely had and 50 probably had congenital syphilis. In the remaining 28 cases evidence of congenital syphilis was lacking.

Turning to the Higoumenakis sign, Grafe finds that its frequency in cases of congenital syphilis ranges, according to different authors, from 30 to 100 per cent. He has found it in 25 per cent. of definite cases of congenital syphilis, and in 15 per cent. of suspected cases. A comb-out of all his polyclinic

patients during a certain period revealed the clavicle sign in 55. Among these 55 were 20 definitely suffering from congenital syphilis and 25 who were not definitely suffering from it. Of the remaining 10 cases 7 were insufficiently investigated as to the presence or absence of congenital syphilis. But there remained 3 with thickening of the sternal end of the clavicle who otherwise were perfectly healthy, and freedom from congenital syphilis was demonstrable throughout three generations. I would therefore seem that the clavicle sign is not proof positive of congenital syphilis.

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The Pharmacopeia and the Physician

THE THERAPY OF DROPSY

H. E. MARVIN, M. D.

Dropsy, or edema, is usually defined as the accumulation of serous fluid in the intercellular spaces of the subcutaneous or deeper tissues and in the serous cavities. The source of this fluid is the blood, from which it has escaped by passage through the walls of the blood vessels. Edema is always but one manifestation—although sometimes the most dramatic and important—of some abnormality or disease process, and its removal by medical means should logically begin with treatment of the causative process. Specific measures for its removal are necessary only if its location or extent render it harmful or uncomfortable to the patient and should ordinarily be employed only after correction or treatment of the underlying abnormality.

There are many conditions with which edema may be associated but only a few of these will be considered in this review, which is concerned primarily with the practical aspect of medical treatment. The conditions to which attention will be devoted comprise congestive heart failure, acute and chronic nephritis, cirrhosis of the liver the Pick syndrome of constrictive pericarditis, vitamin deficiency and marked lowering of the protein content of the blood plasma, whether this is found in malnutrition, in chronic glomerulonephritis or in so-called lipoid nephrosis.

For a clearer understanding of the discussion that follows, it is desirable to review briefly the mechanisms involved in the formation of edema. The opinion first expressed clearly by Starling in 1896 has received the almost unanimous support of investigators in recent years; in its simplest form it may be stated as follows: The capillary wall is a membrane freely permeable to water and to most of the crystalloids of the blood, such as salt, sugar and urea, which pass from the capillary into the surrounding tissue spaces, or from these spaces into capillary, in response to physical laws now well understood.

The most important factor causing movement of fluid out of the capillary is the pressure exerted on it; in other words, the intracapillary blood pressure. If this were unopposed, most of the fluid of the blood would readily pass into the tissue spaces. But it is opposed, as Starling first showed, by a force due to the presence of proteins, chiefly albumin, in the blood plasma. These protein substances cannot pass readily through the capillary wall; by remaining within the lumen they attract fluid powerfully through the process of osmosis, the force so exerted being known as the colloid osmotic pressure of the plasma. Obviously the direction and extent of movement of fluid through the capillary wall must depend on the balance of these two opposed forces; if the intracapillary pressure is higher than the colloid osmotic pressure, fluid will pass out of the blood stream and edema will form. On the contrary, a rise in the colloid osmotic pressure above the capillary blood pressure will result in prompt withdrawal of fluid from the tissue space into the blood.

It is thought that both these processes are operating continuously in health and in disease. It is impossible to assign any constant value for the capillary blood pressure, since this varies in different parts of the body and in response to many influences, but in the capillaries at the base of finger nails. Landis has found that the pressure at the arterial end of the loop averages about 43.5 cm. of water, while the colloid osmotic pressure is about 34 cm. of water. The result of this difference is to force fluid from the capillary. But when the blood reaches the venous end of the loop the pressure has fallen to an average value of 16.8 cm. while the colloid osmotic pressure has risen because of increased concentration due to loss of water. At the venous end of the capillary, then, fluid will be drawn from the tissue spaces into the blood. It is therefore clear that edema may result from either or both of two changes: an increase in the capillary pressure or a decrease in the amount of protein in the blood plasma.

This statement has been purposely simplified and abbreviated but is essentially correct. The mechanism that it describes is not the only one concerned in the formation of edema but is generally regarded as the most important. The other primary

and contributory factors have been lucidly reviewed by Landis, whose studies of the capillary circulation have added greatly to our knowledge. He regards as other primary factors injury to the capillary wall, which increases its permeability and obstruction to lymph channels. As contributory factors he mentions low tissue pressure, high salt intake, high fluid intake, a warm environment and disturbances of innervation. It is well to emphasize that the contributory factors may become of great importance and may actually determine the occurrence or disappearance of edema.

Thus in the capillary bed there are two important and opposed physiologic processes involved in the formation of edema; similarly in the kidney there are two fundamental and opposed processes involved in the formation of urine. It is now believed that the renal glomerulus acts essentially as a filter; relatively enormous quantities of a protein-free ultrafiltrate normally pass through it into the tubules, where most of it is reabsorbed, leaving only a small percentage to be excreted as urine. It is apparent that the volume of urine may be increased by either or both of two processes: an increase in glomerular filtration or a decrease in tubular reabsorption.

With this brief outline of the more important mechanisms in mind, we may consider the treatment of edema associated with various clinical conditions.

Congestive Heart Failure

Congestive heart failure is the most frequent cause of edema sufficient to require treatment; fortunately it is also the condition in which specific treatment is most gratifying. The edema is thought to be due to several factors, which probably vary in relative importance in different cases. The effective filtration pressure in the capillaries is increased by the rise in general venous pressure that occurs in congestive heart failure and also by the muscular inactivity that generally accompanies it. In addition there is increased permeability of the capillaries to water and crystalloids, and in some cases there is a fall in the effective colloid osmotic pressure of the plasma because some protein passes into the tissue spaces. The hypoproteinemia

is probably increased at times by the loss of albumin in the urine and by the low protein diet often prescribed by the physician.

A detailed discussion of the treatment of congestive heart failure is beyond the scope of this article, but it is now generally agreed that this should include complete rest in bed, necessary sedatives, limitation of fluid and of salt intake, and full digitalization. These measures should precede the use of diuretics in most instances, since they will often result in marked diuresis and render further treatment unnecessary. But there are several important exceptions to this statement. If there is considerable fluid in one or both pleural cavities it should be withdrawn at once by means of paracentesis, for such fluid often causes great respiratory discomfort and is but slowly absorbed and excreted, even when are employed. Further more if the edema elsewhere is so extreme as to be the cause of danger or grave discomfort, the mercurial diuretics should be administered at once, without waiting for the effect of digitalis. I am in agreement with Thomson that the diuretic effect of these agents is often just as great without digitalis as with it, and the patient may be spared some days of discomfort if they are used immediately.

Xanthines.—Until about fifteen years ago the xanthien diuretics, sometimes known as the purine base, were the only ones in general use. For practical clinical purposes this group may be regarded as consisting of theophylline and theobromine with their derivatives; caffeine is also a member but has little or no value as a diuretic in disease states. Theophylline may be administered in gelatin capsules containing from 3 to 5 grains (.2 to .325 Gm.) and may be given two or three times a day. Even in this small dosage however, it often causes nausea and vomiting after four or five doses have been given and must then be discontinued. Because of the likelihood of vomiting, it is usually wise to give theophylline for periods of only a few days at a time, even if it is well tolerated; there is some evidence that the total diuretic effect is greater with intermittent than with continuous administration. It is the most potent of the xanthine diuretics but can seldom be given in effective dosage because of its unfortunate side actions. In recent years it has been used far more frequently in

combination with other salts, the best known preparations being theophylline with sodium acetate and theophylline with ethylenediamine (aminophylline). These are usually tolerated better than is theophylline alone and can therefore be used for longer periods, but it is well to omit them for a few days after a period of brisk diuresis. Theophylline with sodium acetate is available in tablets containing from $2\frac{1}{2}$ to $7\frac{1}{2}$ grains (0.16 to 0.5 gm.) those which have an enteric coating are better tolerated by most patients. The therapeutic dose should be determined in each case by actual trial, starting with small amounts in order to avoid the induction of vomiting. The total daily quantities of from 15 to 30 grains (1 to 2 Gm.) can be taken by many subjects without discomfort if given in three or four doses, but amounts less than this often causes satisfactory diuresis. The other preparation theophylline with ethylenediamine, is better known today because of its widespread use in recent years for its supposed effect on the coronary arteries. It is not a potent diuretic but may be of value in preventing the reaccumulation of edema that has been successfully removed by other agents. It is marketed in tablets containing $1\frac{1}{2}$ grains (0.1 Gm.), and six or eight of these a day are required in most cases for any significant diuretic effect. Like other theophylline preparations, this also may cause nausea if given in doses sufficiently large to increase the volume of urine.

The Council of Pharmacy and Chemistry makes the following statement concerning the actions and uses of xanthine derivative:

Actions and Uses.—The council recognizes no therapeutic claim for any xanthine derivative beyond those for diuretic action and for use as a myocardial stimulant. Theobromine and theophylline surpass caffeine in their diuretic, and perhaps in cardiac and muscular, actions. They are therefore generally preferred in cardiac edemas, etc., since they are equally, or more, effective, more prompt and largely avoid the unpleasant side effects (insomnia, nervousness, gastric disturbance) which often interfere with the use of caffeine in adequate doses. This freedom from side effects holds true, particularly for theobromine. Theophylline surpasses theobromine in diuretic

efficacy, but its action is probably not so lasting; it may produce gastric disturbances; renal irritation has been reported. Theobromine is therefore generally preferred, sometimes preceded for a few days by theophylline. If central stimulation is desired, caffeine must be used.

