

The Antiseptic



A Monthly Medical Journal

Edited by

Rama Rau, M.L.C. & U. Krishna Rau, M.B., B.S.

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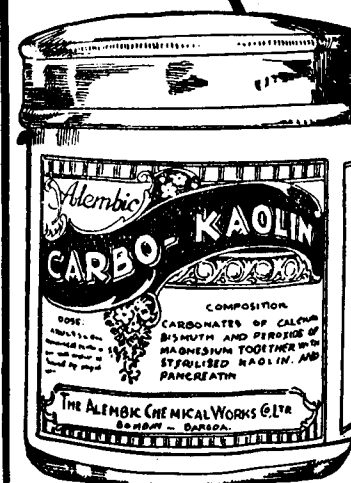
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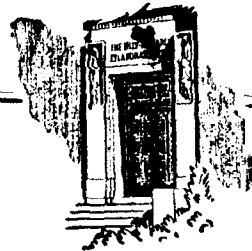
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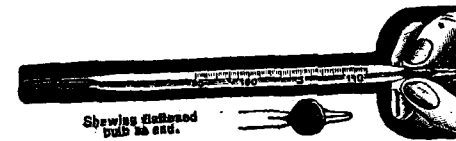
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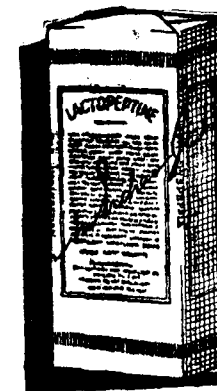
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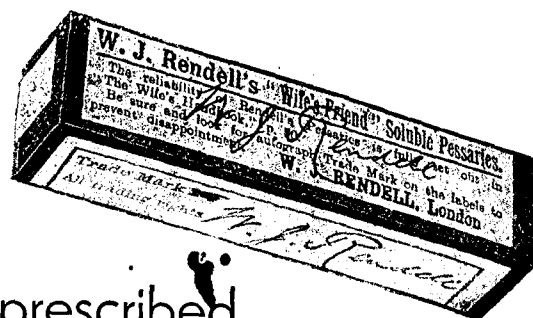
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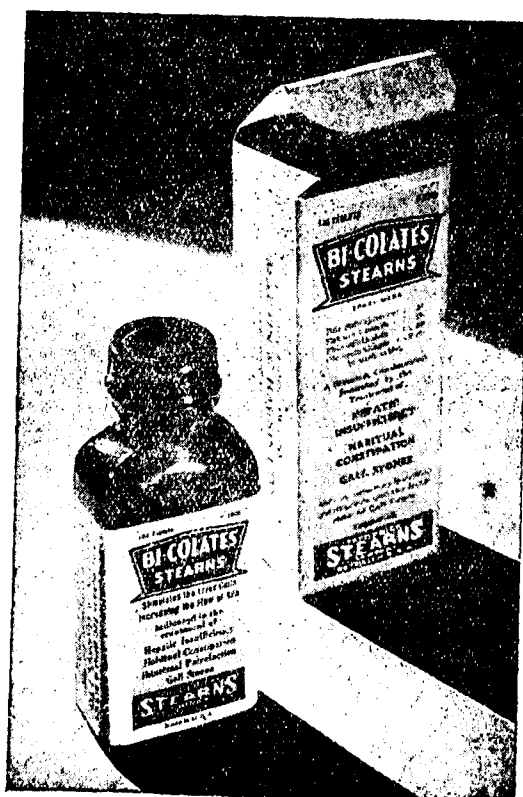
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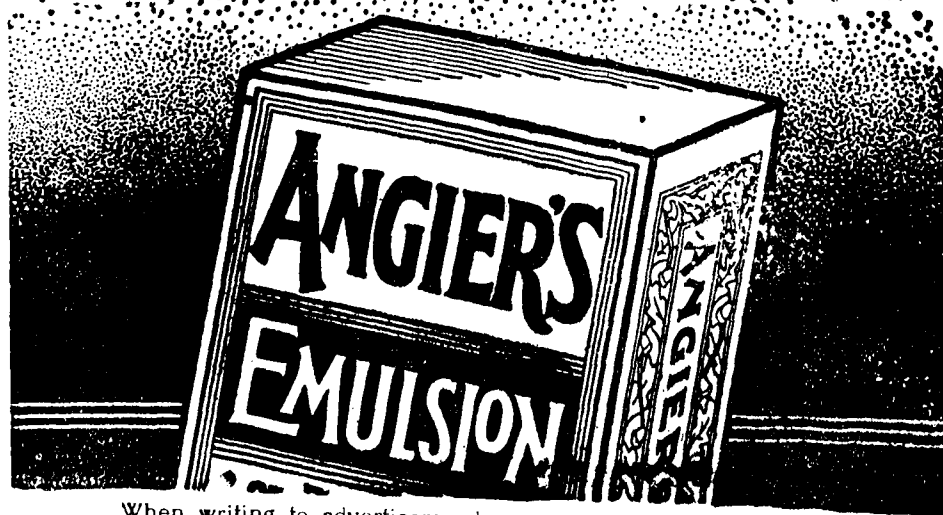
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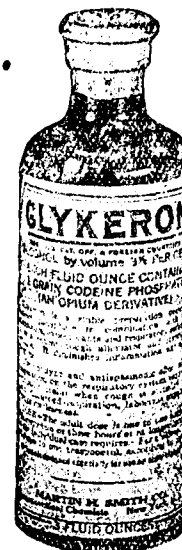
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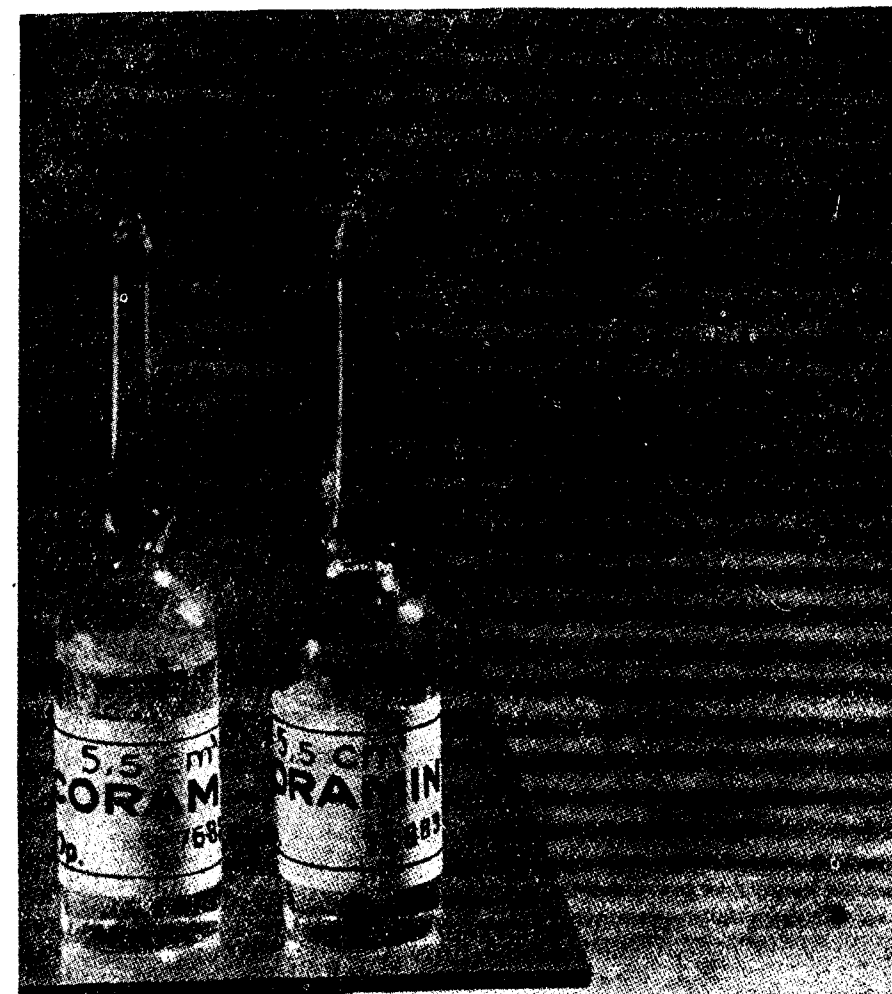
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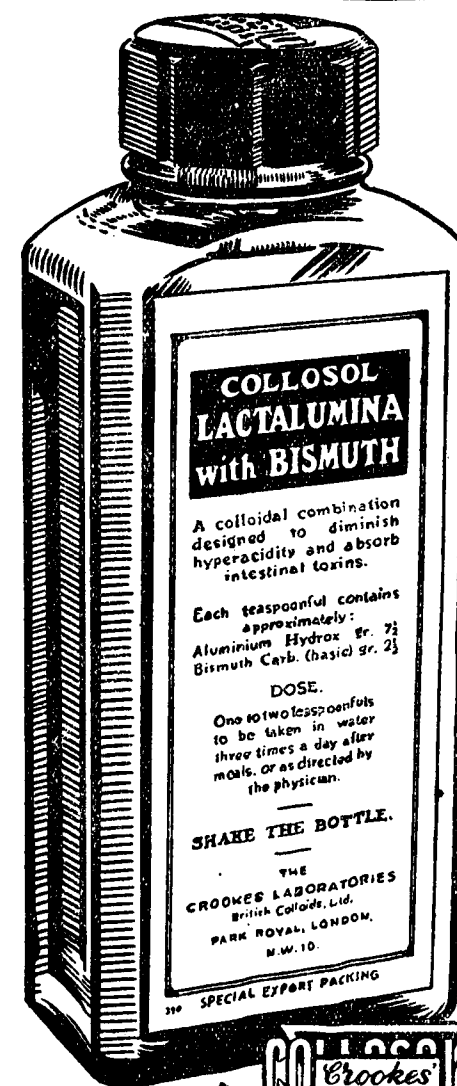
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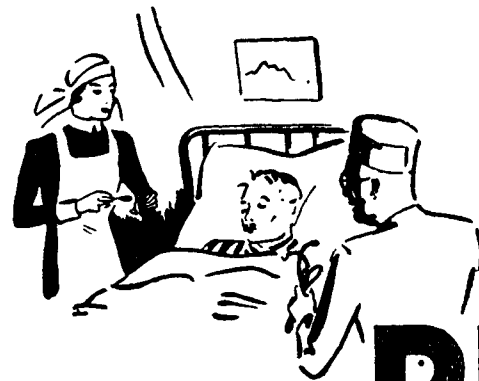
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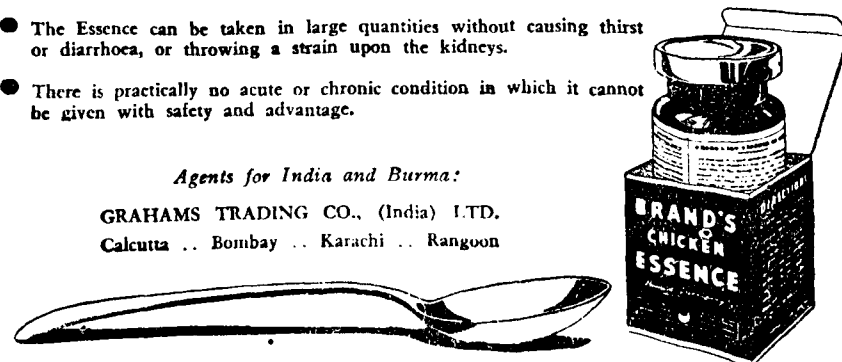
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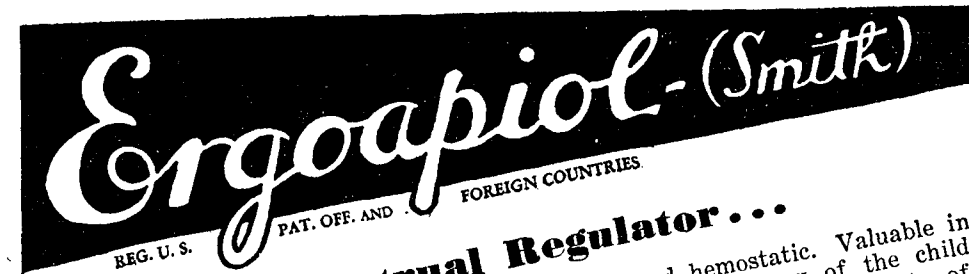
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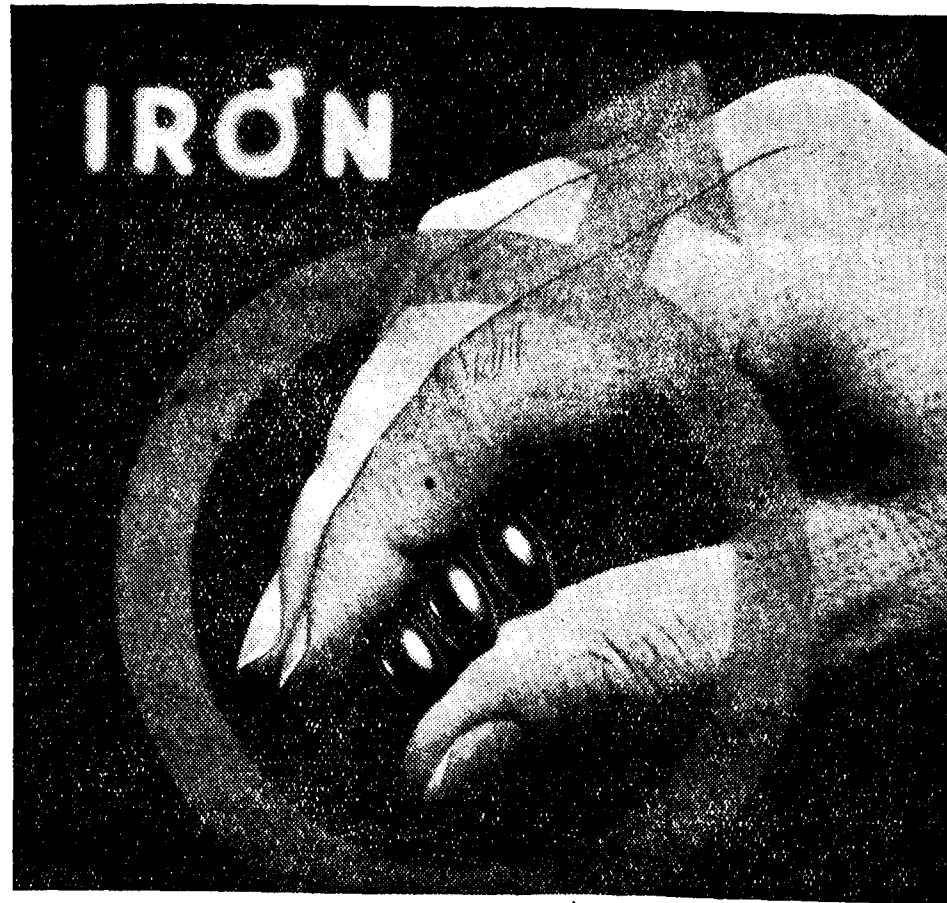
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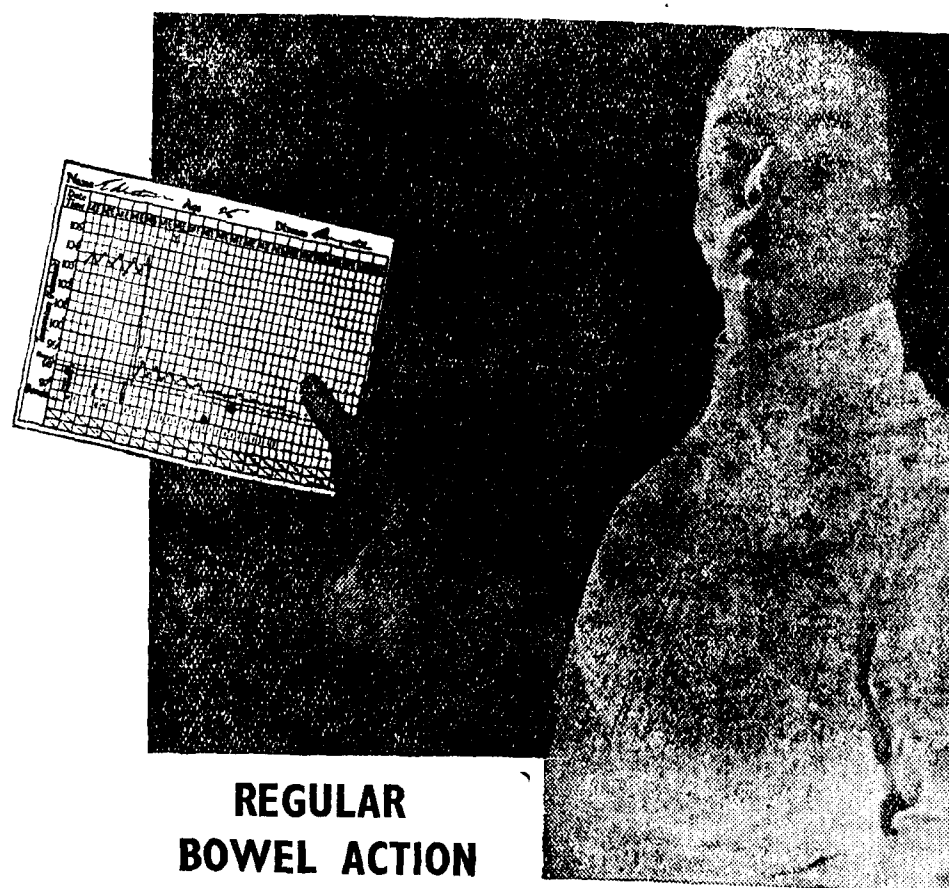
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ORIGINAL ARTICLES

The Present Day Concepts of Epileptic Convulsions And Their Treatment With Snake Venoms*

BY

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LOVATT EVANS (1936) stated that there could be no great theoretical conception in medicine without corresponding underlying physiological principles. The conquest of physiology by chemistry and physics is the aim of the physiologists, and its advent depends upon the success of the efforts to apply to his own subject the findings of chemistry and physics.

Below are discussed the present day conceptions regarding the causation of convulsions. These conceptions have been based on various biochemical and physiological findings and the electrical changes observed in subjects suffering from convulsions.

There is a tendency to look upon epilepsy as a symptom complex or a group of symptoms common to several, rather than a single pathological condition. Convulsions, whose features are indistinguishable from those of epileptic seizures, occur in a number of conditions. In animals, convulsion may be produced by injections of Absinthe or Caffeine. Hypocalcæmia and hypoglycæmia, cerebral œdema or cerebral anæmia are accompanied by generalised convulsions which are epileptiform in character.

Some believe that convulsions are only a 'a release phenomenon' due to the inhibition of the cortical areas which normally exert a controlling influence upon the motor centres, but POLLOCK and DAVIS have shown that tonic or clonic types of convulsions can be induced by means of certain drugs as Picrotoxin in decerebrated animals.