It has been the experience of almost all observers that theobromine and its compounds are less powerful diuretics than the closely related substances just named, but they are often well tolerated in effective dosage and may therefore prove to be far more satisfactory. Theobromine may be administered in capsules in doses of 5 or 10 grains (0.325 or 0.650 Gm.) three times a day and continued for a number of days if nausea does not occur. One of its best known compounds is theobromine with sodium salicylate, which contains approximately 50 per cent theobromine. This is one of the mildest of all diuretics, seldom causes nausea or vomiting and must be given in doses of from 40 to 60 grains (2.6 to 4 Gm.) or more a day. Another preparation is theobromine, calcium salicylate, or theocalcin, which is said to contain 48 per cent theobromine, 11 per cent calcium and 38 per cent salicylic acid. Stewart's study indicated its advantages and these have been confirmed by subsequent experience. It is a potent diuretic, often superior to theophylline in this respect, seldom causes nausea and may be continued without intermission as long as diuresis results. It is available in tablets containing $7\frac{1}{2}$ grains (0.5 Gm.), and the usual effective dose is from three to six tablets a day; larger amounts may be given if necessary.

It is the belief of many students that the xanthines cause diuresis by an action on the renal glomerulus, increasing the filtration but authoritative opinion is not agreed on this. Smith states that, although they increase the filtration rate, this is not an essential factor in their diuretic action, which is to be attributed to diminished reabsorption of water in the tubules. A final statement on this point is not possible as yet. The xanthines as a group are far from negligible; in recent years they have been from overshadowed and to a large extent superseded by the mercurials, but they have an important place in the treatment of the patients with slight or

moderate edema and of those patients who object seriously to intravenous injections.

Organic Mercurials: The mercurial diuretics are unquestionably the most effective available today, even though an occasional patient may exhibit a greater response to one of the xanthines. Merbaphen, the first to be introduced, has been almost completely displaced in recent years by salyrgan, which is regarded as more potent and less toxic. These are organic mercurial compounds containing about 10 per cent of mercury and are effective when administered by intravenous or intramuscular injection or in the form of rectal suppositories. Their effectiveness is greatly increased if acid-producing salts are administered by mouth for several days should be a routine unless the need for the first injection is urgent. Ammonium chloride and ammonium nitrate are the salts most commonly used, but calcium chloride and calcium nitrate are also effective. It has been shown that there is a true synergism between these salts and the mercurial preparation; all four regularly cause a lowering of the carbon dioxide combining power of the plasma and increase the diuretic response. Alkalizing salts cause a rise in the carbon dioxide combining power and a decrease in the diuretic effect, while neutral salts cause no change in either function. The statement is often made that doses of these acid-producing salts as large as from 90 to 120 grains (6 to 8 Gm.) a day must be given in order to secure satisfactory results, but my experience is in accord with that of Thomson, who has found doses of from 60 to 90 grains (4 to 6 Gm.) sufficient. Even these smaller doses will almost invariably cause nausea and vomiting unless administered in the form of enteric coated tablets, which are taken by most patients without discomfort in the doses mentioned.

The mercurials for injection are available in ampules containing 1 and 2 cc. It is customary to give only from 0.5 to 0.75 cc. at the first injection, in case there should be an idiosyncrasy to mercury or some untoward reaction, both of which are rare. Subsequent doses are usually 2 cc. If the patient requires a series of injections it is satisfactory to continue ammonium chloride without interruption and inject the mercurial every third, fourth or fifth day. The results are

almost always satisfactory and sometimes astonishing; it is not unusual to secure a urinary secretion of from 6 to 10 liters in twenty-four hours, and quantities as large as 15 or 16 liters have been recorded.

A few years ago Shelling and Tarr reported that the diuretic effect of salyrgan might be increased by combining magnesium sulphate with it. They recommended the use of 15 c.c. of 50 per cent magnesium sulfate with 2 c.p. of salyrgan and 1.5 cc. of 5 per cent procaine hydrochloride, the whole to be mixed thoroughly in a 20 cc. syringe and injected deeply into the gluteal muscles. There can be no question that this combination is sometimes remarkably efficacious with patients who have shown little or no response to salyrgan alone. To secure such effect, however, it is not always necessary to use such large quantities of magnesium sulfate; a mixture of 2 cc. of salyrgan, 6 or 8 cc. of 50 per cent magnesium sulfate and 2 cc. of 1 per cent procaine hydrochloride solution has often given excellent results. This is about half the total quantity recommended by Shelling and Tarr, and its injection into the muscles seldom causes pain at the time or later. It should be added that the anterior muscles of the thighs are more suitable for such injections than are the gluteal muscles if the patient is confined to bed.

It is generally agreed that the mercurial diuretics owe their effect largely, if not exclusively, to a direct action on the renal tubules, diminishing their power of reabsorption.

Since there was a widespread belief that the xanthines caused diuresis chiefly by increasing glomerular filtration and the mercurials by diminishing tubular reabsorption, it was but natural that attempts should be made to secure a more effective diuretic agent by combining the two substances. In Europe such a combination was introduced as early as 1929; several years later it appeared in this country under the name mercupurin. According to the revised supplement to New and Non-official Remedies 1939, it contains 10 per cent of the mercurial component and 4.86 per cent of anhydrous theophylline, each cubic centimeter contains about 39 mg. of mercury in nonionizable form. DeGraff and his collaborators in a series of important studies have shown that

the addition of theophylline to a mercurial diuretic causes much more rapid absorption from the site of intramuscular injection and also renders it far less injurious to the tissues. Comparative clinical studies have shown that the combination of two substances in a more potent diuretic than is the mercurial alone, and this increased potency is apparently due to the addition of theophylline. The advantages of combining the two have been so apparent in recent years that practically all mercurials now marketed in Europe have been modified by the addition of 5 per cent theophylline. Several years ago salyrgan was thus modified and available under the name salyrgan-theophylline; apparently its content of mercury and of theophylline is approximately the same as that of mercupurin. More recently there has been introduced a combination of the two under the name esidrone, which is said to contain 31.2 per cent mercury in nonionizable form and 28 per cent theophylline, which is chemically connected with the mercury molecule. The reports on its clinical use thus far available are not sufficient to determine whether the great increase in the amount of theophylline in the mixture has caused any considerable increase in its diuretic potency. (The product has not been accepted by the Council on Pharmacy and Chemistry—ED.)

There can be no question that the combination of a mercurial with theophylline is the most powerful diuretic agent now available for most patients with congestive heart failure.

Both salyrgan and the mercurial component of mercupurin are available in the form of rectal suppositories, each containing approximately 0.5 Gm. of mercury and a small amount of local anesthetic to prevent rectal irritation. A cleansing enema usually precedes the insertion of the suppository, and diuretic response is often increased by the preceding administration of the acid-producing salts. Some observers have found the suppositories to be almost as effective as intravenous or intramuscular injections of the mercurials, but most regard them as about one third to one half as effective. (It should be noted that the suppositories of salyrgan have recently been found to result in rectal irritation or ulceration in so many cases that their acceptance has been rescinded by the council on Pharmacy

and Chemistry, and many clinicians have discontinued their use.) Similar unfortunate results have apparently not followed the use of mercurin suppositories, but any such preparation should be used with great caution and should be discontinued immediately on the appearance of signs of local irritation.

There is general agreement that the mercurials should not be used in the presence of acute nephritis or ulcerative colitis. For some years fear was expressed that they might cause serious injury to the renal tubules, and a few such instances have in fact been reported. But the accumulated experience of the past ten years justifies the statement that the mercurial diuretics, especially those combined with theophylline, are safe and highly effective and often retain their full potency after hundreds of injections over a period of many months or years. In the great majority of cases, even of chronic nephritis, there is no evidence that the kidneys have been injured by the mercury.

Potassium Salts—According to Keith and Binger potassium salts were recommended for the treatment of dropsy as early as 1679. In recent years most of the studies relating to their diuretic action have been concerned with nephritic patients, but in 1932 Barker reported excellent results from the administration of potassium chloride to a group of patients whose edema was due to congestive heart failure. He emphasized the importance of placing such patients on a full general diet with an excess of acid ash in which a low ratio of sodium to potassium is maintained. The dose of potassium chloride found to be effective in most of his cases was 5 Gm. (75 grains) a day; this amount was given to the patient each morning in a salt shaker and sprinkled on the food instead of sodium chloride. At the end of the day any salt remaining was dissolved in water and taken by mouth. Twelve of his sixteen patients obtained excellent results, and he observed, as others had done, that no ill effects followed even if very large doses were given for long periods.

In a later and more elaborate study, Keith and Binger found that potassium salts gave "very satisfactory diuretic results" in 48 per cent of their sixty cases and fair results in another 33 per cent, but their figures do not indicate in how

many of these edema was due to heart failure. After a careful study of five potassium salts they concluded that the nitrate was preferable, since it frequently caused diuresis and seldom gave rise to untoward effects. They pointed out that any potassium salt must be given in large doses, amounting to 12.5 Gm. or more of the nitrate a day, but state that smaller doses should be administered first. One of their patients took 24.5 Gm. of potassium salts daily for thirteen days and 871 Gm. in sixty-eight days without complaints or toxic symptoms! The salts may be administered in powder form or in solution, but the most satisfactory method is by means of enteric coated tablets containing $7\frac{1}{2}$ grains (0.5 Gm.) each. Like ammonium chloride and ammonium nitrate, the potassium salts may be used in conjunction with other diuretics to enhance the action of the latter.

A great many studies are in complete harmony in indicating that in the experimental animal, in normal human subjects and in patients with edema due to human subjects and in patients with edema due to potassium results in increased excretion of water, while the substitution of sodium for potassium results in increased retention of water. The exact mechanism responsible for these results, however, is not entirely clear. It is known that potassium is quickly absorbed from the intestine and is promptly excreted by the kidney, which is able to concentrate it as much as fifty times; even after large doses the amount in the blood is seldom elevated appreciably and often not at all. In fact the careful measurements of Barker revealed practically no changes in the sodium, potassium, calcium, carbon dioxide combining power, PH, or cholesterol of the blood during the administration of potassium. In some cases it seems possible that the diuresis is linked with a shift in the acid-base equilibrium, but this cannot be demonstrated regularly.

Bismuth—Ten years ago, Mehrtens and Hanzlik brought forward evidence indicating that certain bismuth preparations injected intramuscularly in small doses act as a diuretic and are almost devoid of toxic manifestations. In the following year Hanzlik and his co-workers cited case reports indicating that bismuth sodium tartrate injected in doses of one half grain

(0.03 Gm.) often caused prompt diuresis which was maintained for from four to eighteen days, the average being six days. It was particularly satisfactory in cases of edema due to heart failure, and in the cases cited it was far more effective than merbaphen or theophylline with sodium acetate. Several years later Stockton reported the results of intramuscular injections of bismuth sodium tartrate in thirteen cases of edema in which there had been no response to treatment with digitalis and the xanthine and mercurial diuretics. Congestive heart failure was present in nine of these. Bismuth sodium tartrate caused marked diuresis in ten cases and moderate diuresis in one; four showed no diuretic response either to this or to other agents. The average duration of diuresis after the injection of a bismuth preparation was four days.

These reports are so encouraging that it is surprising not to encounter further reports in recent medical literature. Untoward actions or toxic effects cannot explain this apparent neglect, for these are absent or negligible; in fact. Hanzlik states that the group of observers at Stanford University has used bismuth preparations in various ways in several thousand cases and in animals in the past twelve years without serious disturbances, injuries or fatalities. It seems probable that this drug, likewise others of undoubted merit, has failed to come into general use because the mercurial diuretics are usually more potent, even though their action is less sustained than that of bismuth.

According to Stockton, bismuth sodium tartrate probably causes diuresis by general tissue action, resulting in mobilization of chlorides and water. He explains the effect of the mercurial diuretics and theophylline in the same way, whereas most students to-day believe that these substances act directly on the kidney. A belief in general tissue action of diuretics was widespread ten years ago but has been largely abandoned in the light of recent studies.

Urea—Although urea has been recommended as a diuretic in renal disease for a long time, its use for the treatment or cardiac edema seems to date from the report of Crawford and McIntosh in 1923. They found it to be of great value in seven of eight cases in which edema was due to heart failure and

recommended it both for the removal of edema and to prevent its recurrence. No toxic effects were observed. In 1932 Miller and Feldman emphasized several of the cardinal virtues of this substance, demonstrating that its diuretic potency does not diminish during months or years of practically uninterrupted use, that there are no demonstrable deleterious effects on the kidneys or other tissues and that it acts, alone or in conjunction with other agents, as an admirable prophylactic to prevent the recurrence of edema.

Large doses are required, varying from 15 to 60 Gm. or more (225 to 900) grains a day. It is administered most satisfactorily in ice cold aqueous solution three times a day immediately after meals. Its unpleasant taste, which is practically its only disadvantage, can be mitigated for some patients by dissolving it in syrups or fruit juices. Syrup of acacia has been especially recommended as a vehicle for urea, its colloidal nature serving to mask the urea quite satisfactorily. Urea is rapidly absorbed from the intestine and is practically devoid of action in the tissues, even in large doses. After it has been taken for a few days the blood nitrogen should be determined to ascertain whether it is being properly excreted. In almost all instances of congestive heart failure, and even of nephritis and nephrosis, it is readily excreted and carries with it large quantities of water. This mechanical diuretic action is thought to be enhanced by decreased reabsorption in the renal tubules.

Urea is an extremely valuable diuretic and deserves wider popularity than it seems to enjoy at present. All available clinical reports emphasize its complete freedom untoward actions and its extraordinary constancy of diuretic effect. While it is usually less dramatic in its immediate results than are the mercurials, it has obvious advantages and may be used to supplement the latter. There are but few patients who cannot take it for at least several weeks at a time, and many continue it for months or years without interruption.

NEPHROSIS.

Despite the enormous literature devoted to the subject of nephrosis in the past thirty-five years, there is not yet

complete agreement among authoritative observers as to the existence of "pure" or "lipoid" nephrosis as a separate disease entity. There is, however, general agreement that the combination of low serum proteins, profuse albuminuria, normal blood nitrogen and edema may properly be known as the "nephrotic syndrome" and that its treatment is the same whether it is regarded as resulting from a specific renal lesion, a nonspecific renal lesion (one stage in the development of chronic glomerulonephritis) or a general metabolic disease. The edema is thought to be due in large measure, as Epstein first pointed out, to the marked hypoproteinemia, which results in great lowering of the colloid osmotic pressure of the blood.

The general principles of treatment include maintenance of the nutrition at the highest possible level by an adequate diet high in protein, limitation of salt and clinical state permits. Practically all known diuretics have been tried in this condition; any of them may give satisfactory results in a given case but most of them prove quite ineffective. Thyroid has been extensively used because of the low basal rate in most patients but is seldom effective in causing diuresis, possibly because the low metabolic rate is caused in most instances by the under-nutrition rather than by thyroid deficiency. The xanthine diuretics have proved useless in the hands of most observers. Encouraging results have sometimes been obtained from the use of potassium salts, as already outlined. Urea also has occasionally been effective in doses of from 15 to 50 Gm. or more a day and deserves a trial if it is tolerated. But there can be little question that the mercurial diuretics are much the most effective in the majority of cases, and they may be used without fear of increasing the renal lesion. They should be preceded by one of the acid-producing salts. In many cases the mercurials also are useless.

Because of the belief that the edema is due largely or wholly to the reduction of serum proteins, many attempts have been made to raise these to normal levels by means of diets high in protein and by the intravenous injection of such substances as whole blood, blood plasma and solutions of acacia. Leiter has stated that this form of treatment, however plausible

it may seem, is inevitably doomed to failure because the amount of material injected cannot be sufficient to cause an appreciable increase in colloid osmotic pressure of the plasma and because it will be rapidly excreted from the circulation, since the glomeruli are much more permeable to colloids than normally. However, Hartmann and his collaborators, Lepore, Landis and Shelburne have all reported excellent results from the repeated and cautious intravenous injection of acacia solutions. The strength of the solutions has usually been from 6 to 15 per cent, in water or in physiologic solution of sodium chloride, and the injections may be given daily or at intervals of from two to four days. In practically all reported cases of benefit from acacia many diuretics had been tried without success. Following the disappearance of edema, a diet high in protein should be continued; Shelburne regards this as an essential part of the treatment.

The administration of acacia is not wholly without disadvantages, and some have stated that these are so serious as to make the use of the substance unjustified. The work of Dick is often quoted in support of this belief, but Shelburne has recently pointed out that this work is open to serious criticism and should not prevent the proper use of a valuable therapeutic agent. Immediate reactions to injections of acacia are infrequent if the solutions are freshly and carefully prepared, but serious reactions have followed the use of impure solutions. It seems clear that if acacia is to be used it should be in a hospital rather than in the patients' home. If other methods of treatment have been tried without success and the removal of edema is highly desirable, recent experience would certainly justify the trial of acacia. If this also proves ineffective, other diuretics should be employed immediately after the acacia, as they may then prove beneficial.

VITAMIN DEFICIENCY.

In the past several years evidence has been presented, chiefly by Weiss and his collaborators indicating that deficiency of vitamins, especially of vitamin B₁, may lead to various types of cardiovascular dysfunction, whether the heart

was previously normal or diseased. The cardiovascular manifestations do not form a fixed clinical syndrome but may include the characteristic signs of congestive heart failure with marked edema. The diagnosis of the condition may be very difficult, but the possibility of vitamin deficiency should be seriously considered when any patient with an abnormal nutritional history develops the syndrome of heart failure with edema in the absence of convincing signs of heart disease. The presence of other signs of vitamin B₁ deficiency, especially polyneuritis, glossitis and cutaneous changes suggestive of pellagra, may give an important clue. According to Strauss "it is rare to observe 'beriberi heart' without at least minimal signs of poly-neuritis." Both Weiss and Strauss emphasize the possible importance of measurements of the circulatory velocity and the minute volume output of the heart, as these are increased in the condition now under discussion and are conspicuously slowed in heart failure due to other causes. The response to specific therapy, however, may provide the first and most convincing evidence of the nature of the condition.