* An address delivered before the British Medical Association, Punjab Branch, Lahore, on 13th Oct. '40, and specially sent to 'The Antiseptic' for publication.

The pathology of idiopathic epilepsy is, however, still obscure. The present concepts of epileptic and other types of convulsions, in addition to ketosis and alkalosis as casual factors, are based mainly on the equilibrium and balance of fluids and salts in the tissue and in the general circulation. Thus, whenever there is a shifting of fluid from the tissues to the general circulation, there is a relative increase of the water and mineral balance of the brain circulation as well. This increase of fluids and mineral ratio in central nervous system acts as a trigger to set up convulsion. Are convulsive seizures a signal indicating gross pathological changes taking place inside the body or are these only a physiological effort on the part of the body to bring back this imbalance to the normal level? Various observations to support these facts are given below. These hypotheses are discussed somewhat in detail and these observations are applied in epileptic cases treated with Snake Venom therapy.

Water and Salt Metabolism.—The blood volume regulation is a question of balance between the fluid within the vessels and the tissues. When conditions arise which tend to lower or raise the volume of blood, counter-forces come into play which restore it to the normal level.

There exists a complete identity between the clinical picture of *Grand Mal* and acute uremic convulsions. In the latter, the attacks are regarded as consequence of oedema of the brain. The brain being enclosed in a hard inelastic capsule, its oedema leads to increased intra-cranial pressure followed by irritation of various centres. Water intoxication is well-known to produce convulsive seizures and even intravenous injections of hypotonic saline solution into animals increase their susceptibility to convulsant poisons. Hypertonic solution on the other hand lowers the intra-cranial pressure and reduces convulsive tendencies. Cerebral oedema, from whatever cause, is likely to result in convulsions. Spinal puncture and diets, poor in water and salt contents, have a favourable effect on these convulsions. FRISCH noticed an increase of body weight and decrease of water and chloride elimination previous to attack of fits of epilepsy. RÖHDE as well as ALLERS noticed even an oliguria before the attacks. This picture is reversed after the convulsions are over. A variation of water content of the serum has also been noticed in active and in inactive periods of epilepsy. MOLLITOR and PICK (1925-26 and 1930), believed that in the presence of excess of water, a water centre in the diencephalon is stimulated resulting in diuresis; if, however, posterior lobe extract of pituitary gland is administered, diuresis is inhibited because of its effect on the centre. MCQUARRIE and PEELER (1931) found that *Grand Mal* seizures could be provoked in children with latent or mild epilepsy by the repeated administration of water and sufficient posterior lobe extract to cause diuresis inhibition. Usually, the administration of water and posterior lobe extract is followed by an evidence of hydremia.

Calcium, Sodium and Potassium Contents of Blood.—Sodium, Potassium and Calcium when in normal proportions in circulation, regulate normal cell functions. CHAMBERLAIN and REZNIKOFF (1925) and HÖBER (1911) noted that Sodium and Potassium Ions had a liquefying effect upon colloidal system. Whereas, Calcium Ions on the contrary, had a consolidating and stabilising effect. It has been shown by BAYLISS, HARVEY and others that Sodium Ion increases the permeability of cell membrane and Calcium

diminishes it. The administration of Calcium diminishes the Sodium in the blood and prevents it from migrating to the inflamed area. Moreover, water follows the direction of the Sodium. Thus, Calcium plays a role in the control of exudative phenomena and perhaps indirectly of water balance.

Local application of Calcium salts in solution, to the motor area of the cerebral cortex results in diminution of electrical excitability as was demonstrated by SABBATINI (1901).

FRISCH and WIENBERGER noticed a considerable lability of Calcium and Potassium contents in the blood of epileptics. The former increase considerably in pre-convulsive periods. Hence not unlike in uræmia, there is also a marked disturbance of mineral metabolism in epilepsy as well. During the quiescent state, there is a continuous and interrupted retention of water and minerals in tissues. Later on, as a physiological attempt on the part of the body to eliminate these retained fluids and minerals, their mobilization takes place. They move from the tissue to the general circulation and consequently, there is a relative increase of pressure in the brain circulation, thus probably acting as a stimulus for convulsions. This may explain as a mechanism of initial stimulus for the initiation of a fit and may be compared with an initial spark as an immediate cause of the explosion of gunpowder. The water and mineral content of blood is reduced again after convulsions are over. Epileptic paroxysms may be occasionally elicited artificially by producing such preconvulsive mobilization and increased elimination by injection of diuretics as Salyrgan or Euphyllin.

Bromides and Luminal.—For the past seventy or eighty years, Bromides have been used extensively in the diseases of the central nervous system, especially epilepsy. Pharmacologically, their action is due solely to the Bromide Ion itself and not, as was once thought, only by removal of Chloride Ions from the body. The action is confined to the central nervous system and can be demonstrated in man and animals by the depression of the reflexes. Further, it can be shown experimentally in animals that the area of response to a strong stimulus, applied directly to the motor cortex, is greatly limited by the administration of Bromides. Similarly, in man it is found that the psychical processes are depressed, though all are not equally affected. Apart from those of the central nervous system, the somatic cells are indifferent to the presence of the Bromide Ions. Moreover, Bromides being salts, their effect is similar to Sodium Chloride in retaining and fixing water in the periphery, mostly in the skin and consequently inhibit its mobilization and accumulation in the general and the brain circulation. Conversely, discontinuance of administration of Bromides is followed by an attack of epilepsy, apparently due to the mobilization of fluids previously fixed in the periphery. *Luminal* has been shown by FRIEDMAN and EPSTEIN to act as an antidiuretic (anti-mobilizational) and hence useful in epilepsy.

Alkalosis and Acidosis.—GEYLIN was the first to connect alkalies with epilepsy. He observed that starvation, diets poor in carbohydrates and rich in ketones reduce the frequency of attacks due to certain changes in acid base equilibrium of blood CO_2 . An increased alkalinity ratio in blood promotes elimination by diuresis and hence leads to mobilization of water and minerals. It is possible that the alkaline shifting, observed in the paroxysmal period, is one of the many, possible factors which may lead to an attack by mobilization of fluids within the organism.

Paroxysmal Cerebral Dysrhythmia.—The brain irritation and other types of nervous irregularities during fits have been demonstrated with the help of Electro-encephalography. The work on Electro-encephalography has been carried in Boston by LENNOX, GIBBS and their colleagues (1936) and in London by COLLA GRAHAM and GREY WALTER (1938). A clear account of their work has been made by DENNY-BROWN. The technique of recording the brain impulses is by fixing small metallic electrodes to the unshaved scalp with celloidin. The inactive electrodes are attached to the ears and their impulses records are compared with those of scalp electrodes. Potentials are magnified and made to operate the ink writing oscillograph. The variations of the brain potentials are thus recorded on the moving paper tape. In epileptics, during *Grand Mal* seizures, the tracings show spikes of short duration.

GIBBS, GIBBS and LENNOX believe that epilepsy is due to the development of *abnormal rhythms within the cerebral cortex* and they suggest that the term "*Paroxysmal cerebral dysrhythmia*" may be employed as expressing in the physiological language the essential nature of the morbid processes. LENNOX and his associates have studied the influence of various drugs upon the encephalogram. They have studied the action of Luminal, Bromide acidosis and alkalosis, etc.

The electro-encephalographic examination of the epileptics showed dilatation of the ventricles of the brain. CAIRNS (1937) cited a case of epilepsy due to cerebral congestion and increased intracranial pressure. GILBERT PHILLIPS (1939) investigated the cortical electrical changes in normal individuals in both awakening and sleeping state and after the effect of drugs modifying the respiration and the cerebral blood supply. Electro-encephalography has been applied to the study of epilepsy, paralysis agitans, schizophrenia, effect of Cardiazol and other convulsants, and for the localization of cerebral scars and intracranial tumors. The electro-grams provide means of determining the intervals between the attacks, the degree of abnormality of cortical activity and consequent susceptibility to further seizures. It also tells us if the patient suffers from *Petit mal*, myoclonic epilepsy, major convulsions or if it is one of the psychical variants only. During such attacks, dysrhythmic waves are detected by electro-grams. If these dysrhythmias can be checked early in its development or kept low, the impending major attacks may be avoided or delayed.

Endocrine Glands.—Endocrine glands, particularly posterior lobe of pituitary gland and ovaries play an important role in the disturbance of water, and mineral metabolism. Water and chlorides are retained in the perimenstruum and eliminated during and after the menstrual periods. It is known whereas, pregnancy has an inhibitory effect. Similarly, BOYDE and WHYTE (1939) have shown that the posterior pituitary lobe promotes retention of water but furthers the elimination of chlorides in frogs. McQUARRIE (1929) reported occurrence of positive water balance and seizures after pituitary injections. Insulin and Cardiazol promote retention of water and hence set up convulsions after administration of large doses.

Disturbances of Respiratory Mechanism.—These lead to disturbance in the water and mineral balance of tissues CO_2 combining power of blood

decreases before and increases after the epileptic attacks. Hyperventilation reduces CO_2 tension of blood and hence leads to mobilization of water and chlorides from tissues and increases diuresis. It has been shown that forced breathing may provoke convulsion in epileptics due probably to reduction of CO_2 tension in blood. Attacks may also be precipitated by inhalation of inert gases as Nitrogen. Repeated inhalation of Oxygen or Oxygen mixed with CO_2 gas often prolongs the interval between the attacks.

Fluctuations in Atmospheric Conditions are also seen to influence epileptic, eclamptic and tetanic convulsions. SMITH (1938) showed that in dogs and rats, sudden and marked drop in barometric pressure was followed by water retention. This water retention or the mobilization which eventually follows may account for the frequency of attacks. During full moon, changes of seasons, as extreme heat and dampy closeness and storms lead to the recurrence of epileptic attacks.

TABLE I.
Table Showing Factors Influencing Convulsions.

	CONDITIONS WHICH MAY.	
	PREVENT SEIZURES.	PRECIPITATE SEIZURES.
Acid-base equilibrium.	Acidosis: by means of fasting, fat diet, ingestion of acids or acid-forming salts	Alkalosis: by means of ingestion of alkalis.
	Breathing high carbon dioxide	Hyperpnea, "blowing off" carbon dioxide.
Chemical constituents	Low chlorides	High chloride
	Calcium High	Calcium low (tetany)
	Sugar normal	Hypoglycaemia
Water balance	Dehydration	Edema (brain)
Sleep	Adequate (8-9 Hrs.)	Inadequate (fatigue)
Emotions	Contentment or satisfaction	Tension, rage, resentment, frustration and boredom.
Oxygen	Rich supply	Poor supply
Permeability of tissues	Decreased	Increased
Intracranial pressure	Decreased	Increased
Intracranial circulation	Unimpaired	Impaired

(J.A.M.A. Vol. 112, page 1250, 1939.)

In the table above, are enumerated various factors which effect convulsive seizures. Therapeutically, there are three measures which are capable of causing immediate attack in epileptics. (1) Injection of diuretics, Salyrgan, Euphyllin and Cardiazol, (2) Production of alkalosis or over-ventilation of lungs, (3) Injection of Adrenalin and manual stimulation of carotid sinus.

Treatment.—From the aetiology and pathology discussed above, it will be seen that the patient should be thoroughly examined in order to find out the underlying causative factors responsible for bringing about fits. In the Calcutta School of Tropical Medicine it was made a routine to examine the stools for protozoa and worms, blood for Wassermann reaction, Walker protein test for finding allergic conditions and sensitivity to protein, blood count and blood chemistry (to estimate Calcium, Phosphorus, Sodium, Sugar, Urea and Creatinin contents, etc.) teeth, ear, nose, and throat examination for any deep-seated infection, skiagram of skull to study the condition of pituitary fossa, etc.

Epilepsy in the great majority of cases is an incurable affection. Therefore the subject needs a strong and firm but kind treatment. He should be allowed a daily pursuit to keep his mind and body busy. Outdoor exercises and manual training suited to his constitution should be encouraged as in healthy subjects, since the life of the patient should be as normal as possible. Every patient or his elderly relative is instructed to keep a diary in which the date and duration of each attack is noted.

DRUGS.—For the present, the most satisfactory aid for the epileptics is the treatment designed to raise the seizure threshold without appreciably depressing somatic and mental functions. Various drugs have been used with different points of view. Some of these were dubiously effective, a few palliative but none so far curative. The latter is due to the fact that we have to look upon epilepsy, like asthma, only as a symptom complex. The convulsions occurring due to various pathological and physical conditions have to be properly investigated and controlled before any definite relief is expected. So far, greatest reliance has been placed only on Bromides, Belladonna and Phenobarbital. Some of the important remedies are briefly reviewed here, before discussing the use of recent anti-convulsants like Diphenyl hydantoin and Snake Venom.

Bromides :—It has been previously mentioned that Bromides have a salt-like action and fix the water locally in the tissues and thus reduce fluid contents of the blood. This drug was apparently first recommended by SIR CHARLES LOCOCK (1857) and since then, it has been extensively used. It acts as a motor depressant. Its Sodium salt is probably less irritant than the Potassium salt. It is best given daily in single dose—preferably in milk—and about 4 to 6 hours before the attack is expected. Addition of Calcium, Belladonna, Borax and Hydrobromic Acid is warmly recommended. Others believe that best results are noted by mixing all the three Bromides. If Bromides are not tolerated, reduce fats in diet. The absorption of Calcium is favoured by administering cod liver oil with it.

Calcium :—Calcium helps in the excretion of fluids from the body and reduces the muscular irritability and the spasmophilic tendency. It has an inhibitory influence not only on the skeletal muscles and on the voluntary nervous system but also on the unstripped muscles of the vegetative nervous system as well. It is often recommended as a good adjuvant to Bromides. It is particularly useful in children.

On the other hand, it is antagonistic to excitatory effect of Sodium and Potassium. A very satisfactory combination of Calcium and Bromides has been developed in the form of Calcium-bromine Galacto-gluconate (Calcibronate-Sandoz). The formula of this preparation is $(C_{12}H_{21}O_{12})_2Ca$.

$CaBr_2 \cdot 6H_2O$. It is highly soluble in water and has an agreeable taste. Its Bromine content is 15.5% and Calcium content 7.45%, the Bromine Calcium ratio being 2 : 1.

Belladonna :—Belladonna or *deadly night shade* has been described by PARACELASUS as a mania-producing plant. It influences the vegetative nervous system and organs of smooth musculature whose motility and tonus it weakens. Atropine is regarded by TANIUCHI and KUYOHARA (1928) as fatigue-producing poison for the sympathetic nerve endings. Belladonna is indicated in the disorders related to the brain as epilepsy, hallucination, acute mania, Parkinson Syndrome (BALDAUF 1938), cerebral irritation and convulsions, etc. The natural Belladonna alkaloidal complex which rotates the polarised light to the left is found to be 200 times more active on the vagus nerve endings than the Dextro rotatory alkaloids. The Levorotary alkaloids of Belladonna leaves are, therefore, more useful than Atropine. **Bellafoline** (Sandoz) acts as a specific sedative to the parasympathetic system. This preparation acts as an anti-spasmodic, anti-convulsive and sedative. If Belladonna and Luminal are combined together (*Belladenal-Sandoz*), these drugs have a synergistic action on one another (*See below*). Belladonna is found to be particularly sedative in *Petit-mal*.

Phenobarbital (Luminal and Gardinal) :—The use of this drug marks the greatest advance in the treatment of epilepsy in recent years. It may be given in as big doses as 2-5 grains. It was first introduced in medicine by HAUPTMANN in 1912. Phenobarbital is particularly successful in controlling the convulsions of unknown origin. Beginning with a small dose, it is gradually increased for 7-10 days, during the periods the attacks are likely and then should be stopped as soon as possible. The only toxic effects noticed after prolonged use are an irritating morbilliform rash. The drug is non-habit forming and may be continued for years. Its Sodium salts may be injected intravenously in large doses (0.3 gm.) particularly in cases of *status epilepticus*. It can also be combined safely with Belladonna, Bromides, Chloral and Cannabis Indica.

JORES and GOYERT (1936) reported that disturbances in the vegetative nervous system invariably involve parasympathetic as well as sympathetic over stimulation. Simultaneous administration of vagus inhibitor as Belladonna and the sympathetic inhibitor as Gynergin (Ergotamine Tartrate) does not diminish the specific effects of these two drugs. Furthermore, the combination of the brain stem sedative Phenobarbital with the above mentioned two drugs will be useful both for the central and peripheral excitation in the case of general nerve imbalance, which has been named as *Neuro-autonomic dystonia* (*vide* Table 2).

TABLE II.

Table Showing the Action of Drugs in Neuro-autonomic Dystonia.

NERVOUS SYSTEM.	ACTION OF DRUGS.	
	STIMULANT.	INHIBITOR.
Sympathetic nerves	Adrenalin (Lævo)	Ergotamine tartrate (Gynergin)
Parasympathetic nerves	Choline; Eserine	Belladonna alkaloids (Lævo) (Bellafolin)
Brain Stem	Caffeine	Phenobarbital. Bellergal.

The combination of these three active neutropic sedative drugs have been introduced in the market under the name of *Bellergal* (Sandoz). This combination has already been reported useful in vegetative neuroses, severe migraine, night sweats of tubercular patients and in dysmenorrhoea and *Petit-mal*, etc. The above combination should be useful in controlling epileptic convulsions. WATTS and SCHWARZ (1937) reported marked improvement in 19% of his patients and moderate improvements in 43% of his cases of epilepsy, who proved refractive to the routine treatment.

Borates :—Borates are used in the form of Sodium Biborate (Borax) in doses of 10-15 grains twice or thrice daily. It is valuable in major nocturnal epilepsy. Sodium Boratortartrate is also recommended, but with no special benefit over Borates. VERJAAL (1939) recommended combined powder of Sodium Borate 0.5 gm., Boric Acid 0.5 gm., Phenobarbital 0.075 gm., given three times daily. The patients treated with this combination were free from attacks for thirteen months, while with Phenobarbital alone, the fits could not be under control in these patients. The undesirable complications mentioned are exanthem, gastro-intestinal disturbances, rise of temperature, albuminurea, emaciation, and alopecia areata. Boron poisoning can be detected by the excessive presence of Boron in the urine.

OTHER DRUGS :—*Thyroid extract*, *Pilocarpine* and *Nitroglycerine* are also recommended. The latter is useful in *Petit-mal* and should be given in 2 to 5 drops doses and increased till the physiological affects are produced. *Adrenalin* injections are said to precipitate convulsion and hence these have been used as a diagnostic agent in epilepsy. It is suggested that the denervation of the adrenal gland (CRILE 1934) may be useful in epileptic fits caused by the irritation of sympathetic nerves.

Diet.—The diets should be simple, dry, and not over-loading. High fat content in diets with excess of cream, butter, bacon, and oils, etc., should be encouraged to the limit of the patient's comfort. Soups, stews and beverages with meals should be prohibited. Of the solid fruits, banana may only be allowed. Fluids should be reduced as far as possible and Sodium salts cut down to the minimum. Small doses of thyroid glands should be continued for over a year. WILDER (1921) reported beneficial effects by ketogenic diets. Ketosis fixes the water in the tissues and probably depresses the activity of the motor cortex. PETERMAN (1927) showed that starvation caused cessation of attacks. The attacks recur again when food is given. During starvation, there is acidosis and increase of ketogenic bodies in the blood. The increase of ketones in the blood is detected by an increase of Acetone in the breath and by the presence of Acetone and Acetoacetic Acid in the urine. The ketogenic diet is rich in fats and low in carbohydrates and protein adjusted according to the individual.

KETOGENIC DIET FORMULA :—*Breakfast* contains fruits 60 gm. (10% carbohydrate contents), bacon 20 gm., vegetables 25 gm. (20% carbohydrate contents), salad 44 gm., butter 44 gm., steak and jelly 40 gm.

Supper :—Vegetables 25 gm., (3% Carbohydrates), salads 25 gm., butter 16 gm., and ice cream. If convulsions persist, reduce carbohydrates to 10 gm., and push in fat to the limit of tolerance and when convulsions are reduced, then increase carbohydrates again gradually. The total allowance of diet should not exceed 1800 to 2000 calories. The basal metabolic

requirements of the patient is calculated according to the Du Bois tables and addition of 20 to 30% of calories allowed for energy exchange.

Anti-convulsant Measures.—It has been stated before that so far no definite causation of the symptom-complex of epileptic seizures is known. Various drugs causing convulsions by acting at different levels of the central nervous system and the drugs which counteract the convulsions have been discussed in the tables III and IV.

TABLE III.
Table Showing Convulsant Drugs and Their Seat of Action.

NO.	DRUGS.	SEAT OF ACTION.	TYPE OF ACTION.
1	Absinth	Cerebral Cortex	Epileptic in type, involving limited group of muscles.
2	Picrotoxin	Medullary centres	Asymmetrical, irregular and clonic.
3	Camphor		
4	Triphenyl Phosphite		
5	Asphyxia	Medullary centres, Mid-brain and Spinal Cord	Irregular and clonic due to stimulation of respiratory centres; Antidotes, Chloral and Barbiturates.
6	Cardiazol		
7	Coramine		
8	Icoral		
9	Strychnine	Spinal Cord.	Symmetrical and well developed convulsions.
10	Caffeine		
11	Sodium 1.3 Dimethyl Butyl Ethyl Barbiturate		
12	Aconitine		
13	Physostigmine	Anterior Cornua of Spinal Cord.	Violent and tonic type of convulsions.
14	Veratrine	Muscles directly	Tonic in type.

TABLE IV.
Table Showing Anti-Convulsant Drugs and Their Mode of Action.

NO.	DRUGS.	SEAT OF ACTION.	TYPE OF ACTION.
1	Bulbo capnine	Central Nervous System	Plastic rigidity, stimulation of simultaneous, antagonistic group of muscles. Indicated in chorea, Parkinsonism and vertigo.
2	Snake venom	Central and Biochemical changes in tissues.	Epilepsy, chorea, Parkinsonism.
3	Magnesium Sodium Amytal	Central	Paralysis of central nervous system, action on anterior horn cells of spinal cord like curara.
4	Scopolamine	Spinal Motor Neurones	Parkinsonism, epilepsy and chorea.
5	Banisterine		
6	Methylene blue		
7	Phenobarbital		
8	Diphenyl hydantoin		

In the cases of epilepsy, the causation of convulsions appears to be based on the mineral metabolism and water mobilization into the general circulation. Whenever this balance is disturbed, convulsions occur. PUTNAM and MERRIT in America (1937) have been working on the basis of anti-convulsant drugs, particularly in connection with their effect on the nervous excitability and fluid contents of the brain. An effort has been made by us to explain as to how the apparent beneficial results are obtained with Snake-Venoms in epilepsy by fitting in, as far as possible, the theory of water mobilization and other physiological and biochemical factors alleged to cause convulsions. An effort has been made by us to explain why improvement occurs in epileptic cases with Snake-Venom therapy on the above bases. We have discussed the physiological and biochemical changes noted in our experimental animals after injections of venom and have tried to show how these observations can be applied against water mobilization and other changes seen in convulsions. Now-a-days, Insulin or Cardiazol (Cylohexyl ethyltriazol) is used to produce therapeutic convulsions. MEDUNA originally thought that there was an antagonism between schizophrenia and epilepsy and on this basis, he started Cardiazol and Insulin convulsion therapy. On the other hand, ESSER (1938) has shown that catatonic schizophrenia and epilepsy can occur together in the same patient.

1. *Sodium Diphenyl Hydantionate*:—Systematic research for anti-convulsants by experimental methods was started by PUTNAM and MERRIT (1937) at the Neurological unit in America. So far, the Diphenyl-hydantoin has been reported to be more effective than Phenobarbital and is without apparent sporadic effects. Sodium-diphenylhydantionate proved to be especially potent anti-convulsant. It is a derivative of glycolyl urea and exists as an odourless white powder with a bitter taste and is fairly soluble in water. It has been tried by them in 200 epileptics. Of these, 58% had complete relief in *Grand-mal* and 27% had a marked reduction. In *Petit-mal* (74 cases), there was complete relief in 35% and marked reduction in fits in 48% in doses 0.2 to 0.6 gm., daily or in 0.1 gm., three times a day, given before meals in capsules. It has been put in the market under the name of *Dilantine-Sodium* (Sodium 5-5, diphenyl hydantionate) in 0.1 gm. capsules, (P. D. & Co.) and also as *Apanutin*. This stuff is also being tried by the authors and its results will be reported in due course. DENNIS WILLIAM (1939) has reported a marked relief in his cases. Its advantage over Phenobarbital is that it does not produce depression noted with later drug after prolonged use.

2. *Dyes*:—COBB, COHEN and NEY (1935) studied the relationship between the cerebral anoxia and certain convulsive phenomena. They used intraperitoneal injections of *neutral red* which is taken up by the spinal motor neurones as an indicator of increased activity provoked by convulsant drugs. Intraperitoneal injections of neutral red has inhibiting effect on the injections of convulsants as Triphenyl phosphite and Camphor. *Brilliant vital red* is more potent than neutral red and is nontoxic. Two cases of epilepsy were treated by intravenous injections of (1% solution) of Vital red. The initial dose was 10 c.c. and subsequent doses were 20 to 40 c.c. given two to four times a week. Urine was examined for toxæmia (albumin, red cells and granular casts). After these injections, sclera, tears, stools and dandruff become red. The skin resumes normal colour within two

months after the cessation of the treatment. Each patient received about 1,500 to 2,500 c.c. of this solution in two months. Their anti-convulsant action is more pronounced in *Petit-mal*. The patients with this treatment remained free for two years. The mechanism of anti-convulsant action is explained in two ways:—anti-convulsants such as *Methylene Blue* and *Brilliant Red* increase the respiratory interchange of cerebral neurones. The oxidative effect of these are responsible for reduction of seizures. Recent study on the permeability of endothelium in dogs has shown that intravenous injections of Brilliant Red definitely reduce the amount of certain substances entering the cerebrospinal fluid. Hence these dyes, by altering the permeability of endothelium act as barrier to convulsions.

3. *Snake-venom*:—Snake-venoms have been employed in the treatment of epilepsy on account of the alleged freedom from attacks of epileptics after being bitten by certain types of snakes. FINKLEMAN (1937) stated that SPANGLER of Philippines (1928) claimed to have cured epilepsy by injections of 1/400 (0.13 mg.) of Rattle-snake venom hypodermically. It has been believed that the snake venom acts as a protein desensitiser on the assumption that most of the epileptic seizures are anaphylactic in nature. The improvement in such cases was indicated by the reduction of the number of the eosinophils. Moccasin venom (1-3000) was used in 0.2 c.c. (0.1 mg.) doses intradermally thrice weekly and increased by 0.2 c.c. till 1 c.c. was reached. BURNETT has used Puff-adder venom for the same purpose. FITS SIMONS in South Africa treated epilepsy with his preparation 'Venene' which is said to be a mixture of various snake-venoms.

MACHT (1938) has done interesting work on the anti-convulsant properties of Cobra-venom and believes its utility in chorea, angina pectoris and epilepsy. BARBER and LOURENDEAU (1939) have shown immediate sedative effect of Cobra-venom in essential epilepsy. CHOPRA and his associates have been testing the therapeutic properties of snake venoms in the Calcutta School of Tropical Medicine since 1932. CHOPRA and CHOWHAN (1935) drew attention towards the use of Russell-viper venom in epilepsy. A number of persons suffering from epilepsy have been treated by these authors in the Carmichael Hospital for Tropical Diseases and in the Out-Patient Department of the Calcutta School of Tropical Medicine. These cases were treated with Russell-viper venom alone and later on with Russell-viper venom mixed with Cobra venom. A reduction in the intensity and the number of attacks has been noted in the cases treated with snake venoms.

So far, no satisfactory explanation has been forthcoming with regard to the action of snake venoms in epilepsy. We have discussed briefly various physiological and biochemical changes noticed in epilepsy and other types of convulsions. CHOPRA and CHOWHAN (1934), while studying the actions of the Russell-viper venom on the circulatory system in cats, observed that after injections of this venom, there was an excessive leakage of fluids through capillary walls. There was also an increase of the R. B. C. counts, not due to induced polycythemia, but due to the altered permeability of endothelial layer of blood vessels and subsequent leakage of blood fluids and concentration of blood corpuscles. CHOPRA, MOOKERJI and CHOWHAN (1937), while studying the physical changes in the blood *in vivo*, after injections of therapeutic doses of Cobra venom in monkeys, noticed that there was a tendency of fall in the surface tension of blood. There was also an

increased relative viscosity of the blood plasma as compared to water and persisted over 24 hours. With fairly high doses of venom, there was an evidence of fall in the pH value of blood within 2 hours and then return to the normal. The effects of the second or higher dose of venom in such cases was to bring about increase of pH value, if it was already below normal or to decrease the value if it was above normal at that time. VELLARD and MIGUELOTE-VIANNA (1936) have shown that the alkali reserve of the blood falls after the injection of venoms of *Nia Tripudians* and of vipers like *Crotalus Terrificus* and *Lachesis Atrox* in dogs. The alteration of pH value of blood probably owes its origin to the alteration in the CO_2 concentration in pulmonary circulation by the actions of venom on the respiratory activity and possibly due to disturbance of carbonate bicarbonate contents of blood, though all these values are small but appear to have important bearing in the case of convulsions. (1) In the case of epilepsy we have discussed above that there is a disturbance of water balance and tendency of fluids to move towards the blood circulation (water mobilization). The reverse movement of fluids towards the tissues is seen with Viper venom. (2) A decrease of CO_2 tension and an increase of bicarbonate contents lead to causation of fits while, after injections of venom, there is an increase of CO_2 and decrease of bicarbonate contents. (3) Electro encephalograms show an irritability of higher centres in epileptics, while Cobra venom depresses the higher centres and has recently been shown to act as a nervine sedative by CHOPRA and CHOWHAN (1939) and as an anti-convulsant by MACHT (1938). All these physiological and experimental observations show that there is an apparent rationale behind the venom therapy in various types of convulsions.

Some work on the biochemical changes in the blood of anthropoid and other mammals, after therapeutic doses of Cobra venom and Russell venom is being done to see if any change similar to the hypotheses discussed above are brought about after therapeutic injection of venom. In the meanwhile, patients suffering from epilepsy and other types of convulsions are being treated with venom injections by the present authors. Of the 30 cases treated with venom, a few typical ones are selected and are discussed. These will be published in a separate paper. The patients were given injections of Cobra and Russell venom intramuscularly twice a week in ascending doses. The dose of Russell viper venom was equal or double that of Cobra venom. For routine treatment, see Appendix, CHOWHAN (1940). In this way, usually 10 to 15 injections of Cobra and Russell venom were administered; where the benefit was observed, the injections were continued for several months, with a period of rest for a week now and then. The patients were also given a sedative like Potassium Bromide with or without whole extract of *Rauwolfia Serpentina*. CHOPRA, GUPTA and MUKERJI (1933) have reported that the latter drug acts as a very good nervine sedative. It was noted that after several injections of venom, the attacks were gradually reduced in number and subsequently, the attacks became milder in intensity and occurred at longer intervals. The epileptics were usually discharged from hospital if their attacks were reduced to one or two in a month and advised to attend the Out-Patients' Departments, where the injections were continued and they were watched for as long as possible. Even after a prolonged course of treatment, there is still recurrence of mild epileptic form tremors or outbursts but the latter are only a poor copy of real pucca epileptic attacks

and should be ignored since, in chronic epileptics, the central nervous system becomes so irritable to nerve stimuli that after the major epilepsy symptoms have been brought under control, still the nervous system remains hypersensitive to extraordinary impulses brought about by excitement, anger, emotions, etc., but these do not lead to the typical convulsive syndrome and hence should be left alone and ignored.

Discussion and Conclusion.—The present hypotheses on the causation of convulsions are discussed by EUGENE FOLDES (1933) and a few of these points have been discussed briefly in the body of this paper. The main causation of the convulsions is based on the alteration of mineral and water balance between the general circulation and the tissues. Water mobilization and its retention in the general circulation lead to increase of tension and oedema of the brain matter. The other features for the causation of cerebral convulsions are the fluctuation of the CO_2 tensions, carbonate and bi-carbonate ratio in the blood. All these features render the higher centres extremely sensitive to nerve stimuli and act as trigger to the onset of convulsions. Observations have been made that whenever there is increase of fluids and salts, and a decrease of Calcium and Phosphorus in the general circulation, convulsive seizures are anticipated. Again, increase of alkali reserves, decrease of CO_2 tensions and reduction of viscosity of blood lead to convulsions. All these features are reversed after the occurrence of convulsions. In the pharmacological experiments on animals, CHOPRA and CHOWHAN noticed that after the injection of Cobra and Russell venom, in cats and other animals, there was a marked leakage of plasma from the capillary walls, increased relative viscosity of blood, increase of CO_2 tensions of blood and a decrease of its surface tensions. The neurotoxin principle of venom has a definite nervine sedative effect and recently Cobra venom has been shown to have marked anti-convulsant properties.

It has also been shown that Cobra venom not only supplements but may even act as choline esterase enzyme. It is not well known that the enzyme choline esterase counteracts the actions of acetylcholine, the chemical factor which acts as a transmitter of the nerve impulses to and from the nerve terminals. Cobra venom may be acting by the damping of the extraordinary centrifugal nervous impulses emanating from brain in epileptic cases.

Marked relief was noticed in idiopathic cases of epilepsy after a few doses of Cobra and Russell venom injections, the attacks were reduced in frequency and they became much milder in intensity after prolonged venom therapy. Whether venoms act like ordinary non-specific proteins or act by physiologically altering various biochemical factors has still to be established. There appears, however, a clear rationale at the back of the venom therapy in epilepsy. Work is being done to estimate all these biochemical changes in epileptic cases but for the present the data at our disposal is too meagre to be presented.

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APPENDIX

Routine Treatment of Epilepsy with Venoms.—The author (1940) has published the routine treatment of epilepsy with snake venom as carried out in the School of Tropical Medicine, Calcutta, Out-Patients' Department. It is reported again for the information of the readers. (1) Cobra venom 1 to 10 mouse units. (2) Russell-viper venom 1 to 20 mouse units. (3) Extract Rauwolfia Serpentina 10 to 20 drops in water twice daily.

Treatment.—Injections of Cobra and Russell viper venom, mixed together in doses as mentioned below, are given intramuscularly.

Dose No. 1	Cobra-venom	1 m.u.	and Russell-venom	2 m.u.
„ No. 2	„	2 m.u.	„	4 m.u.
„ No. 3	„	3 m.u.	„	6 m.u.

The injections are continued till 10 such doses are administered. The patient is then given rest for one month before repeating the above course once again. The dose of Russell venom may be the same as that of Cobra venom; such—3 to 4 courses, later on—one course every six months. Record of the fits, the dates of occurrence and duration of fit to be recorded.

Extract Rauwolfia Serpentina.—10 to 30 drops to be given in an ounce of water at bed time and early morning or when the fits are anticipated. It is a useful nervine sedative and acts as a mild hypnotic and lowers the blood pressure. The doses of Rauwolfia and venom are regulated according to the local and general reaction and according to the response of the patient.

Other Drugs.—Bromides, Luminal and Dilanten may be given in the beginning to control the fits, and the latter drug if fits are very frequent and severe in type. Alternating courses of Dilanten and venoms probably may be more useful than giving either of the drugs alone.

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A Few Observations on the Causation of Goitre*

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DURING the last few years, I came across more cases of goitre than in previous years, and decided to take short notes about each case. That the cases should be coming from the districts situated in the Himalayan Terai where it is so common would not have been surprising. But that the cases should belong to Lucknow, who have never once visited the endemic area and that their number should obviously be on the increase could not fail to attract attention. I have strictly confined my observation to cases who have never visited the endemic places. The cases coming from the endemic area (Terai districts—Gonda, Bahraich, Gorakhpur) now staying or living in Lucknow have not been recorded. The following 59 cases serially observed are all residents of Lucknow except one which belongs to Moradabad. I have confined myself to my own observations avoiding academic discussion.

It may be noted that in private practice, it is difficult to carry on extensive observations. It is also impossible to follow up cases as the frequent change of physician is a common practice here. It has also been almost impossible to persuade patients to undergo prolonged treatment for a painless affair, or remain under observation for any great length of time. My object in writing these lines is to draw to this disease the attention of those who are in a position to make correct observations and carry on research work.

From the study of these cases and the attached statements, the following points appear striking :—

- (1) The greatest incidence occurs between the ages of 11 to 20. (47 out of 59, *i.e.*, 79.66%).
- (2) Majority of cases are females. (32 out of 59, *i.e.*, 54.24%).
- (3) In a large percentage of cases, the goitre made its appearance at the time of puberty, with which it is obviously connected. (40 out of 59, *i.e.*, 67.8%).
- (4) Nearly 6½% of cases occurred at the time of menopause with which they had an intimate connection.
- (5) Nearly 17% of cases were caused by shock or some nervous strain.

The cases observed belonged without exception to poor families, which live in a state of great nervous tension on account of economic difficulties. Not a single case was found to occur in well-to-do families. The general health of these patients was fairly well maintained. The one noteworthy point which struck me was that a fairly large majority had highly strung nervous system complaining of palpitation, irritability, nervousness, etc. This was especially more marked in the 10 cases in which some shock or nervous strain had caused the enlargement of the thyroid gland. The pulse rate on the average was 86 per minute. In only 14 cases it was 100 or

* Specially contributed to 'The Antiseptic'.

above 100. The blood pressure was noted only in 4 cases and was found to be low. The eyes were not bulging or prominent but were found to be normal, in all cases. Only two cases complained of some difficulty in deglutition. An attack of cold, it was stated by some patients, caused a temporary increase in the size in some causing some discomfort in swallowing. It was observed that generally the lobes were more involved than the body of the gland, and mostly the right side was more enlarged than the left. In 14 cases the enlargement on the right side was specially marked. In one case alone, the right lobe appeared to be cystic to the fingers.