General, or nonspecific treatment consists of the application of the measures enumerated previously: rest in bed, limitation of fluids and of salt and the administration of digitalis and diuretics. Some patients respond well to such a regimen, while others show little or no improvement; indeed some of Weiss's patients became worse when placed at rest. Specific treatment consists of the administration of vitamin B₁, preferably this should begin with the intravenous or intramuscular injection of from 20 to 50 mg. of thiamin chloride N.N.R daily, and this method should be employed as a routine in the more severe cases. After improvement has occurred, usually within two weeks, the dose may be decreased to 10 or 20 mg. daily, or the larger doses may be given by mouth. If the symptoms are not particularly severe or have been largely relieved by intensive treatment, brewer's yeast may be used instead of the crystalline form of the vitamin; doses of about 30 Gm. three times a day are recommended.

The response to such a treatment may be prompt and spectacular, with marked improvement in a few days and

complete disappearance of symptoms and signs within two or three weeks, or improvement may be gradual over a period of six or more weeks. Rapid improvement is said to be associated with diuresis, slowing of the heart rate and rise in the arterial pressure. If there is not clear evidence of improvement after adequate dosage of vitamin B for several weeks it is probable that the cardiovascular manifestations are not due to vitamin deficiency. Beneficial effects do not follow the administration of this vitamin to patients with other types of heart failure.

Weiss has properly emphasized that deficiencies are seldom limited to a single vitamin, and these patients often present evidences of inadequate intake of vitamin A and of ascorbic (cevitamic) acid of anemia, of hypoproteinemia and possibly of other dietary deficiencies. These should, of course, receive appropriate treatment simultaneously.

MALNUTRITION.

The edema, often very extensive, associated with serious degree of malnutrition is thought to be dependent in large part on the diminished proteins of the blood plasma and the consequent lowering of the colloid osmotic pressure. It is clear that this condition may be intimately related to and complicated by the vitamin deficiency state just discussed. Diuretics may be employed, but the logical and highly effective treatment is the correction of the nutritional state by means of a proper diet rich in proteins and in vitamins. Unless the patient is dying, the dropsy usually disappears with gratifying promptness.

PICK'S DISEASE

For many years the term 'PICK'S disease' was used loosely and inaccurately and was applied to a number of quite different pathologic states. Now, thanks largely to the clinical reports of White and the experimental and surgical studies of Beck, it is possible to say with conviction that PICK'S disease is actually chronic constrictive pericarditis. For the details of this important advance in our knowledge, their original papers and those of Churchill and of Burwell should be consulted. Among the more important clinical features of the condition may be mentioned gradual onset of dropsy, disproportionate

enlargement of the liver and ascites, increased venous pressure, low arterial pressure and a heart that is normal in size or smaller than normal. A single cause is responsible for all these manifestations: the heart is so encased by unyielding fibrous or calcified tissue as to be unable to dilate and fill properly during diastole. In some cases there is, in addition, a marked constriction of the inferior vena cava. The immediate mechanisms of edema formation are those discussed under congestive heart failure.

The milder diuretics are of little or no value in this condition, although they may occasionally lengthen the interval between abdominal paracenteses. The mercurials, however, may prove extremely useful, as in the case reported by Noth. A man aged 53 in seven and one half years had had forty abdominal paracenteses and 450 injections of mercurial diuretics and had taken 6 Gm. (90 grains) of ammonium nitrate a day for three years. At the end of this time he presented no signs of hepatic or renal injury and had been able to continue an active life as a banker. However, if the diagnosis is reasonably certain and the patient is a good operative risk, the best treatment is surgical resection of the constricting pericardium. This often results in rapid and spectacular improvement and in restoration of the patient to normal activity even after years of invalidism.

NEPHRITIS

The edema of acute nephritis is generally believed to be due in large part to widespread injury to the capillaries, which makes them more permeable than normally. It is theoretically unwise to administer diuretic drugs which might irritate an organ already acutely inflamed, and experience has shown conclusively that they are practically always devoid of beneficial action. In most cases diuretics are clearly unnecessary; if special circumstances seem to make a trial of such drugs essential, only the very mildest, such urea or theobromine with sodium salicylate, should be used.

In chronic nephritis also diuretics are usually unnecessary if one excludes the "nephrotic syndrome" of chronic glomerulonephritis. But if edema becomes a serious problem almost any

of the diuretics previously discussed may be used safely. The xanthines, urea and potassium salts may prove ineffective. The mercurial diuretics, combined with ammonium chloride or nitrate are usually very satisfactory and almost never increase the renal disease. It is unwise to use these if there is acute renal inflammation or much retention of nitrogen in the blood, but extensive edema and nitrogen retention are seldom associated.

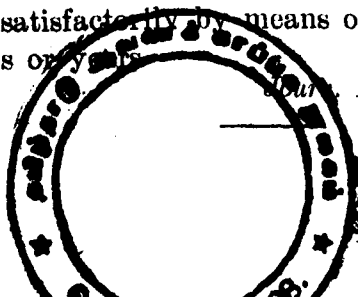
HEPATIC CIRRHOSIS

It is not often that ascites and edema of the lower extremities resulting from portal cirrhosis of the liver can be removed satisfactorily by means of diuretic drugs. It has been almost universal experience that the milder ones, including the xanthines, urea and bismuth, are almost devoid of beneficial action. In occasional cases the mercurials, preceded by acid-forming salts, prove to be fairly satisfactory, but in most instances all that can be expected is a prolongation of the interval between abdominal paracenteses. This, however, is distinctly worth achieving, and a trial is always justified.

COMMENT

Even from the foregoing survey it is clear that the occurrence and removal of dropsy may present involved and baffling problems to the physician. Proper treatment of the underlying disease may result in disappearance of the edema, but often this must be supplemented by control of the diet, by diuretics and some cases by surgical operation. It is highly encouraging to realize that all the specific measures discussed in this article, with the exception of the xanthines, have come into general use in this country within the past fifteen years. Our knowledge of the mechanisms involved in the formation of edema and the occurrence of diuresis have steadily widened, and our use of specific remedies has consequently become more intelligent. It is not often that the disease responsible for dropsy can be wholly cured, as in vitamin deficiency and constrictive pericarditis, but the dropsy itself can often be controlled very satisfactorily by means of medical treatment for many months or years.

Sur. A. M. A. March 2, 1940.



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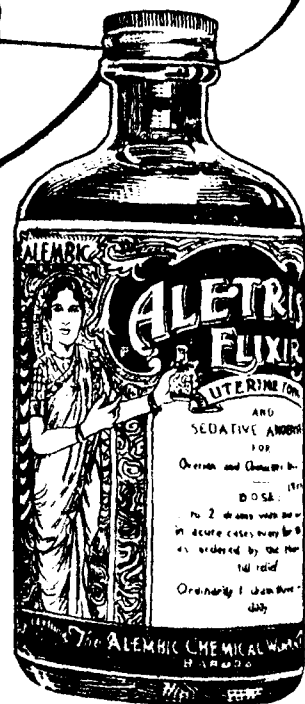


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[No. 9

Treatment of Peptic Ulceration by Rest

Dr. Adolphe Abrahams holds that the essential principle in the "medical" treatment of peptic ulcer is complete confinement to bed for three or four weeks, and that severe dietetic restriction or drug therapy plays an insignificant or negligible part. Whether confinement to bed contributed to healing through physical inactivity (or even posture) or on the nervous side through seclusion from responsibilities and other psychical disturbances, or through both factors, does not matter. The success of several widely differing dietetic treatments may be due to one common factor—the protracted rest—often inevitable from the elaborateness of the details, which in addition have a high suggestive value. Control observations of patients treated solely by rest and a relatively bland diet have shown results at least as satisfactory as in those submitted to the orthodox elaborate regime—results judged by the complete amelioration of symptoms and subsequent radiographic examination.

Confirmation of this view is supplied by the investigations of James Ronald who found it impossible to correlate the variations in acid level with the symptoms and signs of ulcer. Improvement occurred whether the acidity was diminished, unaltered, or increased. No distinction could be drawn on clinical grounds between cases in which hyperchlorhydria was or was not altered during treatment. Indeed, healing could take place although the hyperchlorhydria actually increased. This shows that there is no justification for indicting acidity as the villain in the piece.

(From Cl. Journ., May 1940.)

JK

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N 60. 7. 9

The Chemotherapy of War Wounds

At a meeting of the Medical Society of the British Expeditionary Force Col. L. Colebrook stated that the outstanding lesson of the Great War in the bacteriological field was the predominant part played by haemolytic streptococci in wound infections. Probably this microbe was responsible for 70 per cent. of the deaths. It also gave rise to most of the complications, such as erysipelas, cellulitis and septicaemia. Out of 49 positive blood cultures obtained from men with septic compound fractures of the femur no fewer than 44 were pure cultures of haemolytic streptococci.

Unfortunately we did not learn when and why these infections occurred—whether in most cases the organisms were carried into the tissues at the time of the wounding, whether they were transmitted from case to case in the hospitals, or whether they were due in large measure to dissemination of the microbe by dust or by respiratory tract carriers. The only data obtained were that about 15 per cent. of a series of 365 wounds were already infected by haemolytic streptococci on admission to the casualty clearing station (average about 12 hours after wounding), while a much larger proportion were so infected when examined after a few days at the base. These figures suggest that hospital infection plays a sinister part.