The enlargement in those cases which coincided with puberty or menopause was gradual and moderate and had become stationary. No increase in size was noted after the first year of its appearance. In the 10 cases which were caused by shock or strain, the enlargement was sudden and more marked at the beginning and subsequently, a decrease in size was noticed. In none of these 59 cases, the size of the Goitre attained the large size sometimes to be seen in endemic areas. The greatest enlargement observed was in a case in which the right lobe had attained the size of a large apple.

A glance at the statement No. I, will show that the causes can be worked out as below, showing important factors which appear to be intimately connected with the causation of goitre.

Causative Factor	No. of Cases	Percentage
Puberty ...	40	67.8%
Menopause ...	4	6.78
Shock or Nervous Strain ...	10	16.95
Heredity ...	3	5.10
No special cause discovered ...	2	3.37
	59	100.

The incidence of goitre at the time of puberty and menopause cannot be mere coincidence when it has been observed in such a large percentage of cases. 10 cases gave a definite history of mental shock or extraordinary and severe nervous strain, which was soon followed by the appearance of goitre. In three cases which apparently were due to hereditary causes the mother and mother's mother had large goitres, and their children developed goitre in their very childhood. In two cases no cause could be discovered.

In all these cases excepting two, the causes cannot be dietetic or environmental and no micro-organisms to my mind, can be accused to be responsible when others living in similar conditions did not suffer from this trouble. The intimate relation between the appearance of goitre and puberty and menopause shows that the cause is hormonal. The readjustment of the functions and inter-action of the ductless glands occurring at these periods in life probably occur on abnormal lines leading to the enlargement of the thyroid gland. The absence of any symptoms and the stationary nature of the enlargement lends support to this view. In other words, this enlargement is in some way related to the functional, structural, and hormonal changes that take place at the time of adolescence and menopause. Ten cases having no connection with puberty or menopause can be

• **Statement of Cases Due to Nervous Causes—(Contd.)**

No.	CASE.	HISTORY.	MENTAL STATE.
4	M M 20	A week ago, lost all his property. Very unhappy and depressed. Could not sleep or eat or understand when spoken to for nearly 3 days. Found his neck swollen.	Still depressed and unhappy.
5	M M 13	An intelligent boy. A month ago, fell into bad society. Received shock and fright several times. In spite of punishment at home, could not break away. Was brought for enlarged neck.	Depressed and nervous as if frightened.
6	M M C 8	Six days ago, got frightened and cried and wept for 3 hours. Nothing could console him. Next morning neck found enlarged.	Nervous and shy.
7	M F 16	Attained puberty 3 or 4 years ago. Married after one month of settlement. The month was devoted to arrangement and merriment. Her neck swollen. Great anxiety and trouble due to this defect. Neck more swollen. Subsided after marriage. Still a good sized goitre.	Excitable and hysterical.
8	H F 19	Had Two children 1½ years and 4 months old. Both fell ill and both died at the same time, 1½ months' ago. Pront of the neck became enlarged.	Depressed and morose.
9	M M 28	Death of father leads to poverty. Had to give up studies. Became neurasthenic. During the last 6 months, fell into bad society which caused sexual excitement which was not satisfied. Marriage constantly postponed on account of poverty. Attempted to repair his fortune on the race-course. Lost all. Ran into debt. During the last 5 months, his Sherwanis became useless as their collar could not be buttoned.	Neurasthenic.
10	H F 40	She had a child 15 or 16 years ago. Soon after the birth of the child, her husband died suddenly. She was devotedly attached to him. His death involved her in financial ruin. She was extremely unhappy and worried. At this time, her neck became enlarged.	Depressed and melancholy.

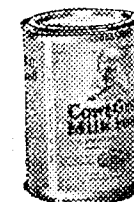
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It is well known, that the wisdom of ancient India has been handed down in the four Vedas, the last of which, the Atharva Veda consists of the facts of the natural sciences, determined at the time by empirical methods. A section of it, Ayurveda treats the science of Life (*i.e.*), the science we call Biology to-day.

Even at that time, (*i.e.*), 3,000 B. C., tuberculosis received detailed consideration in the books dealing with diseases. Pharmacologists, internists, as also surgeons occupied themselves with this king of diseases. The founders of these teachings are said to be CHARAKA, SUSRUTHA, VAGBHATA, SARANGADHARA, etc. These works are available in India and their teachings represent the last word in Hindu Medicine even to-day. We find, in these works, a long and detailed treatment of Gold and Calcium therapy of tuberculosis.

Later, at about 1500 A. D., there came into existence, a work on inorganic substances specially, therapeutics of metals—by BHAVAMITRA, a contemporary of PARACELUS. Just like the latter in Germany, so did BHAVAMITRA in India laid emphasis on therapy of heavy metals and their compounds. Tuberculosis, syphilis, leprosy and malaria were treated with preparations of gold, mercury, copper and iron respectively. The compounds of gold play such an important role amongst medicaments to fight tuberculosis that it can be said that the disease was treated almost entirely with such preparations.

The gold preparations are obtained by different methods. Possibly the oldest method for the preparation of such a gold compound is by its treatment with mercury and sulphur and then subjecting the amalgum thus got to a process of incineration. This purely inorganic compound is easily and relatively cheaply prepared according to well known methods. However, for reasons not far to seek, these preparations are ridiculed by modern medicine as useless.* A further method of preparing gold was by the treatment of the metal with different salts followed by incineration. This method has been almost forgotten and extinct. The third method which deserves our immediate interest, in view of the latest advances in the knowledge of modern gold therapy, is prepared out of gold and some plant extracts. It consists of an organic gold compound whose difficult method of preparation made it easy to keep it a secret. The need for our increased interest arises out of the fact that with this medicament, many remarkable successes have been achieved even upto our modern times. Unfortunately, nothing was known of this type of preparation in Europe owing to its high price and the secrets which surround it. Only recently and after the pioneering works of FELDT and his collaborators, who developed organic gold compounds with very good effects, attention was once again drawn to the Indian gold preparations.

The question of toxic properties and detoxication of their gold compounds and the mode of their administration gave the impetus to further research and improvements in this direction. If to-day considerably detoxicated gold preparations combined with calcium are at our disposal, it does not, in principle, show any great advance over the 5000 year old

* Some Inorganic Preparations of Indian Indigenous Medicine, Part V, Swarna Bhasma and Gold Kusti—by Col. R. N. Chopra, Ind. Jour. Med. Res., Vol. 24, No. 4, April 1937, and Med. Jour. of Australia, page 269, 14th August 1937.

organic and inorganic preparations of India, where also gold in combination with calcium was administered with the only difference in the choice of the route.

Encouraged with the repeated success observed of this Indian gold preparation, we determined to put out the secretly and jealously guarded preparation of India to a first test in the hope of drawing the attention of the bigger scientific circles in Europe to this hitherto relatively unknown science.

The gold and calcium compound, prepared according to the third method from the traditional Indian medicine—which is before us from investigation, consists of a mixture of calcium and gold preparations.

The calcium part again consists of a mixture of oxides, sulphide and carbonate with a total calcium content of 44.9 per cent. In consequence of the presence of free oxides, the liquid extract has an alkaline reaction. This grey white powder is soluble in dilute Hydrochloric acid with the liberation of Carbonic acid gas and small quantities of Hydrogen Sulphide.

The gold part of the preparation with which we are mostly concerned has 64.2 per cent. gold and 6.2 per cent. organic substances and small quantities of iron, calcium, CO₂ and water. (Refer to experiment No. 1). The substance is insoluble in water; for, after shaking it with distilled water for 24 hours, it was filtered and evaporated for determining the dissolved substance with negative result. (Refer to experiment No. 2.). The method applied here for the clarification of the question of solubility was considered to be not exact and sufficient; therefore we adopted another method for its confirmation, by which small quantities of gold in the form of ions could be determined.

When the oligodynamic action of heavy metals and their salts were first observed, it was thought that it was due to the dynamic forces, as the name itself indicates. *Already in 1922, Prof. SCHUMACHER was able to establish that the oligodynamic action is the reaction of the ions. However, it relates to such small quantities, that were not capable of being determined by the then existing chemical methods. As the result of his researches on gold, silver and mercury, SCHUMACHER was clearly able to establish that the reactions, hitherto ascribed to dynamic factors, were in reality none other than the reactions of the ions. According to him, complex-compounds do not exhibit the phenomena, as they do not give out metallic ions. Now, FROMMHERZ and HEISS † inform us that it has been possible for them to prove through a simple and clear reaction, that the oligodynamic consist only of ionic reactions. For silver, whose oligodynamic reaction they investigated, they were able to indicate, even if it is a minimum, their concentrations. "Our investigations also indicate that the oligodynamic effects of silver are caused by silver ions in a concentration of over 2.10⁻¹¹ Mol/l, which originate immediately from silver compounds or are sent out over local currents of surface oxidised chain of concentration or otherwise impure pieces of silver. All oligodynamic phenomena can be explained by this." ‡

By a method which was employed by ROBERT KOCH, for a similar

* Biochem. Z., 134, 308 (1922). † Z. Angew. Chem., 50, 679 (1937). ‡ Ibid.

purpose, we were able to show that our Indian gold preparation possesses an oligodynamic effect. (Refer to experiment No. 3.)

It is, therefore, clear that small quantities of gold from this preparation goes into solution and can consequently be effective within the body. Whether this gold exercises a specific bacteriotropic effect and further whether the small quantities of gold (in comparison with the common form of treatment with Solganal injection in which the body receives greater quantities of gold) can be effective at all, will be shown later.

How do the body-juices react to the preparation under investigation? Above all, depending on the form of administration, saliva, gastric juice, bile and intestinal juices come in question. As the experiment in vitro shows, one part of the gold in the preparation is presented in colloidal form (as free gold and as compounds or possibly as organic complex compounds) and a greater part as a true solution. That at least this part of gold is absorbed by the body, is shown in animal experiments conducted by us. There were 3 questions to be answered, viz:—

- (1) Is the preparation absorbed by oral administration?
- (2) Does the preparation exhibit any toxic properties?
- (3) And are the general inflammatory processes influenced in any manner?

After the administration of this preparation to a series of 10 guinea pigs for 3 days, it was possible to prove traces of gold in their urine; this presence of gold in urine clearly demonstrates that it is absorbed by the gastro-intestinal tract and excreted through the kidneys from the circulation.

That it has nothing to do with a short passage, through the animal organism before being excreted, could be shown by the prepared or treated histological sections of the liver, kidneys and spleen of the killed experimental animals, in which deposition of gold in the cells of the reticuloendothelial system could be demonstrated. (Refer to histo-photographic plates 1 and 2). After feeding the experimental animals for 4 weeks with this medicament, no bad or toxic effects were observed. On the contrary, a remarkable increase in their appetite, an increased activity and better disposition could be established. These subjective observations found confirmation in an abnormal and rapid increase in their weights. This last fact leads one to assume the favourable influence of the preparation on pathological conditions. (For unavoidable reasons, experiments on animals inoculated with tuberculosis could not be carried out). As the experiments conducted by us were broadly based, such experiments are reserved for a future publication. It is, however, of scientific interest to mention here, an experiment in which experimental animals were inoculated with lethal doses of diphtheria toxin. Such of those experimental animals that were treated with gold preparation before and after the inoculation, did not either die or died so much later than the control animals, which were not treated with gold either before or after the inoculation. (Refer to experiment No. 5).

After the determination of the non-toxicity and absorption of this preparation in experimental animals, its favourable influence in general

inflammatory processes could be expected. As this preparation is indicated in India, specially for tuberculosis, its influence in this disease has first of all to be determined. The clinical tests undertaken here, do not, however, imply any elaborate researches, as for this purpose, the time at our disposal was too limited and the number of cases too small. In spite of this, the observations made in the clinic, only confirmed the similarity of the observations made in India, for a long time and in greater number of cases. Further more, one of the objects of this work was to stimulate the interest and help of great authorities and specialists in these problems.

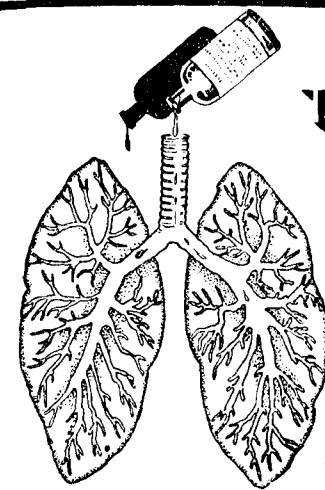
In order to obtain pathological and anatomical material and to find the way which the absorbed gold takes in the human organism and to find such of the human organs where gold deposition takes place, the preparation was given to 3 tuberculous patients with absolute bad prognosis. To test under the same conditions prescribed in India, the compound was administered in the following manner. 133 mg. of gold and 200 mg. of the Calcium preparation were well mixed with butter and given in this form twice a day, followed immediately by two fresh tomatoes.

One of these cases was an advanced cirrhotic form of tuberculosis with cavities in both the lungs. The other was a similar one, with an addition of extensive ulcerative tuberculosis of the larynx. These cases, as already said before, were not intended for observing clinical betterment, due to the particular therapy, but were mainly meant for securing anatomical and pathological materials needed to prove the presence and topographical distribution of the metal in the several organs, as soon as these moribund cases were dead. However, blood-picture, temperature curves, weight, erythrocyte sedimentation test and such other details were maintained in these cases, while their subjective and general disposition were observed and recorded. By way of an example, the weight curve of one of these 3 cases is reproduced hereunder. From this, it will be clearly seen as to how the rapidly falling weight was arrested after 10 days' administration of the medicament and after a further two weeks, a gradual raise in weight curve will also be noted. The improvement in the general disposition of the patient also becomes obvious, simultaneously with the increase in the body-weight.

In addition to all these, the urine was tested every day for the presence of gold and it was found positive in all cases. Without necessarily drawing premature conclusions, it is interesting to note that there is a drop in the temperature on the 3rd day, though on the 2nd day, there was a sharp rise.

Just as in the case of experimental animals, an increased appetite could be noted in the human also. From the 4th day onwards, they showed an abnormal hunger, which was hard to be satisfied and necessitated feeding even during night times. As all these patients were suffering from a lack of hunger before treatment with the gold preparation, it is natural to assume that the increased appetite is due to its influence.

As it was not expected that the treatment would arrest the rapid worsening of the extensive pulmonary, laryngeal and intestinal lesions of the 2 patients who were already in an advanced state of the disease, the



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Experimental Investigations over the Pharmacological and Therapeutic Properties of "Calcii Aurum"*

An old Indian Gold Preparation of Hindu Medicine

BY

C. DWARAKANATH, L.I.M. (MADRAS), Z. T. (HAMBURG UNIVERSITY),
Madras.

AND

DR. PHIL. HERBERT SCHOLZ (UNIVERSITÄTS KRANKENHAUS,
HAMBURG, EPPENDORF)

SINCE the discovery of FELDT, in which the complex organic compounds of gold, of principle R. S. Au are detoxicated and found still effective, the number of gold preparations appearing on the market are on the increase; very many of these are destined to a short existence and only a few satisfy high expectations of them.

The fact that increasingly keen discussions take place over the therapy of the different gold preparations, enables us to determine two things, viz:

- (1) That gold has undoubtedly a helpful influence on all chronic inflammatory processes including tuberculosis.
- (2) That it seems always desirable to improve over the compounds of gold and the modes of their administration.

Unfortunately all the existing gold preparations have more or less high toxicity, requiring greater care in their use, and in many cases, even prevents their application. A further disadvantage with these gold preparations with the exception of Solganal dragees, that have been recently and slowly introduced in the form in which they are administered is that they are given only intravenously or intramuscularly with considerable inconvenience to the patients.

An ideal gold preparation, therefore, must possess the following properties:—

- (1) Simplest (*i.e.*) oral administration.
- (2) Good absorption.
- (3) Minimum toxicity combined with maximum beneficial influence in tubercular process.

In view of these obvious requirements, it is interesting, while modern medicine is still engaged in the solution of this problem, that thousands of years ago in ancient-India, a gold preparation was developed through empirical methods, which satisfied our requirements to a great extent and we need not feel ashamed of a comparison with the synthetic gold preparations of modern times.

* Specially contributed to 'The Antiseptic'.

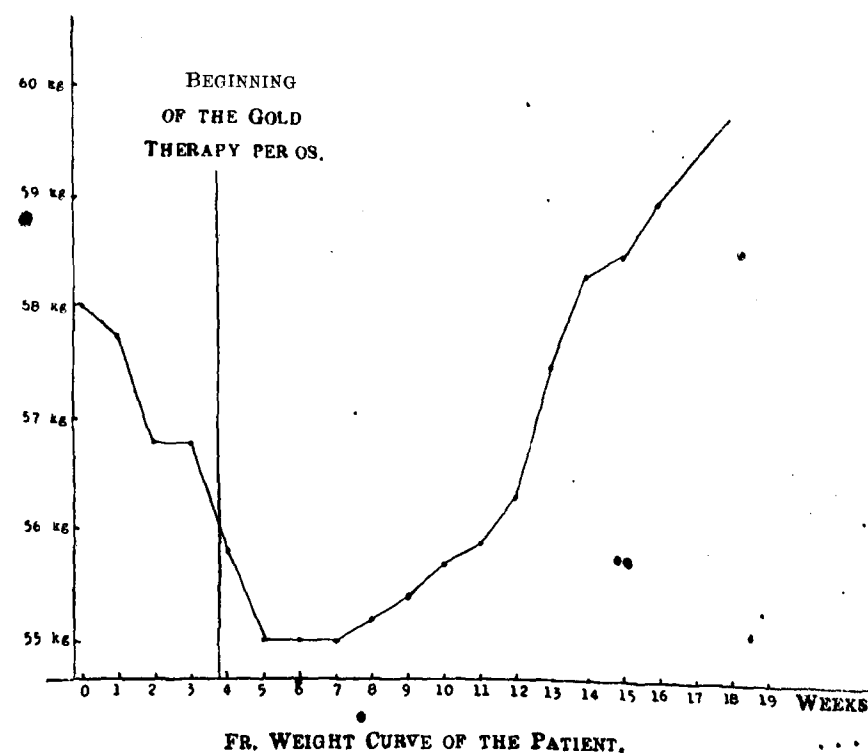
1. This work was completed by the author, at the Faculty of Medicine, University of Hamburg, Germany, under the direction of Prof. Dr. H. M. Berg, Director of Innere Medizin, during the year 1937.

patients died. Sections of their liver, spleen, lungs and kidneys were taken for histochemical tests for the presence of deposits of gold. Gold was found in all the sections and in the following places—in the liver chiefly, in Kupffers' schenstern cells, in pulp cells of the spleen, and in the reticulo-endothelial cells of the Henles fubuls and the kidneys. (Refer to micro-photo plates 3—5).