To control these infections would be no easy task, but there is great hope in the fact that these streptococci (and some of the gas gangrene bacilli) have proved highly susceptible to sulphanilamide and sulphapyridine (M and B 693). The striking results obtained in erysipelas, puerperal fever, meningitis and pneumonia, with the unquestionable effects in experimental infections of animals, give good reason to believe that these new remedies will prove valuable in controlling the acute invasive phase of infections by haemolytic streptococci.

It is possible that early administration soon after the man is wounded may prevent many of these infections from developing—or, failing complete success in that, may render them

non-invasive, and therefore much less dangerous to life. Experiments justify this hope. Mice have been completely protected by a single injection of sulphapyridine given within a period of 24 hours before they were infected with haemolytic streptococci. Others showed good protection when sulphanilamide is present in the circulating blood at the time the streptococci reach the tissues they are prevented from causing an acute infection. That is the essential point to keep in mind in prophylaxis for the wounded. Clearly, if the microbes are implanted in the tissues at the time the man is hit, as is almost certainly true for gas gangrene bacilli, prophylactic treatment must be started at the earliest possible moment, particularly in view of the fulminating course of those infections.

In planning preventive measures against infections by haemolytic streptococci, on the other hand, we are up against the difficulty that infection probably is not always caused at the time the man is wounded, but may occur in hospital during the next few days. A single prophylactic dose given by mouth shortly after the injury would be almost all excreted within 10 to 20 hours. Therefore to maintain the necessary concentration in the blood during the whole period of danger, administration must be continued for at least 4 days. By the end of that time the injured tissues would presumably be walled off by the processes of repair, and if infection did occur it would be much less serious.

Attempts had recently been made by Fuller and James to find a method of securing slow, continuous absorption from the alimentary tract in order to obviate the need for frequently repeated doses. From their estimates of the concentration of sulphanilamide in the blood after various methods of administration the following method is advocated:—

First dose—1·5 gm. (three tablets of sulphanilamide) dissolved in about 100 c.c. of hot citric acid solution (roughly 1 per cent) or hot lemon.

Second dose—0·5 gm., whole or partially crushed, at 4-hourly intervals for 4 days.

Total—13·5 gm. in 4 days.

The blood concentrations obtained on these doses in men suffering from shock would have to be checked up to ensure that they correspond sufficiently with those obtained on normal men—Fuller and James. Any toxic effects resulting from these doses should be noted. If they were well borne, but did not suffice to prevent infection larger doses could be tried later.

The dosage required for infections already established does not differ much from those of civil practice. There is some evidence that sulphapyridine is more effective than sulphanilamide for gas gangrene. In order to expedite its absorption, the first three doses (1 gm. each) should be given well crushed and so far as possible dissolved in about 100 c.c. of hot citric acid or lemon at an interval of one to three hours. Six to 8 gm. should be given in the first 24 hours, and the amount reduced slightly on the next day if the clinical condition is much improved. For haemolytic streptococcal infections 1 gm. doses of sulphanilamide should be given 4-hourly for the first day or two and the amount reduced *pari passu* with the clinical improvement. For severe infections as much as 8 gm. should be given on the first day. The drug should be continued for 4 or 5 days after the temperature had dropped to normal and the clinical condition had become satisfactory, but it should not be continued after that time just because there were still haemolytic streptococci in the discharges.

In the Spanish war different observers came to very different conclusions as to the value of such treatment because sulphanilamide was given indiscriminately in all kinds of wound infections; some due to haemolytic streptococci (presumably) and some not. The same thing happened when red prontosil was first introduced in Germany and "tried out" in puerperal fever. The obstetric surgeons who used it were not fully alive to the fact that only about 50 per cent. of puerperal fever cases were infected by haemolytic streptococci, the rest being due to a heterogeneous group of organisms—anaerobic and faecal types of streptococci, *B. coli*, *B. proteus*, staphylococcus. Later experience of puerperal fever showed that these heterogeneous infections were influenced little, if at all, by sulphanilamide or red prontosil.

To avoid this pitfall in the present war we should attempt to restrict chemotherapy to wounds known to be infected by haemolytic streptococci or gas gangrene bacilli (and perhaps some severe infections by staphylococcus). There would be serious difficulty in doing this because we often could not afford to wait 24 hours for the result of a bacteriological examination. Often an examination by film alone would suffice, but if it did not, treatment should be begun as soon as there were signs of acute infection, and a swab taken from the wound at the same time. The bacteriologist should be asked to report as early as possible as to the presence or predominance of haemolytic streptococci and not to bother about other organisms (except the gas gangrene bacilli), which might take longer to identify. If haemolytic streptococci were not present treatment could be discontinued. But this plan might be quite impracticable in times of heavy fighting.

There is the danger of producing agranulocytosis. This condition (which has a mortality rate of about 50 per cent.) is closely related to the amount of drug given and the duration of treatment. The average total dose in the recorded cases had been about 50 g. and the duration of treatment 20 days. Occasionally, however, much smaller doses and a shorter period of treatment have been recorded. It seems to occur just as often in association with sulphapyridine as with sulphanilamide. The use of these drugs on a large scale under war conditions calls for special vigilance. Wounded men might be given a prophylactic course at the front and a second course when they arrived at the Base, and possibly a third in England. Such second and third courses appeared to be particularly dangerous. The risk would be greatly diminished if treatment was given only to cases known to be infected by haemolytic streptococci (or gas gangrene bacilli) and if treatment was stopped soon after the acute febrile phase had passed. It is the general experience that if an infection does not respond to these drugs within 4 days it seldom does so later.

Recognition of the beginning of agranulocytosis is often difficult—indeed, the diagnosis can be made with certainty only by a rapidly falling leucocyte count. The onset is usually

insidious—moderate rise of temperature, increasing prostration, and perhaps some head-ache. The typical agranulocytic angina is often not present, or develops only as a terminal event. A white cell count and a rough estimate of the polymorphs should be made in every case receiving large doses of these drugs on the seventh day of treatment, and, if a second or third course is given, on the first and third days of such courses; also at any time if the patient's general condition is unsatisfactory or if a sore throat develop.

(From *Cl. Journ.*, May 1940).

LIVERITES

FOR

Infantile Liver and Spleen Disorders.

It is preferred because:

1. It is both prophylactic and curative,
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Diagnosis of the Carcinoma of the Lung

Clinical Feature

In primary carcinoma of the Lung every aspect of the case must be reviewed; symptoms and signs are nowhere more important, and the use of X-ray is becoming so general that one rarely ventures a negative opinion without them. They are often invaluable in solving some mysterious and apparently slight signs produced by an early neoplasm.

Ancillary Investigations

The use of X-rays in examination of intra-thoracic lesions is essential, especially for the early diagnosis of neoplasms. Besides the more obvious changes—masses of growth, effusion and so on—the following points should be borne in mind in examining a chest film.

The symmetry of the two sides may be lost—bronchial stenosis leads to shrinkage of the hemithorax. The comparison of the rib spaces on the two sides is useful. Crowding of the ribs is indicative of massive pulmonary collapse if associated with mediastinal displacement, general loss of translucency of the lung parenchyma and elevation of the diaphragm. The position of the mediastinum, of the heart and of the line of the trachea are valuable guides to mediastinal displacement. The relative positions of the diaphragm on either side. By screen examinations alterations in movement and on the film a high or low level are seen. Chest films are usually taken in the position of full inspiration.

The typical shape of a pleural effusion has a sloping upper level, highest furthest from the hilum. With carcinoma of the lung atypical shapes occur. Fluid and air, e.g. in a hydro-pneumothorax or abscess cavity, show a horizontal "fluid level."

Lateral views are essential to show shadows in the posterior mediastinum and with antero-posterior views help to locate a tumour within the chest. Erect and recumbent positions and oblique views are also frequently helpful.

An effusion which obscures the underlying lesion may sometimes be aspirated and replaced by air. The little residual fluid collects at the bottom and a growth may become evident. Occasionally the induction of an artificial pneumothorax is useful in the absence of an effusion, so that it can be seen whether the tumour is within the lung or growing from the chest wall.

Lipiodol bronchography is of the utmost value and bronchial stenosis, especially, can be visualized in this way.

Bronchoscopy is a further valuable method of investigation. It can be carried out under local anaesthesia, usually with little disturbance to the patient, and by its means, the growth may be seen and a biopsy made—the most definite way of establishing the diagnosis. The majority of carcinomas of the lung, occurring as they do in an area of the bronchi, close to the bifurcation of the trachea, are frequently visible to the bronchoscopist at an early stage.

Summary

Radiology must in all cases be employed alongside the discovery of symptoms and signs. X-rays by themselves and in conjunction with lipiodol injection offer a valuable means of making a diagnosis.

(From Cl. Journ., Apr. 1940).

The Treatment of Blood Disorders

A SUMMARY

ON

THE USE OF TRANSFUSIONS

(From the debate at the Conference on Therapy by the members of the Departments of Pharmacology and of medicine of Cornell University Medical College and the New York Hospital).

DR. DU BOIS: Every one seems to be agreed that to-day we are riding the crest of a wave of enthusiasm for transfusion; that transfusions are used too freely and often in conditions in which they appear to do little or no good.

The purpose of additional blood in most cases in which transfusion is indicated is to alleviate anoxemia due to anemia. The oxygen and carbon dioxide combining power of the blood is augmented by this process; the burden placed on the heart by severe anemia is reduced. There are also other uses for transfusion. In the hemorrhagic states new blood may introduce those elements which aid in the coagulation of blood. There is considerable doubt whether transfused blood is of specific value in combating infections, but on the other hand a transfusion may tide an anemic patient over a crisis, after which he may be better able to combat the infection.

Transfusion is indicated when the red blood cell count falls to about 2 million cells per cubic millimeter and the hemoglobin to about 5 to 6 gm. per hundred cubic centimeters. In sudden severe hemorrhage, however, transfusion is indicated immediately, although the red cell count and the hemoglobin may not have fallen appreciably because hemal dilution has not yet occurred.

Transfusion may be contraindicated in bleeding peptic ulcers and in the presence of pulmonary edema and of cardiac decompensation. If absolutely essential in these conditions, the blood should be administered slowly and in small amounts.

The indications for transfusions in infants are much the same as in adults. They are also useful in the treatment of

premature infants, severe malnutrition and gastrointestinal intoxication. In infants it is important to type the blood and perform compatibility tests before each transfusion because frequently the blood group is not established at birth.

Hemolysis does not appear to decrease the value of stored blood seriously in most instances, but the thrombocytes deteriorate rapidly and fresh blood may be preferable to preserved blood in the treatment of some of the blood dyscrasias, especially the hemorrhage states.

Reactions to transfusions may occur even when scrupulous attention is paid to typing, compatibility and the apparatus. Urticaria, jaundice or chills are not particularly serious, but jaundice with a chill may indicate a severe type of haemolytic reaction. These appear to occur less frequently with the direct method of transfusion.

(From Journ. A. M. A., June 15, 1940).

Nicotinic Acid for Pellagra and Allied Conditions

Coodall used nicotinic acid in the treatment of three cases of true pellagra, twelve of nicotinic acid deficiency and miscellaneous cases of allied conditions. Nicotinic acid was given in varying dosages according to the severity of the case. Of the twenty patients eleven were cured, seven were improved, one did not finish the course of treatment and one obtained no improvement. The author states that although pellagra is quite a common disease in Bengal there is a much larger group of cases of nicotinic acid deficiency, especially among Anglo-Indians, showing such symptoms as sore tongue, anorexia, stomatitis, diarrhoea and mental dullness, which respond well to nicotinic acid therapy. Certain cutaneous conditions such as infected scabies, show improvement with nicotinic acid therapy because this medication increases the blood supply of the affected area.

(Indian Medical Gazette, Calcutta, March 1940).

Treatment of Gonorrheal Arthritis

Culp evaluates the efficacy of various therapeutic measures employed at the John Hopkins Hospital in the treatment of gonorrheal arthritis during the last twenty years. The unimpaired function of the joint as the end result was the chief criterion used. Only those cases in which there was no doubt about the true etiology of the arthritis were included. They have been unselected otherwise. Forty-five of the cases were chronic, fifty subacute and 105 acute. Of the methods employed, sulphanilamide, intravenous injections of mercurochrome and fever therapy give the best results. Of twenty-nine patients treated with intravenous injections of mercurochrome 69 per cent were discharged as being well or markedly improved. Excellent results were obtained in cases of chronic, subacute and acute involvement. Only 53 per cent of the nineteen patients given fever therapy were well or markedly improved. Most of these were given only one session of fever. Several patients had severe reactions, and one died while undergoing treatment. Cures were effected in the chronic while undergoing treatment. Of the twenty-two patients treated with sulphanilamide 68 per cent left the hospital well or markedly improved. Most of the cases were acute and showed amazing improvement despite bone changes in a few instances. Results were less striking in cases of subacute and chronic improvement. Chemotherapy appears to be more efficacious than any other treatment. Sulfanilamide and intravenous injections of mercurochrome are recommended for the routine treatment of gonorrheal arthritis and seem to be of about equal therapeutic value. Both often result in surprisingly rapid cures. The thirty-four patients whose treatment was limited to bed rest and sedatives did poorly. Baking, diathermy, massage, prostatic massage and passive motion failed to cure any of the forty-nine patients. Poor results were obtained in the remaining forty-one cases with aspiration and the injection of air, hot compresses, manipulation under anesthesia, immobilization, incision and drainage or vaccine (typhoid or antigonococcus).

(Journ. of Urology, Baltimore, May 1940).

Ultraviolet Irradiation in Grip

Vitebisky reports the effects of ultraviolet irradiation in 625 cases of grip observed during the epidemic of 1935-36. The treatment was begun on the first day of sickness in 308 cases, on the second in 170, on the third in 112 and on the fourth in thirty-five. It consisted of a daily suberithemal dose of ultraviolet rays to the anterior and the posterior surfaces of the thorax. The minimal number of exposures was three and the maximal six. The temperature fell to normal after the first exposure in 55 per cent of the first group, after two exposures in 12 per cent. In cases in which the treatment was begun on the second day of illness, the temperature came down to normal after one exposure in 51 per cent, after two exposures in 30 per cent and after three exposures in 19 per cent. In cases in which the treatment was begun on the third and the fourth day, the temperature came down to normal after the first exposure in 17 per cent, after the second in 30 per cent and after the third and fourth in 53 per cent. It is thus apparent that the earlier the treatment was begun the quicker was the return of the temperature to normal. Along with the lowering of the temperature there was noted improvement in the subjective and the objective symptoms. The number of the sick days in instances in which the treatment was begun on the first or second day amounted to three, which is from one and a half to two times less than in cases in which irradiation was not given. A favourable effect was likewise noted on diffuse postgripal bronchitis in a group of forty cases in which the treatment was begun on the third or the fourth day. The treatment here extended to from six to ten exposures. There was not a single instance of bronchopneumonia or any other complication.

(Vrachebnoe Delo, Kharkov, No. 1, 1940).

The Pharmacopea and the Physician

THE THERAPY OF RICKETS

EDWARDS A. PARK, M.D.,

Baltimore.

Rickets can be prevented and cured in two ways: by irradiation of the skin with ultraviolet rays and by ingestion of vitamin D. How does it happen that the disease yields to two methods of treatment which seem so totally dissimilar? The answer is that, owing to a device of nature, the two lead to the same final result, namely the absorption of vitamin D into the blood. The skin is full of 7-dehydrocholesterol. Active ultraviolet rays, impinging on the skin, convert the 7-dehydrocholesterol, which is the provitamin form of D, into the vitamin form. The vitamin is then absorbed into the blood. If vitamin D is fed, it is absorbed from the small intestine. In the former case the vitamin was manufactured on the surface of the body as the result of chemical action of light; in the latter it entered the alimentary tract ready made.

What is a unit of vitamin D?

The accepted standard unit for expressing the strength of Vitamin D, as adopted by the League of Nations Health Organization and by the United States Pharmacopeia, is defined as "...the vitamin D activity of 1 mgm. of the International Standard Solution of irradiated ergosterol found equal to 0.025 micrograms of crystalline vitamin D." This is the international unit (I. U.), accepted as the U. S. P. unit. The Steenbook unit is no longer used and need not be defined. In administering antirachitic agents one should think in terms of units of vitamin D since that is the only way in which the dosages of the various substances containing vitamin D, which differ from one another so much in volume, can be reduced to a common denominator. For example, 1 teaspoon (4 cc.) of cod liver oil contains approximately 350 units, 1 quart (liter) of reinforced milk 400 units and 1 mg. of calciferol 400,000 units.

Vitamin D in foods.

Vitamin D is contained in only a few foods ordinarily eaten by us, namely certain oily fishes and eggs. Eggs from all sources contain the vitamin. Hen's eggs contain such variable amounts that they are not reliable sources. February eggs have been reported as yielding 100 units vitamin D and June eggs 390 units per hundred grams. Drake states that it requires at least five egg yolks to furnish the vitamin D equivalent of 1 teaspoon of cod liver oil.

The foods that comprise the diet of the average person are almost lacking in vitamin D, since muscle meat, including the fat, kidneys and other glandular organs, fruit, sugar, cereal and vegetables (the leafy ones as well as seeds, bulbs and tubers) contain none or at the most traces. The amount in milk is negligible. Average butter is estimated as containing only 80 units per hundred grams, making its potency about one one-hundredth that of the average cod liver oil. Liver may contain a very small amount but not enough to have any practical value.

One can summarize this by saying that, although the diet may occasionally furnish appreciable amounts of vitamin D, most of the time it furnishes virtually none. The only proper attitude is to regard the diet as being completely devoid of the vitamin.

The available sources of vitamin D.

Cod Liver Oil.—According to the United States Pharmacopeia XI cod liver oil must contain at least 85 units per gram. However, probably all cod liver oil marketed in this country contain at least 100 units per gram. Some of the superior brands may contain two or even four times the official minimum standard. One teaspoon of cod liver oil, 4 Gm. supplies at least, therefore, 400 units. As already mentioned, the vitamin D in cod liver oil is probably chiefly activated 7-dehydro-cholesterol.