The quantitative determination of gold in the aforesaid organs were then undertaken. The method elaborated in Bio. Chem. Z. 260, 143 was adopted, according to which the metal was filtrated with Thiosulphate after its separation and oxidation. It was found giving the following quantities: spleen 98.6 mg., lungs 246.5 mg., liver 573.5 mg., kidneys 269.7 mg. From the fact that the gold of this preparation is chiefly deposited in the reticulo-endothelial system, it is concluded that the favourable effects observed may be caused by the rising of the immunity of the organism.

The influence on the infectious process could further be confirmed by clinical observations made on cases with better prognosis.

In addition to the increases in appetite, weight, etc., just mentioned (considered to be nonspecific influence of the medicament), there was one case which particularly expressed the definite increase of body resistance. It is the same case whose weight curve is shown below.



This case was treated by the specialists in the clinic for a fairly long time and found to have tuberculosis of the larynx and lungs, with pleurisy and effusion of right lung. In this case, after the administration of our gold preparation by mouth for over a period of 3 months, we were able to observe

healing proliferative process with the absorption of the pleural effusion. In another patient, whose treatment with Solganal had to be stopped after the 2nd injection owing to the patient's increased uneasiness and vomiting, and impairment of the appetite, the Indian gold preparation was tried perorally. As in the case of Solganal injection, the patient did not show any consequential unpleasant effects. On the other hand, the appetite increased and a betterment in the general disposition was observed. What was hitherto an exudative form of pulmonary tuberculosis, showed a clear tendency for fibrosis—as evidenced by X-ray and clinical tests.

In conclusion, it can be said that in the peroral administration of the Indian gold preparation, a general improvement and a partial arrest of the tubercular process was observed even after a short treatment. It must also be mentioned that the much feared latent tubercular process, especially the flare up in the intestines, or the kidney complications were not observed. As has been already mentioned, we are far from exaggerating the value of clinical observations, and we would like chiefly to invite the attention of workers to this method of gold therapy of Hindu Medicine for tuberculosis and submit the preparation for a discussion.

Experiments.—1. *Analysis of the gold preparation*:—The gold brown powder is taken up by aqua regia and investigated analytically, whereby the following results were obtained: Gold 64.2%; Organic substances 6.2%; Water 1.2%; Ferrum 4.9%; Calcium 3.6%; Carbondioxide 0.3%.

2. *Determination of its solubility in water*:—One gram of the gold preparation is shaken for 24 hours with 80 c.c. of distilled water and this is dialysed in an electric rapid dialyser. For this purpose, an apparatus manufactured by the firm, SCHOTT GEN JENA (Electric rapid dialyser 5401) was employed. After dialysing it for 8 hours, and evaporating the dialysed fluid, no trace of gold was found.

3. *Proof of the oligodynamic effect of the gold preparation*:—In a culture of Staphylococcus aureus, a fine gold wire (999) previously heated red hot, and a small quantity of the gold preparation under investigation, were placed in different places. Simultaneously, another dish with the same culture was set under the same experimental condition, to which were given a trace of the only German peroral Solganal dragee in addition to the fine gold wire (999) and a trace of the Indian gold preparation, heated red hot on the flames and the organic complexes destroyed in 3 different places.

As was to be expected, the gold wire did not show any oligodynamic effect; while a bacteria-free field developed around the Solganal nucleus. A similar field was also obtained around the Ayurvedic gold preparation. The same did not happen around the Indian preparation which was heated in the flames and the organic substances destroyed.

4. *Absorption in vitro*:—Since it was found that the preparation was insoluble in water and partly soluble in HCl., it had to be determined if the body juice and other organic compounds with which it is likely to come in contact in the human organism, were able to dissolve the gold in that preparation. The absorbability of the medicament depends to a very large extent on this. Therefore, 1 gram of the gold preparation was added to 6 c.c. of gastric juice, 2 c.c. each of saliva, gall bladder bile and duodenal secretion of a normal man and kept in an incubator for

48 hours at a temperature of 37° Centigrade. Then it was diluted with an equal quantity of water, and passed through a bacterial filter. (SCHOTT, GEN. JENA). After thorough washing, the filtrate was freed of colloidal admixtures by an immediate ultra-filtration. The ultra-filtrate was investigated quantitatively for gold. 2.5 to 3% of the gold employed, remained in the ultra-filter while in the filtrate which was transparent, 9.2 to 10.5% of gold was found in solution.

If, under the experimental condition in vitro, some 10% of the gold goes into solution, it only represents the minimum of gold going into solution. For, in living organisms, greater quantities in soluble form for absorption can surely be expected.

5. *Animal experiments*.—10 grown up guinea pigs, of weights 400 to 500 grams were maintained in experimental animal cages. Each one of them was given daily 30 mg. of the mixture of Calcium and gold preparation in the ratio of 2:1. The animals were trained to swallow the medication by placing on the tongue a thoroughly prepared mixture, in a glass spoon, previously dipped in a saturated solution of sugar. After a few days, all the animals started taking the medicine with avidity. As control 10 similar animals were given the same quantity of sugar solution without gold preparation. Their urine was collected and examined for trace of gold as mentioned hereunder. 10 c.c. of the urine were ashed after adding 2 to 3 c.c. of concentrated nitric acid in a porcelain crucible on Bunsen flame and the residue heated red hot. When the crucibles were cooled, the ash was dissolved with very dilute HCl and set on a water bath for drying. The residue thus got was dissolved in distilled water.

To a 100 c.c. of a freshly prepared 0.5% methylene blue (medicinal and chemically pure Merck's) was added 7 drops of concentrated HCl and 5 c.c. of a 10% solution of Rougalit (standardised dye stuff 1. g.) and heated till the blue black solution became colourless.

When a few drops of this colourless Leucomethylene is added to the solution of the residue in the crucible, it at once turns blue if gold is present. As the oxidation of the Leucobase is possible not only through gold ions, but also through mercury, silver and copper, it is imperative in these experiments on animals to carefully avoid the contamination with these metals. The catalysis of the Leucobase is described by Prof. SCHUMACHER in Biochem. Z. 134, 398, 1922. For analytical proof for traces of gold, this reaction described was used here for the first time. The experimental animals began to excrete gold in their urine from the 3rd and 4th days. After feeding them for 4 weeks with the medicament, they were killed and their organs examined histochemically for gold. Fairly large deposits of gold was found in the kidneys, liver and spleen as is already shown in the microphotographs 1 and 2. At the end of the experiments, the gold treated animals increased in weights of 90 to 160 grams while the control animals gained on an average 50 grams.

6. *Treatment of animals with the gold preparation before and after the inoculation with diphtheria toxin*.—Four series of 6 animals each were taken for this experiment.

Series A.—Were inoculated with a lethal dose of diphtheria toxin without administering gold either before or after the inoculation.

Experimental Investigations over the Pharmacological and Therapeutic Properties of "Calcii Aurum"—C. Devarakanath and Dr. Phil. Herbert Scholz.

Microphotograph 1.

Spleen: (x 1000) of normal guinea-pig after 30 days of administration of Gold by mouth.

Microphotograph 2.

Kidney (x 1000) of normal guinea-pig after 30 days of administration of Gold by mouth.

Series B:—Were inoculated with the toxin, and was followed by gold therapy; these were not treated previously with the medicament.

Series C:—These animals were treated with the gold medicament for 2 weeks and then inoculated with the toxin.

Series D:—These animals were treated with the gold medicament, on the 15th day the toxin was inoculated. This was followed by further daily treatment with the medicament.

Result.—*Series A*:—Died on the 3rd day.

Series B:—Died on the 4th and 5th days.

Series C:—Died on the 8th and 9th days.

Series D:—Died suddenly on the 14th day and 16th day without showing the symptoms of the disease.

Conclusions.—1. The ancient Indian medicine fully appreciated the value of gold in the therapy for infectious inflammatory conditions and in particular tuberculosis. One such preparation, "Calcii Aurum", traditionally known in India to be of value in the treatment of tuberculosis, was taken up for our investigation.

2. After the quantitative analysis was made, that it can be brought partly into solution by the biochemical fluids of the organism as saliva, gastric juice, gall bladder bile and duodenal secretion in vitro, and that it possesses oligodynamic effect was shown.

3. By the animal experiments, it was shown that the gold in the preparation is absorbed by the body when administered by mouth and that it is excreted with urine after its circulation through kidneys.

4. The preparation has no toxic effects.

5. In normal animals (guinea pigs), gold was found deposited in the cells of the reticulo-endothelial system.

6. In animal experiments, an increased appetite and a general feeling of well being could be observed after administering the preparation for a short time. After treating them with the medicament for 4 weeks, a considerable increase in their weight was noted.

7. The increased residue stimulated in the animal against toxic inflammatory process was demonstrated with the help of inoculation experiments with diphtheria toxin. Those treated with gold showed greater and more successful resistance to the toxin.

8. A new method for proving even small quantities of gold in organic and inorganic substances was worked out and applied.

9. It was shown that the gold is absorbed and deposited in the reticulo-endothelial system in human subjects also.

10. Increased appetite and a feeling of general well being, a lowering in the temperature and a good increase in weight were also observed in the tuberculous patients.

11. The treatment with this preparation can also be considered in cases where injectable Solganal treatment is contra-indicated.

12. Points 9, 10, 11 were also observed in patients whose processes were so advanced that a recovery could not be thought of. In cases with better prognosis, clinical and X-ray indications of improvement and the arrest of the tubercular process could be observed.

Filariasis*

BY

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AND

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A MAJORITY of the population of Surat proper is being infected with the filarial disease in one form or another, and with a more or less permanent disability or disfigurement; moreover, the manifestations of the disease are so varied that many a time, the real diagnosis is missed as will be seen from the case-notes given at the end of this article. As regards the treatment-part of the disease is concerned, there is very little to do once the disease has well-advanced.

Of the genus *Filaridæ*, MAYLOR describes six species known to be parasitic in man, but only *Filaria bancrofti* appears to be capable of giving rise to any morbid change. The habitat of these adult *Filariae* is the dilated lymphatics of the extremities, and trunk and at times the lymphatic glands, where in time they may be calcified. The embryos often known as micro-filaria are about the size of a R. B. C. and passing up through the lymphatic channels, they reach the blood-stream where they may be found between the hours of 6 P.M. and 2 A.M. and hence the term *Filaria nocturna* in contradistinction to the term *F. diurna*, another name for *Filaria loa loa*, which appear in blood-stream by day only. The embryos of *Filaria bancrofti* retire by day to the lungs and large vessels but if the sleeping-habits of their human host are changed, the periodicity of the embryos is reversed as well. It is a well-known fact that an abundant number of micro-filaria may be detected in the blood of persons at night without causing any pathological condition whatsoever and secondly, that in those with marked elephantiasis and chyluria, there may be an entire and permanent absence of these embryos from the blood. Of the adult worms, the male measures 1" while a female worm is about 3" long. Sexes are often found coiled together in cyst-like dilatations of the lymphatic spaces or glands; the sheathed embryos are born viviparously and that, as a result of injury to the parent worm and resulting extrusion of these embryos, the blocking of the lymphatic channel occurs with the various manifestations of the disease accordingly.

Life-Cycle.—Blood containing embryos of *Filaria bancrofti* is being taken up into the stomach of *Culex* mosquito, wherein the activity of the contained embryos is markedly increased and within two hours' time, the embryo forces its way out of its sheath and passing up to the thoracic muscles of the mosquito, it begins to grow in length and change into a larval form within a period of two weeks. It then reaches the proboscis ready to return to its human host when next this *Culex* mosquito bites a man. These infective filarial larvæ are simply deposited near about the puncture on the skin caused by the bite of this mosquito and thence they effect their entrance into the skin and lymphatics by their own active

movement, contrary to the mode of infection by malarial parasites. The larvæ thus enter their definitive host—man, and proceed to lymphatic vessels or glands where they attain sexual maturity. Females are then fertilized by males and begin to give off sheathed embryos from the uterine opening near the anterior end. If too many embryos are taken up by the *Culex* mosquito, the insect is apt to die as a result of too heavy an infection and so, the chances are that a person harbouring an enormous number of micro-filaria may be less dangerous than one harbouring a smaller number.

Demonstration of Micro-Filaria in Blood.—1. Make a thick blood smear on the slide and allow it to dry and then wash under water till the hæmoglobin is dissolved out—put under the microscope, close the diaphragm and look for micro-filaria.

2. *Staining preparation*:—Make 5 to 6 drops of blood on a slide, mix them well with a needle and spread by a circular movement to the size of a pie; dry it over a flame and immerse in water to wash off the hæmoglobin, dry and stain with Leishmann's for parasites or immerse the dried slide in alcohol for .2 minute, dry again and pour Meyer's Hæmolum, apply heat slowly, cool and wash with water—dry and look for *Filaria*.

DR. GANDHI describes the clinical picture as under, and cites some of the interesting cases that he observed: "Majority of the persons who are infected with *Filaria Bancrofti* show no symptoms at all; these symptom-free cases are usually discovered accidentally when blood is being examined for any other disease or when a filarial survey is being undertaken. It is only when damage to the lymphatic vessels or glands has taken place that the obstructive symptoms appear. In general, whatever part of the body may be affected, a patient with acute filaria is comes with the following clinical picture: painful and tender, cord-like swellings of the affected lymphatic trunks appearing like red, congested streaks in the superficial skin with painful and tender lymphatic glands draining the area. This may last for one or many days, accompanied by rigors, high temperature, back-ache, head-ache, vomiting and sometimes even delirium. This is what is called filarial fever. Obstruction to lymphatics manifests differently at different anatomical areas". The following appears to be the most rational classification of filariasis:—

- (1) *Filarial lymphangitis*.
- (2) *Lymphatic tumors*:—(a) Varicose lymphatic glands. (b) Filarial tumors of testicle and spermatic cord. (i) Filarial orchitis and epi-orchitis; (ii) Lymphatic varicocele. (c) Filarial cysts.
- (3) *Lymphorrhagia*: (a) External; (b) Internal.
- (4) *Elephantiasis*.

1. *Filarial lymphangitis*:—It is for this condition that a majority of the filarial patients visit the out-door for treatment. It may be the first attack or an acute attack of lymphangitis over already existing chronic lymphangitis. The patient gets local and general symptoms of acute infection of lymphangitis as already mentioned under 'clinical picture'. The course of the disease may lead to complete subsidence of local and general symptoms or may leave behind cord-like lymphatics or may develop

* Specially contributed to 'The Antiseptic'.

into an abscess. The writers had a few occasions to see cases ending fatally with symptoms of septicæmia.

2. *Lymphatic tumors*: (a) Varicose lymphatic glands. Most commonly affected lymphatic glands are inguinal and femoral. Axillary and others are rarely or never affected.

(b) Filarial tumors of testes and spermatic cord.

(i) Filarial orchitis:—The patient gets acute pain in the testes with severe back-ache and fever with rigor. There are signs of acute orchitis and a small acute hydrocele may be recognised. This may end in chronic orchitis or abscess formation or may leave behind filarial hydrocele.

(ii) Lymphatic varicocele:—The lymphatics of the spermatic cord are dilated, tortuous and very often accompanied by hydrocele.

(c) Filarial cysts:—The writer had occasions to see two cases of cystic tumors—the fluid on microscopic examinations showed plenty of micro-filaria. This condition is unfortunately not described in any text-book.

3. *Lymphorrhagia*:—This means extrusion of lymph or any fluid from lymphatic system i.e., chyle. This may be met with into two different forms. (a) External lymphorrhagia; (b) Internal lymphorrhagia.

By internal lymphorrhagia is meant the flow of or exudation of lymph which has taken place within the body-cavity, such as vesical, tunica vaginal, pleural and very rarely peritoneal, leading to the conditions like chyluria, hæmatochyluria, lymphuria, chylous hydrocele or lymphocele, chylous ascites, and chylous diarrhoea—the latter two conditions are very rare. External lymphorrhagia:—This condition is very commonly met with on scrotum and labia majora. It may occur on any part of the body which is studded with dilated lymphatics.

A man gets acute attacks of filariasis, the scrotum gets swollen and small clear vesicles appear on the affected scrotal skin. These vesicles may burst and give out chyle or lymph. If it is profuse and continuous exudation soiling the clothes, it gives rise to a condition resembling weeping eczema. If the exudation is not sufficient to have continuous flow, the lymph dries on the skin and forms crusts on the surface. The same condition may occur in the case of females on labia majora.

4. *Elephantiasis*:—This is one of the most common conditions found in filarial localities, where people take none or very little treatment for filariasis. It is characterised by focal thickening of the affected part in progressive character by various attacks of acute lymphangitis over the chronic one. The condition is progressive. The skin becomes thick, hard and deformed and the swelling is described as "solid œdema" i.e., not pitting on pressure. The most superficial layer of the affected skin remains either smooth, or becomes scaly, moist or dry. This condition is most common in (a) lower extremities (b) scrotum (c) upper extremity (d) penis (e) labia majora and clitoris (f) breast and (g) rarely face and head.

Dr. GANDHI has a few rare and interesting case notes of filariasis which are as under:—

1. *Filarial cysts*:—He has seen two cases of filarial cysts—one in

axillary region and the other in kidney region. Both of these cases were seen at the K. E. M. Hospital, Bombay, on operation table, when he was an anæsthetic there. The axillary case came to the hospital for a soft fluctuating tumor in the right axilla, neither painful nor tender, giving the feel of cystic hygroma in the neck. The whole cyst was dissected out; the cyst wall was very thin—the fluid could be seen clear through the cyst wall. The cyst reached as far as middle of the clavicle under the pectoralis major. The fluid was immediately sent for the pathological examination and, to the surprise of all, the fluid was found to contain many living micro-filaria.

The other cyst was a huge one in the lumbar area, giving the appearance of hydro-nephrosis. The patient was operated and the fluid showed micro-filaria in plenty.

2. Dr. GANDHI was called upon to see a case at about 3 p.m., of a male patient aged about 45 years. The patient was restless, tossing about, complaining of acute pain along the transpyloric line; his temperature was 103°, pulse 130 and resp. 35. Physical examination revealed an acute attack of filarial scrotum. Abdomen was tender and somewhat rigid in the right upper quadrant and there was a ball-like protuberance in the epigastrium; within half an hour of his seeing him, he got profuse hæmatemeses; three times he vomited blood within 6 hours, which was controlled by usual treatment of hæmorrhage, viz., injection of Morphia gr. ¼ and injection of Cal. Gluconate 10%, 10 c.c. and Co-agulen Ciba 5 c.c.; continuous ice-compresses to the abdomen. This was a case of hæmorrhage during an acute attack of filarial scrotum. He had the opportunity to follow up the case till now i.e., nearly 5 years. After the subsidence of hæmatemeses and malæna, the patient had no peptic ulcer complaint; neither did he give history of peptic ulcer before. A few months after his first attack the patient had another attack of filariasis and had hæmatemeses on the first day of the attack which was controlled by the usual treatment. The patient got fever with rigor some days after the last attack. It was malaria but this time he had neither hæmatemeses nor malæna. This is an unusual case of hæmatemeses and malæna during the filarial attack. During the last five years, the patient had several attacks of filarial scrotum; majority of these were accompanied by malæna, as vomiting was controlled by injection of Morphia during the very start of an attack. The patient is still living healthy without any sign of malignancy stomach, or peptic ulcer or cirrhotic liver. This case illustrates filarial hæmatemeses just as we come across filarial hæmaturia, although the former is very rare.