Cod liver oil is effective in rickets, infantile tetany and also osteomalacia, as was pointed out clearly years ago. It is universally obtainable and safe and in addition contains vitamin A (about 600 units per gram). The great disadvantage of cod liver oil is its fishy taste. Another disadvantage is its

lack of concentration. Since it is not practicable to give more than a 4 teaspoons (16 c. c.) daily, the maximum dosage is limited to 1,400 units. Cod liver oil is amply sufficient to prevent and to cure rickets in almost all instances. The older child or adult will not take cod liver oil because of its unpleasant taste, provided the oil is given early and regularly. When the infant refuses cod liver oil, the fault usually lies with the mother or others who by words or actions communicate their feelings. If begun early and given regularly, ordinarily no difficulty is experienced in administration until toward the end of the first year. If the use is allowed to lapse, however, difficulties almost always arise. It is a common experience to find that when the cod liver oil is stopped for the summer its resumption in the fall is impossible. If the cod liver oil is aspirated, it may produce lipoid pneumonia. For this reason it is inadvisable to give it to premature infants or infants with a very low vitality.

Many patients object to cod liver oil on the ground that it gives rise to digestive disturbances, especially in summer. The oil rarely does this and can be administered in hot weather without difficulty. However, some infants cannot take it, and in very rare instances hypersensitiveness has been reported. If infants do not readily take cod liver oil, it is wiser to turn elsewhere.

Cod liver oil is best administered from the spoon. It may, however, be floated on orange juice and the two fed with a spoon. It is possible in this way to give as much as 4 teaspoons in a single dose.

Vitamin D Milk.—Vitamin D can be placed in the milk in three different ways: first by ultraviolet irradiation, second by feeding the cow irradiated yeast and third by adding a concentrate of vitamin D directly. The advantage of incorporating vitamin D in the milk is that it is taken automatically. The disadvantage is that the amount of the vitamin is determined by the milk requirement.

In other words, the vitamin D may be insufficient though the milk sufficient. The requirement for vitamin D seems to be dependent on age rather than on weight.

(a) *Irradiated Vitamin D Milk*: Activation is accomplished through exposure to active ultraviolet rays from artificial sources. The irradiation is carried out in such a way that standardization is at 135 international units per quart. Attempts to obtain a higher potency have failed because of the production of an unpleasant taste. As already stated, the form of the vitamin in irradiated milk is probably activated 7-dehydrocholesterol. Irradiated milk is marketed fresh and also in evaporated and dried forms. The latter are standardized so as to have a potency of 135 international units to the reconstituted quart.

(b) *Metabolized vitamin D (Yeast) Milk*: This is produced by feeding irradiated yeast to the cow. The standardization is 430 units per quart. The form of vitamin D is viosterol, as already stated.

(c) *Fortified Vitamin D Milk*: Vitamin D in the form of a concentrate derived from cod liver oil or the oils of other fishes or viosterol is added directly to the milk. Fortified vitamin D milk is standardized at 400 units per quart. The form of vitamin D in the milk varies naturally with the supplement.

Vitamin D Bread. This contains 460 units in the form of viosterol per 24 ounce loaf, would yield 115 units.

How to use vitamin for the cure of rickets

Although the doses of vitamin D which are sufficient to prevent rickets in a given case can be relied on to cure the disease, the cure may take place too slowly. It is better, therefore, to use sufficiently large doses to end the disease abruptly. The vitamin D milk are not sufficiently powerful antirachitic agents when the cure of rickets is at stake. If cod liver oil is employed, the curative dose in the ordinary case of rickets is 1,000 units (3 teaspoons) daily. This dosage in the form of cod liver oil, the highly concentrated fish oils or viosterol preparations, will bring advanced rickets under control within a period of from three to four weeks in the great majority of cases. If doses larger than 1,000 units are required, it is best to turn to the concentrated preparations of vitamin D. In the case of premature infants, it is sometimes necessary to give as much as from 10,000 to 20,000 units to bring the

disease to a complete termination in a short time, and in the case of some older children in whom the rickets is found to be obstinate it may be necessary to raise the dose to 60,000 units daily or even in excess of that amount. In any case, when the rickets has been stopped, as can be determined by means of repeated x-ray films or by measurements of calcium and inorganic phosphorus in the blood serum or, as can often be surmised from clinical examination alone, the dose of vitamin D can be reduced to protection levels. However, in the case of some infants and older children in whom the tendency to rickets seems to be especially highly developed, large doses of vitamin D may be required indefinitely. In the case of premature infants the need for large doses is usually temporary.

How to use vitamin D for the cure of Tetany

Since the initial action of vitamin D in some cases is to cause a depression of the serum calcium at the same time that it causes an elevation in the level of the inorganic phosphorus, it is advisable during the first few days of treatment also to give calcium in some form. If calcium chloride is chosen, it is usual to administer from 3 to 4 Gm. as an initial dose. This is to be followed by 1 Gm. four times a day for two or three days and then 1 Gm. twice a day. The administration of calcium can be stopped at the end of a week or ten days. But the vitamin D treatment should, of course, be continued as already described.

The use of Sunlight for protection against Rickets

In the temperate zone in the summer, sunlight can be relied on to protect against rickets, except in rare instances, provided the child is exposed outdoors. The infant cannot receive too much ultraviolet light from the sun's rays, if the blood who "burns" is expected. Infants, as they grow older, should be placed outdoors on every suitable occasion and should be allowed to profit by the sky shine, even when direct shine is not available. In the winter, sunlight cannot be relied on for protection from rickets. Indeed it is best to regard winter sunshine as almost devoid of antirachitic rays and hence to substitute other methods of protection. Sunlight in the

summer is capable of curing rickets. But it is better not to rely on it for that purpose but to adopt other means which are measurable and certain in their results. These other means are the administration of vitamin D, as already recited, or exposure of the body to radiations from artificial sources of ultraviolet light.

Advice with regard to the best ways to expose infants to sunlight has been furnished in great detail by the United States Children's Bureau. Practical points are these: In spring, fall and summer, under favourable weather conditions, the baby can of course be exposed outdoors. In cold weather, however, it may be necessary to expose him indoors. In the latter even the baby must be placed in the direct rays of the sun (direct shine) with the window open. Care must be used to protect the eyes. This can be accomplished by varying the position, so that the direct rays do not shine into the eyes. A good plan in cold weather is to begin with exposure of the cheeks only and then extend to one extremity at a time. Large areas of the body can be exposed, a part at a time, without danger. Exposure of only a small part of the body for a short space of time is sufficient to produce a general antirachitic effect, if the sunlight happens to be rich in antirachitic rays. In warm weather large surfaces of the body can be exposed with impunity. It is important to remember that sky shine is as valuable as direct shine and at times more valuable and that it is available on cloudy days; also that in winter in the temperate zone only in the noon period are active rays available and at best they are of low intensity.

How to employ the Artificial sources of Ultraviolet light

Treatment with the quartz mercury-vapour lamp may be conducted as follows: The lamp is placed at a distance of 2 or 3 feet from the body which of course is uncovered, and exposure of the front and back carried out alternately. The exposures are at first for one minute and are increased by one minute at each session until a total of ten minutes is reached. The treatment is carried out every day or every other day. It must be continued for at least a month. At the end of this time periods of exposure may be reduced to from two to three

minutes every other day, or some other treatment may be substituted. For the prevention of rickets the irradiations may be carried out every other day and the duration of each session limited to two or three minutes. Treatment with the carbon arc lamp is conducted in a similar manner.

The quartz mercury-vapour lamp is more apt to cause burns than the carbon arc lamp. The burns produced by ultraviolet light are, however, exceedingly superficial (sunburn), and the inflammation disappears in a few days. When either lamp is used, the eyes must be protected. Irradiation with ultraviolet lamps is especially valuable in conditions in which vitamin D cannot be absorbed well from the intestine, e.g. obstruction of the bile duct. It also has been used to advantage in the protection and cure of premature babies. The quartz mercury-vapour lamp and the carbon arc lamp may be used to supplement administration of vitamin D. When the carbon arc lamps are used, a curative effect may be obtained even though no tanning is produced. The quartz mercury-vapour lamps cause tanning. Tanning is a useful sign that ultraviolet light is producing an antirachitic action. Obviously, the use of the quartz mercury-vapour lamp and of the carbon arc lamp is contraindicated in blonds who "burn" and do not tan. For such individuals it is better to rely on the administration of vitamin D.

How to induce rapid Healing

In so-called thoracic rickets, described by Park and Howland, the weakness of the thorax is a menace to the life of the child. In such cases it is advisable to supply rigidity with the least possible loss of time. In the case of a baby aged 8 months suffering from very advanced rickets, one can give daily doses of 50,000 units of vitamin D. When the healing begins, as can be detected by means of x-ray films or calcium and inorganic phosphorus determinations, the dosage should be reduced to the ordinary curative levels. Several investigators have tried the use of enormous single doses of vitamin D, e.g. 600,000 units, and have reported that no bad effects result. It has been shown recently that after a single large dose of vitamin D the vitamin remains in the body for a number of weeks. I do not recommend the single dose method. To the infant as much

as 50,000 units of vitamin D can be given daily with safety for two or three weeks. If the dose is continued longer, one must watch for toxic effects.

How to determine that vitamin D Therapy is succeeding

The best way to determine whether vitamin D is succeeding is by measurements of the calcium and inorganic phosphorus in the blood serum or x-ray examination or preferably both. If the level of the calcium is normal and the inorganic phosphorus rises to 5 mg. per hundred cubic centimeters or above, one knows that a curative effect has been obtained. In cases of ordinary rickets, treated with the usual doses of vitamin D, a rise in the inorganic phosphorus level of the blood serum can be expected on about the tenth day. If very large doses of vitamin D are given, the rise in the level of inorganic phosphorus of the blood serum may occur as early as the fifth or sixth day after the beginning of treatment. Under ordinary conditions the first evidence of deposition of lime salts at the ends of the long bones occurs about the twenty-first day. But if very large doses of the vitamin are given signs of deposition may be found on the tenth day. When enormous doses of vitamin D have been given, doses in the hundred thousands of units, the signs of deposition in the x-ray films have been reported on the fifth or sixth day. If the physician is obliged to rely on inspection and palpation in order to gauge the effect of antirachitic treatment, it is very difficult to be certain that the cure has begun. The recession of the deformities is a very gradual process. Perhaps the most obvious clinical indication that the treatment is successful, but one that is hard to appraise, is improvement in muscle function. The child begins to make efforts to walk or to sit up. He seems stronger or more active. Very gradually the deformities of the cartilage-shaft junctions vanish and the bones seem to have acquired an increased degree of rigidity.

If the x-ray appearance is used as a guide to the effectiveness of treatment, it is important to remember that the filling in process of the ends of the bones in extreme rickets requires from two to three months and that the pattern of the lesion will remain visible in the roentgenogram for months after the disease has been completely arrested.

Signs of toxicity of vitamin D

One need not fear that the dosage of vitamin D will be toxic unless renal insufficiency exists or unless the dosage is extremely large. To adults, enormous doses of vitamin D, have been given over long periods without apparent injury. The symptoms of overdosage seem to be nausea, headache, diarrhoea, loss of appetite, frequent micturition and nocturia and lassitude. In the case of the ordinary full term baby more than 3 months of age I regard 50,000 units as lying in the danger zone if given for more than two weeks. For small premature babies I believe that signs of overdosage ought to be watched for if more than 20,000 units is given daily for more than two weeks. Reed assures me that the toxic effects of vitamin D are independent of its action in raising the calcium and inorganic phosphorus concentration in the blood serum. However, in treating rickets with correction of the disturbance of the calcium and phosphorus metabolism as the main objective, the elevation of calcium above 12 mg. per hundred cubic centimeters is an indication of that the dosage has been exceeded and ought to be reduced. With a rise in the serum calcium, a rise in inorganic phosphorus takes place. But this may not reach even the normal level. If the vitamin D therapy is continued, undoubtedly the inorganic phosphorus, as well as the calcium, will become much elevated, and metastatic calcification will occur. In rickets great aid is furnished by the x-ray examination alone. If the x-ray film reveals shadows which indicate healing, the inference can be made that the vitamin has begun to act and that the desired effect of treatment has been gained.

Examination of the urine may reveal evidence of overdosage. Albright and his collaborators noted in their cases of intractable rickets under treatment with enormous doses of vitamin D that the urine was loaded with calcium and contained many calcium casts such as have been observed in cases of hyperparathyroidism and were able to infer from the presence of the calcium and the characteristic casts in the urine that the dosage of vitamin D had reached toxic proportions.

(From *Journ. A. M. A.*, Aug. 3, 1940.)

The Trichinopoly District Medical Association

Trichy Dt. Branch of the Indian Medical Association

Quarterly Statement of Account for the period
1-6-40 to 31-8-40

RECEIPTS			EXPENDITURE		
	Rs.	A. P.		Rs.	A. P.
Cash on hand	14	15 3	Clerk's Salary	54	0 0
Cash with the Bank as			Office Rent for 3 Months	15	0 0
per last statt.	193	3 9	Postage & Telegrams	7	3 3
Fixed deposit with the			Miscellany Ptg. charges	67	13 9
Trinity Bank Ltd.	200	0 0	Printing & Stationery	4	7 6
Members' Subscn.	150	4 0	I. M. A. subscription	9	0 0
Advt. charges recd.	22	15 6	Miscellaneous exps.	6	12 9
Interest on Fixed Deposit	5	0 0	Bank commission on		
Miscellaneous receipt	0	8 0	cheque	0	4 0
			Fixed deposit with the		
			Trinity Bank Ltd.	200	0 0
			Cash on hand	25	15 9
			Cash with the bank	196	5 6
TOTAL	...	586 14 6	TOTAL	...	586 14 6

TRICHINOPOLY, }
1-9-40.

T. N. SUBRAMANIAN,
Hony. Treasurer.

Trichinopoly Municipality

Details of Public Health Activities during July 1940

I. Vital Statistics:

Number of births registered	...	...	...	424
Number of deaths registered	...	...	...	344
Number of deaths from fever	...	...	...	10
Number of deaths from respiratory disease	...	...	...	22
Number of deaths under one year	...	...	...	83
Estimated birth rate	...	...	...	35.6
Estimated death rate per mille	...	...	...	28.9
Number of deaths from child birth	...	...	...	3
No. of deaths from Alimentary disease	...	...	...	49
Infant mortality rate	...	...	...	195.7

II. Infectious diseases:

	Attack.	Death.		Attack.	Death.
Cholera	Nil.	Nil.	Measles	5	Nil.
Smallpox	23	6	Tuberculosis not known		27
Chickenpox	1	Nil.	Pneumonia	Do.	31
Typhoid	10	5	Diphtheria	1	1
No. of anti-cholera inoculation done	...	...		...	Nil.
No. of anti-typhoid inoculation done	...	...		...	827

No. of vaccination done:

Primary Vaccination	...	...	...	891
Re-vaccination	...	...	...	5282
Total	...	...	...	6173

III. Maternity and Child Welfare

(1) No. of cases visited by Woman Medical Officer.	(2) No. of houses visited by Health Visitor.
(a) Labour	1
(b) Ante-natal	4
(c) Post natal	114
(a) Infants	...
(b) Pre-school	...
(c) Ante-natal	...
(d) Post-natal	...
(3) No. of labour cases conducted by Midwives	...

IV. Propaganda.

No. of lectures with magic lantern demonstration	...	58
No. of lectures without magic lantern demonstration	...	21

V. Food adulteration.

No. of samples taken	22	No. of samples reported	
No. prosecuted	6	adulterated	6
Amount of fine imposed	nil	No. convicted	nil.

VI. Meat Inspection:

	No. passed	No. condemned
(1) Sheep	9170	148
(2) Goats	2654	6
(3) Cows and Heifers	417	2
(4) Bulls and Bullocks	133	9
(5) Buffaloes	32	1
(6) No. of dogs caught	221	
(7) No. of dogs destroyed	200	
(8) No. of dogs released	9	

VII. General remarks:

K. P. THOMAS,
Health Officer.

Trichinopoly Municipality

Details of Public Health Activities during August 1940

I. Vital Statistics:

Number of births registered	...	...	...	414
Number of deaths registered	...	...	...	332
Number of deaths from fever	...	...	...	5
Number of deaths from respiratory disease	...	...	...	73
Number of deaths under 1 year	...	...	...	78
Estimated birth rate	...	...	...	34.8
Estimated death rate per mille	...	...	...	27.9
Number of deaths from child birth	...	...	...	8
No. of deaths from Alimentary disease	...	...	...	55
Infant mortality rate	...	...	...	188.4

II. Infectious diseases:

	Attack.	Death.		Attack.	Death.
	Nil	Nil	Measles	Nil	Nil
Cholera	9	2	Tuberculosis	not known	27
Smallpox	2	Nil	Pneumonia	not known	28
Chickenpox	4	2	Diphtheria	2	2
Typhoid	...	...	No. of anti-cholera inoculation done	...	Nil
No. of anti-typhoid inoculation done	...	...	No. of anti-typhoid inoculation done	...	675
No. of vaccination done	...	...	Primary vaccination	...	965
Re-vaccination	...	...	Re-vaccination	...	10566
			Total	...	11531

III. Maternity and Child Welfare:

(1) No. of cases visited by Woman Medical Officer.	(2) No. of houses visited by Health Visitor.
(a) Labour	(a) Infants
(b) Ante-natal	(b) Pre-school
(c) Post-natal	(c) Ante-natal
	(d) Post-natal
(3) No. of labour cases conducted by Midwives...	

IV. Propaganda:

No. of lectures with magic lantern demonstration	...	58
No. of lectures without magic lantern demonstration	...	10

V. Food adulteration:

No. of samples taken	...	...	...	26
No. prosecuted.	...	...	...	9
Amount of fine imposed	...	...	...	Rs. 65
No. of samples reported adulterated	...	...	...	9
No. convicted	...	...	...	6

VI. Meat Inspection

	No. passed	No. condemned
(1) Sheep	8202	103
(2) Goats	3225	8
(3) Cows and Heifers	393	4
(4) Bulls and Bullocks	136	5
(5) Buffaloes	41	1
(6) No. of dogs caught	102	
(7) No. of dogs destroyed	71	
(8) No. of dogs released	15	

VII. General remarks:

K. P. THOMAS,
Health Officer.

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Thio Calcin ... oz. 1.

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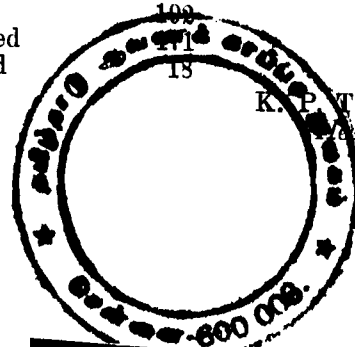
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