3. The case below described is from the memory of Dr. GANDHI's old partner, Dr. K. V. HORA, L.M.S., illustrating and giving clue to some Indian herbal medicine which still requires identification for the treatment. Thirty years back, a case of elephantiasis of right leg was admitted into Sir J. J. Hospital, where Dr. HORA was a student then. The leg was for amputation. When the patient knew of the amputation business, he absconded from the hospital. After an year, he came to the O. P. D. for some other complaint where he was recognised. His leg was found to be half cured. He was then questioned as to what was done to his leg. He said, "a Sadhu gave me some green leaves—the juice of which was applied to the leg—the watery substance began to pour out of the leg continuously for days together and here is the result."

4. Another interesting case was of an unmarried carpenter girl, aged 18 years, admitted to the Hindi Mission Hospital, for acute unilateral swelling of the whole inferior extremity, reaching as far as 2" above the inguinal ligament and pitting on pressure, the knee-joint being greatly swollen and tender and of 6 days' duration. The history of the case was that she first got high fever with rigor, followed by painful swelling of the knee and extending to the thigh with the appearance of red areas on the skin of the thigh. The movements were limited and the knee was in the position of extension. The case was puzzling and thinking it to be pyoarthrosis, the joint was incised and opened up with the escape of very little reactionary (inflammatory) synovial fluid and there was complete absence of expected pus! The two incisions took a long time to heal with no relief of symptoms, except that the swelling in the thigh and leg became a little less after a month or so, with no relief at knee joint. Now the suspicion arose of T. B. knee joint; the sliding traction was applied for the stiff joint and to relieve the pain; It was discontinued as there was no relief. As the case was not at all progressing well and as she was going down in health every day, the relatives took her home after nearly 2-3 months with false ankylosis in extended position and persistent swelling of the knee joint and greatly emaciated. She was then treated at her residence with the injection of milk, Prontosil and massage, advised to take a good deal of nourishment. The patient progressed well with this line of treatment, resulting in great relief and regaining her former strength. Now this is a case which started initially as an acute filarial lymphangitis of the lower extremity which could easily be mistaken for pyoarthrosis or T. B. knee joint or septic femoral thrombosis, if the various manifestations are not kept in mind. The relief obtained would have been very great, if the case were treated on the medical line with rest to the joint and with a food little more raised than the body, with Sulphonamides and foreign protein therapy, etc.

We propose to deal here with the medical line of treatment only. The patients coming under this category are those with acute lymphangitis and those with lymphangitis leading to elephantiasis. The prophylactic treatment consists of (1) destruction of the mosquito concerned (*Culex* variety) and mosquito breeding places by proper use of culicides and culifuges (2) avoiding residence in filarial districts (3) avoiding the mosquito bites by the use of mosquito nets or rubbing the whole body at night with oils of Eucalyptus or Citronella. The curative treatment: Till the present date, no drug exists specifically potent to destroy adult filaria in human carriers. It is very difficult to treat those in whom the disease has well advanced and the symptoms are due to mechanical obstruction of the lymph channels. A general practitioner is very often confronted with this type of cases coming for treatment with the hope of rapid cure of their weighty appendages or at least alleviation of the feeling of weight or a removal of disfigurement, and many drugs like Arsenic, Antimony, and Iodides have been tried to no satisfaction; so, the only treatment that is left to us is to give symptomatic relief. Three conditions seem to be essential to form a curative treatment of filariasis. First, the destruction of micro-filaria circulating in the blood and adult worms abounding the lymph channels in human carriers before the stage of solid oedema is reached; second is to cure solid oedema, which seems possible by the use of some

yet unidentified herbal remedy, thirdly, the avoidance of bites by *Culex* mosquito.

We, however, intend to deal here with the treatment purely from the view point of a general practitioner, as he is apt to receive the following two types of manifestations, more often at his dispensary. The majority of these patients come with the acute attack of lymphangitis. The treatment consists of:—Locally soothing lotions such as—*R* Plumbi Subacetatis 3 ii p.; aqua ad 3 xx for compresses to the affected part or Lotion Catamine and orally give the following:

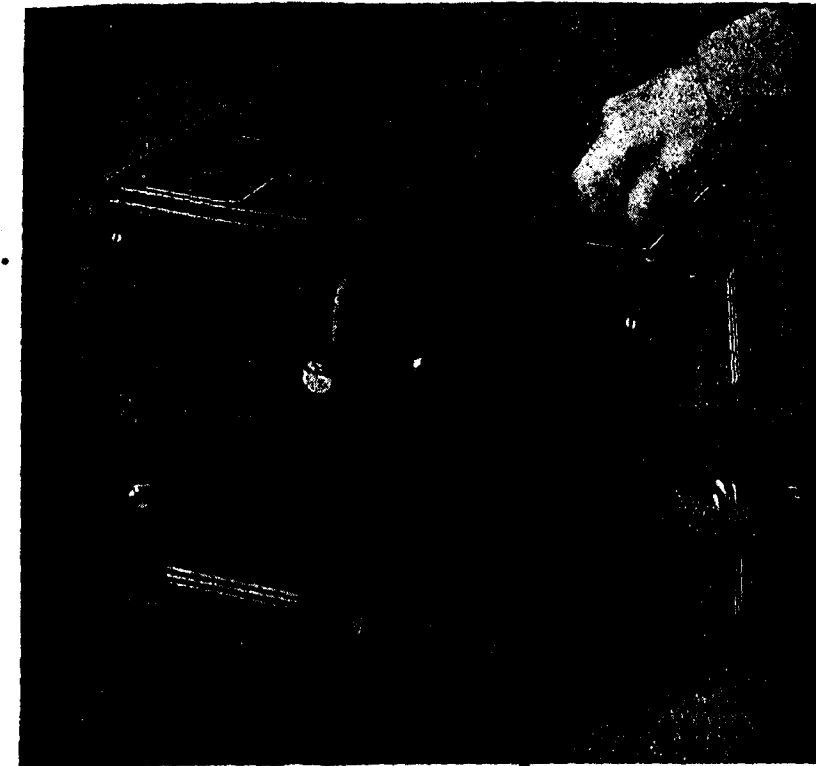
<i>R</i>	
Soda Salicylas	... gr. xxx.
Soda Bicarb.	... gr. xxx.
Pot. Brom.	... gr. xxx.
Tr. Card Co.	... 3 i.
Spt. Am. Arom.	... 3 i p.
Aq. Chlorof. ad	... 3 iii. 1/3 T.D.S.

This mixture will relieve the temperature and back-ache—the two main symptoms of acute filarial attack. Sulphanilamide 7½ gr. t. d. s. is usually prescribed with the mixture. The preparation that we generally use is the Septanilum Tablets (Glaxo Lab.) or Inj. Urea-Sulfazide 5 c.c. intramuscularly (Union Drug House) if the parenteral route is selected for its administration. The rationale of this drug in acute filariasis is very easy to understand if it is remembered that the acute symptoms of lymphangitis are not due to the obstruction of lymphatics but are mainly due to the infection by Streptococci and to a lesser extent by Staphylococci, and for that very reason, it was advocated to use Strepto-Staphylo Vaccines in acute filariasis. The advent of Sulphanilamide has greatly changed the whole outlook of such acute Streptococcal affections and to-day, it is the most powerful weapon that we possess to fight against the so-called most virulent bacteria. We have used Urea-Sulfazide injection in 5 c.c. doses intramuscularly on majority of occasions and found it to be the most useful preparation in aborting the acute attacks. To our observation, the drug is only useful in cases with fever. We have been successfully using this preparation for the last 1½ years and it was the chief drug that was used in the case of filarial scrotum with hæmatemeses that has already been cited in this article. Another interesting point about this patient is that the intervals between the acute attacks were greatly lengthened by only one injection of Urea-Sulfazide, which was tried after unsuccessfully giving 12 injections of Faudin which proved absolutely useless in this particular patient. (A brief reference to Sulphanilamide treatment of filariasis will be found in *Practitioner*, Jan. '40.)

Treatment of Chronic Cases.—This is the type that is most tiring and disappointing; tiring, because it requires a great deal of patience on both sides to show some result and the treatment generally proves to be a lengthy one and it is disappointing, because one always loses a chance to watch the results of his treatment as the patient comes in expectancy of a rapid cure and disappears soon after taking a short treatment, of course with no results. Various drugs are used for this type of cases—such as: (1) Milk with Iodine; (2) Arsenic with Iodides; (3) Arseno-typhoid Vaccines in graduated doses; (4) Antimony. Out of these four remedies, we

have found some good results with Arsenic and Iodide. The preparations that we generally use are:—(1) Entodon; (2) Sulfarsenol intravenous; (3) Arsenic with Hydrarg Iodide (Walker's) intravenous. In private practice, it is very difficult to get a patient taking treatment till recovery or good deal of relief is achieved. But we had an occasion to observe a case of filarial serolin who was advised operation, getting better with increasing doses of Sulfarsenol intravenous. The patient has very small scrotum and no discomfort now. It will be seen from a case of elephantiasis, nearly labelled for amputation, getting cured by only a local application of a fresh juice extracted from some Indian plant and this shows a possible existence of such a verbal remedy that will cure elephantiasis. India possesses many indigenous drugs which are largely used by quacks to cure many so-called incurable diseases, but they are still lying in the dark, because, we, allopaths, have a tendency to laugh at these curious cures by such quacks. Instead, if we try to scrutinize the plants they use or persuade them to co-operate with us, it is no wonder that new remedies may be discovered to cure many so far incurable diseases. In support of this queer statement regarding the existence of such remedies in the hands of these quacks—of which, our science of allopathy does not take any cognisance, let us remind the readers of the story about the discovery of digitalis—one of our chief armamentarium at the present day; It was originally an "old woman's medicine for dropsy". Another similar example is of the insanity roots distributed by one Marwari gentleman at Bombay. Dr. GANDHI had an occasion to observe personally the marvellous results with the use of these roots. These roots are now known to many and a great deal of experimental work is being carried out by many different workers to find the various alkaloids contained in this plant. Himalayan Drug Co. have already placed on the market their preparation Serpina Tablet—a product of these roots. It is a promising remedy for high blood pressure, hysteria and insanity. We have tried it on all these cases with very satisfactory results. It is no wonder then, that such a herbal remedy may be discovered as a cure for elephantiasis in future. It is a matter of great delight that today we possess great research scholars like BREVET. COLONEL CHOPRA, taking keen interest in the indigenous drugs of India and that there is every hope that a day will come when such an unidentified plant may be brought to the light as a successful cure for elephantiasis through the efforts of such ingenious brains.

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CASES AND COMMENTS

On a Case of Recklinghausen's Disease Complicated by Cold Granulia

BY

DR. A. DE SOUSA E FARO

Professor of the Medical College of Nova-Goa.

AND

DR. SOARES DA VEIGA.

Government Radiologist to the Medical Services of Portuguese India.

History of the Case.—When two years ago, the patient;..... was operated in the Santa Casa de Misericordia's Hospital at Ribandar, by the Surgeon, D. J. DE REGO, with one of us (A. S. F.) as assistant, for a subtotal hysterectomy on account of a fibromyoma, we had been struck by the coexistence, in the same patient, of numerous pigmented cutaneous tumors, whose neurofibromatous nature could be diagnosed at first sight.

The patient went away without giving us the opportunity to study her case, whose history is the following:—

Health rather precarious since childhood, with diseases common at this age. Her relatives did not notice whether she showed some manifestations in relation to her actual condition then. At puberty, it was clearly seen that her skin was covered by some pigmented spots and at the same time, numerous roundish tumors, more or less soft, invading the body, having the same colour as that of the skin and becoming later on, somewhat irregular in shape. No other member of the family was affected by this disease. During the interrogatory, the patient did not show any sign of mental deficiency; on the contrary, she remembered vividly the most insignificant details of her life and her replies were clear and intelligent.

The reason why the patient came now for consultation was her extreme asthenia, growing worse and worse in the last months, a persistent small cough, notwithstanding her temperature nearly normal and strong dyspneic condition: *lack of air, I am thirsty for air*, were the expressions used by the patient. This dyspnea which laid her in a very deep weakness, increased at the least effort, causing her a state of anxiety and provoking or increasing her cough accesses. No or practically no expectoration. She had never noticed any blood in the sputum. Weight greatly diminished, lastly.

With these short anamnesis, we observed the patient.

Actual Condition of the Patient.—On dorsal and abdominal regions hepatic spots; on the left flank regional melanoderma of Addisonian type; the whole tegument covered by tumors—from which a perfect idea is given by the joint photo—with or without a pedicle, soft, most of them roundish, their base in the hypodermis, their size varying from that of a pea to an orange; at the same time, but rarely, some hard nodules along the course of the nerves, some of them roundish, others fusiform (these ones mostly along the course of the superficial nervous branches on the

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EDITORIAL

The New Year

1940 is gone, never more to return and 1941 has dawned with fresh hopes, and with fresh vigour. "The Antiseptic" enters on its thirty-eighth year, with a fairly long record of uninterrupted and, if we may be permitted to say so, unstinted service to the medical profession in India.

The present War which started fifteen months ago in Europe, has now practically enveloped the whole world, the old and the new, and there is no knowing when or where it will end. Meanwhile, there is considerable loss of men and money and not only the Military but also the Civil population—men and women, young and old—are living in a state of panic and nervous tension due to ruthless air raids by the totalitarian States. The British and the Allies have borne these onslaughts with a heroism and fortitude, which is unparalleled in the history of the world, ancient or modern. The enemies are bewildered and there are already signs of weakening among them. The recent successes of the British in the Balkans in conjunction with the Greeks and in Libya in Africa are the forerunners of a complete victory yet to come. India's contribution to the War in men, money and materials—not to mention medical service—is typical of her hoary tradition and loyalty to the Empire and with such ample resources and grit, we hope and trust that Britain will soon emerge victorious and glorious and introduce a "New World Order", where there will be a federation of all human beings on earth, whose motto will be "The Fatherhood of God and Brotherhood of Man".

By way of retrospect, the year 1940 witnessed the long-wished for legislation for the regulation of Drug Trade in this country. The Bill was introduced in the Central Legislative Assembly in March 1940. But it contained many lacunae, which made it a measure of mere eye-wash. We pointed out these lacunae in our Editorial of March '40, which were attended to, subsequently, though not in entirety, by the Select Committee, and the Assembly. Still, it is a far off cry to say that India is self-supporting

fore-arms, flanks, forehead and neck), painless and having the size of a nut or less.

Mental state unaltered, somatic development normal without dystrophias neither malformations. No sign of disendocrine syndrome, no stigm of heredolues. Urine without sugar, glycemia normal, Kahn negative.

The biopsy of tumors shows: neoplastic proliferation of peripheral neuroglia, specially of Schwann cells and ameylinic fibres. We are dealing with a pure Schwannoma without any sign of sarcomatous degeneration.

Characters of Recklinghausen's Disease.—In 1882, VON RECKLINGHAUSEN was able to isolate a systemic embryonic dystrophias, hence a congenital disease, often hereditary and familiar, appearing in infancy or adolescence, and characterised by three cardinal symptoms; (a) cutaneous and sub-cutaneous syndrome; (b) psychic troubles; (c) osseous dystrophic alterations.

(a) The cutaneous and sub-cutaneous syndrome is constituted by regional or diffuse pigmentation of hepatic spots, lenticular spots and Addisonian melanoderma, more or less associated; moreover, there are tumors, more or less voluminous, some of them cutaneous, caused by *naevi molluscum*, others formed by nodules, hard and fibrous, reaching the nervous sheets of the cutaneous nerves, either from the rachidean or from cranial or sympathetic system—*neurinomes*—(originating a proliferation of peripheral neuroglia—*neuro-gliomatosis peripherica*—and not a generalised neurofibromatosis, (a name improperly given to the Recklinghausen's disease), due to an anomaly of the mesenchymatous tissues and therefore in relation to other congenital deformations; (b) the psychic troubles observed in this disease are very slight and concern the intelligence and memory which become deficient. There are no real mental troubles; (c) the osseous dystrophias in this disease are also very slight, the patient being generally of small size or showing deformation of vertebral column.

There may be some association with disendocrine syndromes and this has led some authors to the conclusion that internal secretions are disturbed in the course of the disease, whilst others claim that the serious osseous troubles, going so far as the decalcification as in osteomalacia, rightly suggest the glandular origin of the disease (ovarian or testicular, hypophyseal or thyroid deficiency).

More frequent, however, are the clinical forms, where two cardinal symptoms or even one only may appear—often the nervous tumors are lacking and the affection is characterised by the existence of *naevi molluscum* associated to cutaneous pigmentations; sometimes, the cutaneous spots co-exist with neurones, or the *naevi molluscum* with neurones.

The beginning of the disease occurs in childhood or adolescence (exceptionally late forms in adults are found), does not interfere with a long survival even when the pathological elements do not show any tendency to regression or cure. Death may occur either on account of a sarcomatous degeneration which, according to HOFFMANN and THOMSON, is rather rare, but not exceptional, or through infectious phenomena.

In certain cases, nervous anomalies are found in the hereditary anamnesis of the patients (epilepsy, idiocy, mental retardment) which seem to

play an important role in the genesis of the disease. Heredodysphilia should also constitute an important etiologic cause, as some psychic and dystrophic anomalies are attributed by authors to the action of the toxoplasma.

Our case, a monosymptomatic clinical form of Recklinghausen's Disease—Differential Diagnosis.—In our case, the cutaneous and sub-cutaneous syndromes are very clear, but the psychic troubles and osseous dystrophias are lacking. We are, therefore, dealing with a monosymptomatic clinical form of Recklinghausen's disease—as confirmed by the histopathological report on the biopsy of one of the tumors.

Anyhow, the existence of such tumors may be due to other causes and we will try to make a clinical differential diagnosis with other syndromes which may give a similar pathological appearance.

1. *Lipomata*:—Rarely congenital, appear generally during the adult age. When multiple, they are frequently symmetrical, and are constituted by polylobular masses, of a rather pasty consistence. Not being painful, they cause, however, a disagreeable sensation to the patient when pressed by palpation. They are generally well limited by a capsular membrane.

2. *Cysticercosis*:—When superficial, the vesicles take the form of small roundish nodosities, subcutaneous but adhering to the skin—the tumors are much smaller, and show a characteristic localisation, viz., in the anterior chamber of the eye; finally, this disease has a rather peculiar geographic distribution (Germany, Poland, Rumania, etc.).

3. *Cold abscess*:—Generally of a tuberculous nature, ossifluent, having its seat near a bone or articulation. Indeed, it is not from this type of abscess that confusion may arise, but from a "*subcutaneous tuberculous cold abscess, apparently primitive*" whose seat is anywhere in the body and which may be only differentiated by the general characters of cold suppurations which are frequently bacilliferous and by the inoculation of the pus to guinea pig. Such confusion is not, however, possible when the cold abscess, after its adhesion to the skin, arrives to the stage of ulceration, evacuation and fistulae formation.

4. Finally, the *nodular disseminated form of sporotrichosis* showing liquid tumors, of a torpid evolution analogous to that of cold abscesses. The softening of the nodule is progressive in sporotrichosis, occurs after a certain time, may be exteriorised by a central depression at finger pressure and the pus contains *sporotrichum beurmanni*.

All these hypotheses having been eliminated, our patient is diagnosed as suffering from Recklinghausen's disease.

Cause of the Dyspnea of our Patient.—But how to explain her intense dyspnea which gave her that outlook of permanent depressive anxiety? Were we in the presence of some thoraco-pulmonary alterations caused by the disease itself or by some coexistent pulmonary pneumophatia?

Let us come back again to the history of the patient: when we observed her for the first time, she had said that she was practically always apyretic, but pressing forward the questions, we knew that the absence of fever was intermittent and that sometimes her temperature was slightly above normal; that, despite her intense dyspnea, the accesses of cough

were not accompanied by expectoration, which was nil; her general state was fair in spite of her meagreness. On auscultation, we found the respiratory signs slightly altered, rough and dull, with some ronchi and crepitations. The discrepancy between the physical signs and the intense dyspnea, led us to find out the solution in bacteriological—as we were induced to believe that it was due to a more or less serious impregnation by Kocks bacillus—which was negative as it might be expected—or in radiological examinations.

While awaiting the results of both these examinations, we made a revision of what is known on the thoraco-pulmonary alteration due to peripheric neurogliomatosis. As it is well known, during long time, in this disease, importance was not attached but to the cutaneous alterations. Later on, came the idea of seeing what occurred in the nerves deeply situated and today, by means of radiological exploration—which, on this case also, was done with this purpose—it was possible to observe with detail the osseous alterations accompanying the neurofibromatosis. So, the neurinomata, provenient of intercostal nerve, give rise to the appearance of "tumors on thoracic wall" and such tumors, as they grow with preference in the interior of the thorax produce a corrosion in the neighbouring ribs.

Such is not the case in our patient, as can be seen in the X-ray images.

The hypothesis of tumors provenient of the nerves of pulmonary hilar region, however not impossible, was not probable in our case as, according to SCHILLING and PERGER, such tumors, owing to their development in the interior of the lung, could only give the radiological image—but not the clinical aspect—of hydatid cysts, whose roundish and well limited form is so different from bronchial neoplasm. Clinically, the short expectoration which accompanied her persistent cough, had never been hæmorrhagic, as it occurs in pulmonary tumors; neither the dyspnea of asphyxic type of our case had any resemblance with the habitual dyspnea of pulmonary neoformation. Finally, no phenomena due to vascular or recurrent nerve compression were observed, neither the least effusion in pleura, indicating a propagation to or an irritation of this serosa.

Radiographic Image.—The radiographic image confirms our opinion as far as concerns Recklinghausen's disease, and gives some interesting elements not only on this disease but as well as on the concomitant pulmonary stage which caused the patient's dyspnea.

The cranial radiography shows the cella turcica increased, the destruction of the posterior clinoid processes and of the dorsum of the same cella. On lateral radiography, a kind of finger impressions are noticed showing the increase of intracranial pressure (Rad. I).

The radiography of dorso-lumbar column does not show any kyphoscoliosis neither osteoporosis of vertebral bodies. A myelography which was done showed that the Lipiodol stopped at the level of the first sacral vertebra—a normal myelogram. The hypothesis of any neurinoma which might cause the detention of the contrasting substance or the corrosion of vertebral bodies was excluded.

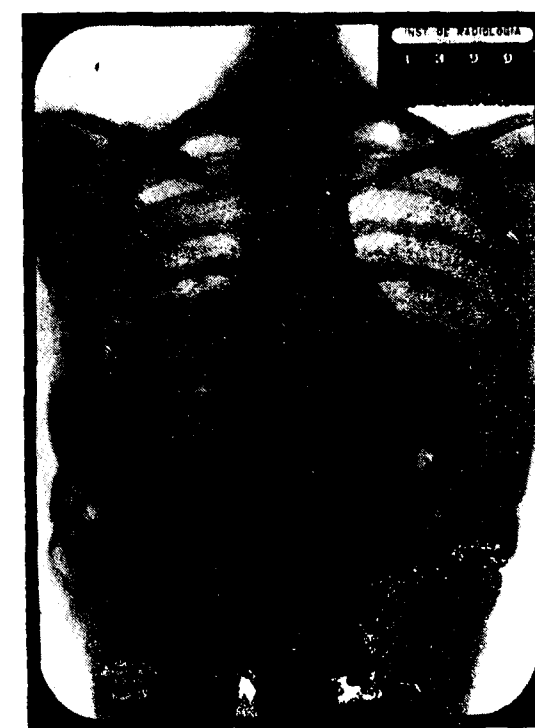
The thoracic radiogram shows: (a)—no tumor on the thoracic wall.

A Case of Recklinghausen's Disease Complicated by Cold Granuloma

By Dr. A. de Sousa e Faro, and Dr. Soares da Veiga.



Rad. I.
Increased cella turcica,
Destruction of the posterior
clinoid process and
of the dorsum of the same
cella. A kind of finger im-
pression showing the in-
crease of intracranial
pressure.



Rad. 2
Miliary Tuberculosis

A Case of Recklinghausen's Disease Complicated by Cold Granulia*By Dr. A. de Sousa e Faro and Dr. Soares da Veiga.*

Rad. 3.

Thickening of the periosteum, nodules of hyperostosis and slight osteoporosis of the upper third of bones of the right leg.



Clinical Photograph.



Clinical Photograph.

neither any destruction of ribs in connection with such tumors; (b)—in in hilar region no image supporting the presence of tumors of the nerves of the same region (note that such tumors show the characteristic aspect of roundish and well limited formations, as drawn through a compass and with an uniform tonality resembling that of true hydatid cysts; (c)—the aspect of the tele-radiography in our case is that of small roundish shadows some of a strong density, alternating with others less dense; on the base of the right lung some nodules, similar to those above described, lose however their roundish and miliary outline and appear under the form of nebulous shadows. On the right hilar region, there are small cavitary spots with funicular appearance (*funicular images of Shinz*).

The left hemidiaphragm shows the appearance of a tent due to pleuro-pulmonary fibrosis (Rad. II).

The pelvic bones do not show any abnormality. The lower members show on the superior third of the bones of the right leg strong thickening of the periosteum, nodules of hyperostosis and slight osteoporosis. (Rad. III).

In conclusion: the bony lesions found in our case are: turcic cell destruction, periostitis osteifaciens, local hyperostosis, and osteoporosis. There is, moreover, the aspect of a miliary infiltration-granulia in the lungs,

We are, therefore, dealing with a case of granulia, developed in a patient of neurofibromatosis: let us see what clinical type does this granulia belong to.

Granulia, Its Clinical Types.—The study of granulia was very easy sometime ago as, basing on the classical conception, all our knowledge on the matter was considered definite.

But, since the facts were examined with more detail by the clinicians, together with the study of histological and radiological elements, our ideas on the disease began to lose their primitive precision. Anyhow, what exists indeed is a slight discrepancy which concerns more the words than the facts, as will be seen below:

The generalised granulia has been considered for a long time—as is done even now by some authors—as “resembling more closely to an acute infectious disease than to the pulmonary tuberculosis” and produced by a “sawing of granulations” in different viscera, characterised by the outburst of very serious general symptoms (typhoidic evolution) causing death in a short time (4 to 6 weeks).

The pathogenesis of Empis' disease is attributed to a generalisation through the blood vessels. Anatomically, the fundamental lesion—granulation—possesses also special characteristics: its dissemination occurs, more or less regularly, in different viscera; its localisation is interstitial, occurring thus in the conjunctive spaces, near the vessels; its aspect is follicular, hence constituted by an aggregate of giant cells. In itself the clinical aspect offers an unusual intensity of symptoms and the prognosis is very severe.

According to the old conception, at the site of the generalised granulia of Empis with acute typhoidic evolution, there are “localised forms” reaching exclusively or at least pre-eminently such or such viscera, specially the lung. It is in such a case that the granulia provokes the

apparition of acute functional signs which do not correspond to the habitual poverty of physical signs; this particular form has been named "*acute tuberculous asphyxia*" Needless to say that some authors contest the existence of these localised forms and others consider them as peculiar affections to be clearly separated from the true generalised granulia.

More recent Conceptions.—In modern science, there is agreement only concerning pathogenesis which all accept to be through the blood current and for BEZANCON "this aetiological definition would be the best". The views on the clinical aspects of the disease are not uniform and on the histopathology, nothing agrees with the teachings of the classical doctrine. For a better comprehension may we remind that the two great processes of the development of tuberculosis viz "the pneumonic lesion (or exudative) and the follicular lesion (or productive)", are defined by their histopathological characters and by their topography.

Histopathologically, the follicle—as already well known—is constituted by a small caseous, and bacilliferous centre, surrounded by a crown of nuclei whose origin has been much discussed, and all this circumscribed by a double zone of epithelial and lymphoid cells. Its topography is also very characteristic, as it shows a remarkable affinity for the interstitial elements of the lung, hence for the interacinous and interlobar septa, mostly on the neighbourhood of the vessels—reason why the *follicular tuberculosis* is also named *vascular or interstitial tuberculosis*. On the contrary, the pneumonic lesion, at least in its beginning, is essentially an exudative bronchoalveolitis, fibrino-leucocytosis, comparable to a local pneumonia from which it differs by a fundamental character: its tendency to a caseogenous necrobiosis, reaching firstly the elements of the exudate and simultaneously, or later on, the endothelial cells of the alveoli, extending further on the interstitial septa and the elements contained therein.

So, it must be concluded, that the tuberculous follicle shows a clear preference for the interstitial elements, while the pneumonic process attains firstly the respiratory elements.

After these statements, let us see what BEZANCON, LETULLE and BRAUN have observed at the microscopical examination of the micronodular foci in the lungs. Two types of lesions were seen: (1) tuberculous granulation, of follicular type and interstitial topography: (2) miliary tubercle representing a minute focus of bronchoalveolitis, a true pneumonia in miniature (the pneumonic nature of certain miliary lesions had already been stated by TRIPIER). On the basis of these purely histological statements, the authors found themselves authorised to describe two varieties of tuberculosis of micronodular disseminated foci: "*the true granulia*" characterised by the tubercular granulation, and "*miliary tuberculosis*" characterised by the miliary tubercle.

Objections of Rist and his School.—However, RIST and his school, confirming the existence of both these species of granulations, and accepting to a certain extent, the well-founded remarks of the precedent authors, demonstrated that it was not advisable to base only on histological statements and bring the extremism to the point of creating on such base two varieties of tuberculosis of micronodular foci, as generally, both these types are associated, and it is very frequent to see the coexistence of

both tuberculous granulations and miliary tubercles. Still more interesting is the statement of RIST that certain cases take the mask of a pneumonic, exudative type, not only in cases of pulmonary localisation, but also in those of typical generalised granulia.

More recently, BENZANCON and DELARUE admit the polymorphism of micronodular lesions and leave aside the designation "granulation and tubercle" to use the expression "*miliary nodule*", justly to give the idea that there is an unity among the micronodular tuberculous lesions: So, the histopathological lesions should be (1)—a *miliary follicular nodule* (corresponding to the old tuberculous granulation); (2)—a *miliary exudative nodule* (corresponding to the old miliary tubercle) and (3)—a *fibrous miliary nodule* a form of senility or better of cicatrisation of the above forms. These authors even believe that these different types correspond, indeed to the different ages of the same nodule, the exudative type being younger and most frequent in acute types, the other nodules being older and found in resistant clinical forms (one must not forget that some authors hold that the histological variety is attached to the stage of the resistance of the organism, specially of its allergia).

Concerning the localisation also, there is not a perfect agreement with the old conceptions, as, in many cases, the follicular granulation may be intra-alveolar, while the exudative process invades the interstitial spaces.

Clinical Classification of our Case.—Notwithstanding the lack of agreement on the clinical aspects of granulia, let us try to classify our case.

The classical granulia or Empis' disease is characterised mostly by its pathogenesis—sudden and acute dissemination through blood vessels,—and by the clinical aspect that is not found in our case. In Empis' disease, according to French and German authors, the granulation in the lungs belongs to the type of minute exudative foci, whose frequency is as great as the case is more acute.

In some cases of micronodular disseminated foci with or without fever, there is a small effusion of pleuritic liquid, on one or both sides—special anatomical forms with a great histological polymorphism, and not liable to generalisation. Such is not our case.

There are finally cases, of a rather torpid evolution, where the occlusion of micronodular tuberculous lesions occurs more or less regularly in the lungs, but with a general state more or less satisfactory. The physical and functional signs are discrete and as the fever may totally lack, such cases are improperly named *cold granulia*. The micronodules are disseminated in the lungs but show different evolutionary stages, corresponding to their different ages: so, a great polymorphism is seen (productive, exudative, fibrous and mixed nodules). Among these lesions, fibrous formations are seen (hence the designation *fibrogranulic lesions*), which never occur in children. Often a cicatricial nodule, a torpid or active cavern, true focus of dissemination, is noticed, hence sometimes bacilli in the sputum. In such a case, the diagnosis is arrived at through radiology and, such has been our case where, by lack of general symptoms, the intense and rather suffocative dyspnea was certainly due to the fibrous element.

Excepting in children, where the cure is frequent, the constitution of a

radiological image of *cold granulia* is extremely severe. Our patient died soon after.

The patient belonging to our private practice, it was not possible to push further the anatomo-pathological study of the case, by post-mortem records.

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Triple Hernia in an infant of about one month

BY

P. K. DAS, M.B., D.P.H. (CALCUTTA), L.O. (MADRAS)

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MOTHER of a Lashi baby observed, on the 6th day of the birth of the child, swelling of the left scrotum. She thought it to be an insect bite. But when she noticed that the swelling sometimes disappears but reappears and increases in size on crying or during defæcation, a doctor was consulted who diagnosed it to be a hernia. After 4/5 days, the same doctor was again consulted, when the mother noticed a similar swelling on the right scrotum and the doctor found it to be hernia. I was consulted on the 28th day of the birth of the child, when the mother noticed another similar swelling a little to the right of the umbilicus. I found that there were 3 hernias—two inguinal and one umbilical. The inguinal rings were very big, the intestine comes down through both the rings generally at the same time, when the child is kept in standing posture for 5/7 minutes, by the movements of the child's hands and legs.

The general health of the child is poor and there was no other congenital defect.

I am reporting this case as triple hernia is very rare.

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in the matter of Drugs and Medicine and unless the Government of India put forth their heart and soul and start or subsidize Pharmaceutical Industries in this country, and take the fullest advantage and opportunity which the War has given, the same old trouble will continue and the "Drug Act" will be in practice, a "Dead Act".

It will not be out of place, here, if we venture to offer a few remarks on the Indian Medical Council. Ever since the nominated official President was replaced by an elected President in the person of Dr. B. C. Roy, the Council is animated with a feeling of dignity and self-respect and is endeavouring its best to raise its head and tear itself off from the shackles of the British Medical Council. We have very recently in our December '40 issue, alluded to the various handicaps with which it is tied up and the measures taken by the Council to secure its freedom, and we hope ere-long, it will realise its objective and negotiate, in regard to reciprocity, as an equal with the other Medical Councils not only of the British Commonwealth but of those of the rest of the world.

During 1940, "The Antiseptic" true to its programme, brought out three special issues, (1) on Genito-Urinary Diseases, (2) On Diabetes and (3) On Respiratory Diseases. In the absence of any adverse criticism or comment, we must presume that they have all been well-received.

By way of prospect, we have only to say, that despite the present unsettled conditions of the world with regard to paper and other printing requisites and fall in advertisements, we have decided to carry on, bringing forth three more special issues, as in the past.

We seize this opportunity and offer our heart-felt thanks to all our subscribers, advertisers and contributors for all the forbearance, patronage and loyalty, they have shown us in the past, and wish them all a happy, peaceful and prosperous NEW YEAR.

Medical Men in Conferences

DURING the week-end of December last year (1940), three separate Conferences of medical men in India, were held at three different centres, (1) under the auspices of the Indian Medical Association at Vizag, (2) of the All-India Medical Licentiates' Association in Bombay and (3) of the Licentiates of Indian Medicine, at Madras. It is indeed deplorable that no common platform could be found for all of them, at least for the first two of them, which would have meant a saving of so much of time, money and energy and which would have brought about a solid, united body of medical men, standing shoulder to shoulder, and pressing the powers-that-be for the conferment of their due rights and privileges. Dr. K. S. RAY, in his admirable presidential address delivered at the Conference of the Indian Medical Association at Vizag, which covers the whole range of Medical Politics and which none but a close student of Medical Politics like him could ever produce, had emphasized this aspect of the question when he said: "Apropos of my remarks on expansion, I feel I must say a few words on the question of amalgamation of our two Associations—the Indian Medical Association and the All-India Medical Licentiates' Association. It

is a consummation devoutly to be desired. The accession of strength to the amalgamated body would render its influence almost irresistible. No medical man could afford to remain outside its membership, no authority could fail to give it ear."

We have, times without number, advised, in the columns of the Antiseptic the fusion of these two bodies and we are at a loss to understand what stands in the way of its accomplishment. The Indian Medical Council, whatever might have been its past prejudices against the Licentiates, has, since it came under the dynamic power and influence of its present President, Dr. B. C. Roy, cast off those prejudices and are out and out for a compromise. This is evident from the following utterance of Dr. K. S. RAY: "In the words of the late SIR FAZLI HUSSAIN, these objects (of the Indian Medical Council) were to secure 'efficiency at home and honour abroad'. So far as efficiency is concerned, although the Council claims that the object is now on the way to fulfilment as most of the Indian Universities are following the curriculum laid down by it, in my opinion, efficiency cannot be complete unless the training of 80% of the medical practitioners in India, viz., the Licentiates who do not come under the fold of the Council is also raised to the uniform standard laid down by it." The Licentiates are also desirous of a compromise, as can be judged from the short and sweet welcome address of Dr. U. B. NARAYANA RAO of Bombay. It is high time, therefore, that our Licentiate brethren should seize this opportunity and grasp the hand of friendship extended by the graduates and merge the Licentiates' Association into the larger body of the Indian Medical Association and present a united front for the amelioration of their lot.

Another noteworthy point in Dr. K. S. RAY's address is the stress laid on Medical Research in India. Despite huge sums of money spent annually for research work in medicine under the Indian Research Fund Association, 'there is hardly any work of outstanding merit which can be held out before the world as epoch-making or as creating a landmark in the Science of Medicine'. We agree with Dr. RAY when he says that, 'if genuine workers are to be attracted to this Fund, the stuffy official-controlled air of the place must make room for a freer atmosphere'. His appeal to the rich and well-to-do and to the philanthropic people of India to endow their charities for research in medicine is timely and we trust will not be lost on them.

Dr. RAY is enthusiastic on two other points about which mention must be made here, viz., (1) the compilation of an Indian Pharmacopoeia and (2) the introduction of a system of compulsory Health Insurance. These are really laudable objects which deserve the closest scrutiny and attention not only of the medical profession but also of the general public and the Government.

With regard to the Ayurvedic and Unani systems of medicine, Dr. M. R. GURUSWAMI MUDALIAR, who opened the Conference of the Licentiates of Indian Medicine, in Madras, observed: "What we have got now of the Science of Ayurveda is only a compilation of fragments picked up here and there by clear-headed and patient workers in the field. It is only part of the knowledge that was at one time prevalent. It is our duty, therefore, that we once more take up the task of improving knowledge from

whatever source it might be". This is a clear indication of the imminent need for delving into the hoary past and discovering the hidden treasures of Indian Medicine, thus setting up a basis for the compilation of a complete Indian Pharmacopœia, which would be a happy blending of the two systems of medicine, •Allopathic and Ayurvedic or Unani. Dr. GURUSWAMI MUDALIAR went even further and said that in the treatment of human diseases, the stars and planets should also be consulted, as they exercise a potent influence on human beings. The welcome address of Dr. (Miss.) K. V. LAKSHMI BAI is constructive and thought-provoking while the presidential address of Dr. SHAKOOR SAHIB sets forth the various grievances of the L.I.M.'s, requiring immediate attention and redress at the hands of the Government.

GLEANINGS FROM MEDICAL PRESS

Medicine and Therapeutics

Some Basic Principles in Leprosy Treatment.—E. MUIR writes in the *Leprosy Review*:—

In any well-established case of the leprosy of the lepromatous type, treatment must aim at two objectives: (a) to strengthen and stimulate the cells to act more vigorously, and (b) to break down the triple defence of the bacilli. Care and restraint must be exercised, however, in bringing about the latter, and it must be carried out gradually and only in proportion as the cells have been stimulated and strengthened to deal effectively with the bacilli set free and brought into close contact with them. Otherwise, the bacilli are likely to be carried to a distance and form fresh foci and thus extend the disease.

Keeping in mind these two objectives and the proviso that the bacillary triple defence must be broken down only with care, let us examine the various possible remedies and procedures for the treatment of leprosy.

1. *Stimulation and strengthening of the cells*:—In considering this we should be helped considerably if we knew the reasons underlying the immense difference referred to above between individual patients and the degree of their cellular reaction and resistance to invading bacilli. Is the degree of resistance hereditary? Is it dependent on the degree of infection especially in early childhood? To what extent is it affected by the condition of endocrine glands such as the supra-renal or thyroid? The writer has seen a slight but long-standing single lesion become negative and disappear under thyroid treatment in a few weeks time.

Of one thing there can be no doubt, that the general health of the patient profoundly affects his resistance to the disease. Deterioration of health not only favours the spread of formerly stationary lesions, but it not

infrequently results in tuberculoid lesions degenerating into those of the lepromatous type. On the contrary, it is seldom that a lepromatous case recovers (at least without serious deformity) unless he has continued for a considerable period in uniformly first class health.

The appearance in the neural type of leprosy of what is commonly known as the 'major tuberculoid lesion', which especially in its more outstanding form is of the nature of a suddenly sensitized minor tuberculoid, is frequently followed by complete healing of the lesion or lesions which resolve and leave only scars. This apparently allergic phenomenon seems to correspond to extreme activation of the local cells, enabling them to destroy the comparatively few bacilli present.

We know very little of the action of the most widely used remedy in leprosy—chaulmoogra oil and its derivatives. There is no reliable evidence that it acts directly on the bacillus. Does it activate the cells to destroy bacilli? When injected intradermally into skin lesions there is little doubt that it stimulates the cells locally; but what about its more generalised action? These are questions awaiting further investigation.

Local applications to the skin have the effect of stimulating the phagocytic cells and at the same time of freeing the bacilli and bringing them in contact with the cells. Unna in an article strongly advocates the vigorous use of various types of applications. He recommends iron baths, beginning at a temperature of 30° C and gradually heating; hot douches; friction with oil; ironing the skin with a hot iron, the skin being protected with a layer of flannel. These forms of treatment can be repeated day by day to different parts of the skin surface.

Various kinds of caustics can be used. One of the commonest is the application of a 1 in 3

solution of Trichloroacetic Acid. Carbon dioxide snow is particularly valuable in elevated nodules. One of the methods recommended by Unna was shaving off the outer parts of the skin, including nodules, with a razor after freezing with ethyl chloride. Cotton swabs soaked in a styptic are then applied and are fastened on with plaster. The next day the same part is again frozen and a caustic is applied. A small part of the nodular surface is thus dealt with daily. In ulcerating nodules, as distinct from trophic ulcers, a useful form of treatment is daily painting with 1 in 3 Trichloroacetic Acid till the leproma is absorbed and epithelium begins to grow at the edge.

Pressure is another form of local application useful in reducing at least the grosser forms of lesions. It can be applied by means of elastic bands, elastoplast or split bicycle tubes. Unna recommended applying pressure over a dressing of zinc oxide and glycerine.

As mentioned above, intradermal injection of hydnocarpus oil or its preparations forms a useful method of stimulating the local cells apart from any more general effect that the absorbed oil may have.

To get good results a combination or alternation of these forms of local treatment may be used, but passive applications should always be accompanied by active exercises. In the Mkambati Leprosy Institution in South Africa, where unusually good results are obtained, the patients spend a considerable time every morning in bathing, inunction and various applications, and carefully regulated exercises; these are all done communally and under expert supervision. This is in addition to agricultural work in which they employ themselves for much of the rest of the day.

Active physical exercises have the effect of improving the metabolism and the general health. At the same time they can be used to prevent and remove the deformities of hands, feet and other parts of the body. Removal of dead bone in the feet, hygiene of the nose and the gums and teeth, care of early lesions of the eyes—all these are of the highest importance; failing them, the patient tends to become immobilized and his general resistance deteriorates in consequence.

None of the above recommendations are likely to be of much value unless they are backed by satisfactory nutrition. Not only must the diet be carefully balanced and regulated, but accompanying diseases which interfere with nutrition must be sought out and removed.

2. *Breaking down bacillary defence*:—Both the passively received applications and the active exercises mentioned above, if carefully and skilfully regulated, have the effect of strengthening and stimulating the cells and of breaking down the triple defence mechanism of the bacilli so as to bring the latter in contact with the cells judi-

ciously and only in such numbers as they are able to deal with effectively.

It should be mentioned here that we have a drug in our possession which has a specific effect in breaking down the defence mechanism of the bacilli—potassium iodide. This drug has been used from time to time, and as often abandoned on account of its dangerous qualities. In some lepromatous cases even a fraction of a grain has the effect of causing an acute generalized reaction with febrile symptoms, swelling up of leproma of skin, mucous membranes and nerves; though in most cases larger doses are necessary to produce such an effect. The liver, testicles, lymph nodes and any part of the body where masses of bacilli exist are liable to take part in the reaction. Iodide does not appear to have any effect on single bacilli, and large doses may be given without reaction in cases of the neural type with tuberculoid lesions in which, on careful examination, only single bacilli or occasional clumps of two or three are found with difficulty. In apparently neural cases, however, it may cause reaction in affected nerve trunks, presumably because they contain large clumps of bacilli. It would appear that iodide has the effect of dissolving or breaking up the mucoid glue referred to above, which surrounds the bacilli and helps to isolate them from the surrounding living tissues. How it acts we do not know; but apparently it is not by direct action. For no reaction results from injection of iodide solution direct into leproma in a strength far in excess of the concentration that can be produced in the tissues by giving large doses by the mouth. Iodide can be used safely in the following two categories: (a) In lepromatous cases with first class physique in whom the bacilli have been reduced to such small numbers that repeated routine examinations of skin and mucosa fail to find them. In such cases the administration of iodide in increasing, carefully regulated, doses breaks up the defence mechanism if the bacilli in residual foci show their presence by causing local nodules or macules, and enables the activated cells to destroy the broken up clumps; (b) In lepromatous cases with good general health, but with a fairly large infection as shown by microscopic examination use minute fractional doses beginning with one-tenth of a grain or less, to be repeated, it may be a week or a month later, only when all signs of reaction from the last dose (including rise in sedimentation rate) have passed away, and raised in amount only when the previous dose fails to produce any appreciable reaction. The essential is that bacilli should not be set free and brought in contact with the living tissues in greater numbers than the cells are able to destroy.

Much has been written in recent years about treatment of leprosy with various dyes such as mercurochrome, methylene blue, trypan blue, fluorescine, etc. The way in which these dyes act when given in repeated doses over a considerable period is illustrated by the following case of advanced

lepromatous type and many years standing. The treatment consisted of fluorescein 10 grains a day for seven months, methylene blue 4 grains a day for six months, and trypan blue 4 grains a day for over one month. These were given in the order mentioned, occasionally being discontinued for a few days. The lepromatous areas both cutaneous and subcutaneous showed intense staining and later began one or more at a time, to become inflamed and to suppurate. After discharging pus full of acid-fast bacilli each area in turn died down, leaving more or less marked scars. The same process occurred in the nose, mouth and throat. From time to time there was severe gastro-intestinal disturbance which suggested that a somewhat similar occurrence was taking place in internal leprosy. The patient began to cough up large quantities of pus apparently from the trachea. So severe was this condition on one occasion that his life had to be saved by an emergency tracheotomy; but after he had worn the tube for a few months it was possible to dispense with it. During this period the patient was having almost constant fever. One eye had been destroyed some years previously and the other eye was badly infected and had very little vision; this now became entirely destroyed. Gradually the leprosy, which had involved both skin and subcutaneous tissue over large areas of the body, disappeared leaving only scars; fresh inflammatory areas ceased to appear and the patient, though blind and crippled, appeared to have either discharged or absorbed the entire infection within a period between two and three years. His health recovered, his appetite was good, and he slept well.

I cannot recommend massive treatment with dyes. Former reference has been made to similar results from prolonged treatment with mercurochrome. Smaller doses do not appear to have a curative effect and doses sufficient to cause evacuation of leprosy are apt to be extremely dangerous. It would seem as if extremely concentrated dye in leprosy acts as an irritant foreign body and results in its own evacuation, the bacilli and the remainder of the leprosy sharing in the process. The action of dyes given in small doses over a short period to control leprosy reaction is a different matter; used in this way they are safe and of considerable value.

We are able with available treatment to control neural leprosy if diagnosis is made in time and the patient is willing to cooperate. What is most required is a means of activating the cells in early lepromatous cases before the disease has progressed to the stage of the patient described above, in which treatment with chaulmoogra and other remedies is seldom successful. Attempts at immunization in lepromatous cases by injection of lepra bacillary emulsion have been found useless; indeed the multiplication of lepra bacilli in the tissues has an inactivating rather than an immunizing effect.—*Leprosy Review.*

Sulfathiazole in Bubonic Plague.—Sokhey and Dikshit found sulfathiazole to be effective for plague in mice. Sulfapyridine also had some action. In human cases of plague the most important factor which decides the issue is the development of septicemia. Septicemia develops in mice from forty-eight to seventy-two hours after the induction of infection by the subcutaneous route. Therefore the authors started the administration of the drug at four different stages of the infection: at the time the infecting injection was given and twenty-four, forty-eight and seventy-two hours later. Twenty animals were used in each experiment. The mice were observed for at least thirty-one days. Plague organisms were never found in the organ smears and blood cultures of animals dying during the period of administration of the drug, but they were found in animals dying after the drug had been stopped, the only exception being in the experiments in which sulfapyridine was given in 10 mg. doses once a day for ten days. In this case some animals which died during the period of administration of the drug showed the presence of plague organisms. In human plague spontaneous recovery invariably results if the lymph glands prevent the spread of infection to the blood stream and the infection remains localized. The occurrence of such cases in different outbreaks is from 20 to 50 per cent. If the organisms pass the lymph glands and a septicemia results, death invariably follows unless an effective agent can be given to control the infection. The effective agent must be given before extensive destruction of the tissues of the organs has resulted. When the mice were given the drug before septicemia had set in, that is before forty-eight hours after infection, as little as 10 mg. of sulfathiazole twice a day for ten days saved nearly 80 per cent of the infected animals, and even better results were obtained by doubling this dose. Sulfapyridine produced about the same action as sulfathiazole in the early stages of infection with doses of the same order. When the administration of the drugs was started after septicemia had set in, a dose of 20 mg. of sulfathiazole twice a day for ten days cured approximately 80 per cent of infected animals when the drug was given forty-eight hours after infection and 65 per cent when given seventy-two hours after infection. Doubling this dose produced even better results the survivals becoming 90 and 80 per cent, respectively. These results are as good as those obtained with the Haffkine Institute antiplague serum. It is in this group of animals that sulfathiazole shows much more definite curative action than sulfapyridine. With the largest dose employed (40 mg. twice a day for ten days), when treatment was started forty-eight hours after infection, sulfathiazole cured 90 per cent of infected animals, whereas sulfapyridine cured only 10 per cent. Similar results were obtained when treatment was started seventy-two hours after infection. Since plague is much more severe in the mouse than in man, it is

hoped that sulfathiazole will prove even more effective in human infection.—J.A.M.A.

Status Asthmaticus.—WELL and CLIMO cite seven cases of status asthmaticus treated with sulfanilamide. Six of these responded promptly by rapid relief of symptoms. In the exception the sputum showed a preponderance of pneumococci but after treatment with sulfapyridine relief was prompt. One of the patients with chronic bronchitis and emphysema had staphylococci in his sputum but nevertheless he responded to sulfanilamide therapy. In this type of case sulfathiazole might be expected to give better results. The authors do not suggest that sulfanilamide and its derivatives will relieve all cases of status asthmaticus or that they will actually cure asthma. There may be cases of status asthmaticus which result from an overwhelming contact with some extrinsic substance of antigenic quality in which they do not know what effect sulfanilamide may have. In cases of status asthmaticus which result from respiratory infection, sulfanilamide and sulfapyridine seem to offer the possibility of dramatic relief. The authors do not yet feel certain about the optimal dose of sulfanilamide and its derivatives. They have used the following schedule for adults: 20 grains (1.3 Gm.) every six hours for two days, 15 grains (1 Gm.) every six hours for three days and 10 grains (0.65 Gm.) every six hours for seven days. There is still a question as to how long treatment should be continued. It is not known whether this method will be as efficacious in cases of chronic bacterial asthma or so-called bronchitis with asthma, even in the absence of status asthmaticus. The principles underlying the two conditions are similar and should respond to similar therapy. This method of treating status asthmaticus may afford relief to some patients with less prolonged hospitalization and less expensive medication than has been possible in the past. When the indications for the use of these drugs, the proper dosage and the duration of treatment have been well established, the outlook for the asthmatic patient may be improved considerably and the late complications of asthma—chronic bronchitis, bronchiectasis, emphysema, pulmonary fibrosis, cardiac hypertrophy and myocardial damage—prevented.—J.A.M.A.

Serum Sickness in Diphtheria.—Hertel reports the drastic decrease (from a preceding average of 17.4 per cent. to one of 3.7 per cent) in serum sickness complicating diphtheria observed during the course of nine and a half years and coincident with the adoption of a combined intravenous and intramuscular injection procedure, supported by a regimen of fruit and vegetable juices and daily enemas. The study was confined to 1,095 consecutive cases of diph-

theria exhibiting 135 instances of serum sickness, three fourths of which occurred in children under 14 years of age. The greatest incidence of serum sickness was observed during the months of January, February and March. It was treated by slowly administering intravenously from 2 to 3 cc. of serum solution (from 2,000 to 3,000 international units) followed by intramuscular injections. The treatments were seconded by a complete withdrawal of the usual food, replaced by abundant juices. Twice daily enemas medicated with glycerin were administered. Istizin was given as a laxative. Subjective symptoms such as pruritus usually disappeared within twenty-four hours. Treatments were continued for three days after the cutaneous manifestations had disappeared, a vegetable and fruit diet bridging over the next two days before normal food ingestion was resumed. Recurrence following the violation of dietary directions promptly yielded with a return to the regimen. The author attributes the success of the therapy to the two phase injection plan, to vitamin C replenishment by vegetable and fruit juices of the seasonally impoverished system and to detoxication through intestinal washing out of bacteria. The increasing incidence of serum sickness with age may confirm bacterial implications. He believes that the therapeutic aids usually employed for controlling serum sickness involve needless distress to the patient and should be replaced by a more physiologic regimen.—J.A.M.A.

The Treatment of Alcoholism.—Formerly heavy drinking was considered to be a mode of behavior that was a unit in itself, and concerned morals rather than physical medicine. Today the physician approaches the problem from both a physical and psychiatric point of view.

Acute Alcoholism.—The degree of the acute effects of alcohol on the human body is in proportion to its concentration in the tissues. When the concentration of alcohol in the blood reads 500 milligrams per 100 c.c. of blood, respiration is slowed to a dangerous degree.

When alcohol is taken by mouth, it is distributed throughout the body, and in a uniform manner according to its solubility in the various kinds of tissues. Its effect depends on its concentration in the tissues. A given amount of alcohol will therefore affect a 125-pound man twice as much as it will one weighing 250 pounds.

When alcohol is taken on an empty stomach, it is absorbed with greater speed than when it is mixed with food. Fatigue, exposure, recent infections, and general debility increase the susceptibility to the intoxicating effects of alcohol. Also a certain amount of tolerance is acquired by habitual drinkers.

The characteristic postmortem finding of acute alcoholism is hyperemia of the gray

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matter, associated with edema and flattening of the convolutions. A chemical analysis of the brain substance is the only approved way to establish the presence and amount of alcohol which it contains.

In uncomplicated acute alcoholic intoxication the principal objects of therapy are:

1. The oxidation of alcohol.
2. The promotion of its elimination.
3. The restoration of depleted water and minerals.
4. Sedation.

Gastric lavage given to a comatose patient may flood the lungs and produce pneumonia. The fatal concentration of alcohol in the blood is 500 milligrams in 100 c.c. of blood. In these cases a mixture of carbon dioxide and oxygen may be needed in order to stimulate breathing. The comatose patient must be kept warm throughout the course of the treatment, for a vast amount of heat is lost through the dilated skin vessels. If vomiting is excessive, the loss of hydrochloric acid from the stomach may result in a severe alkalosis.

The treatment of the "hangover" is not essentially different from that of the acute stage of intoxication. Any of the following drugs is excellent:

1. Soda bicarbonate—50 grains.
2. Saturated magnesium sulphate— $\frac{1}{2}$ ounce.
3. Seidlitz powders—2, together with 10 grains of aspirin.

For the restless patient, excellent sedatives are:

1. Sodium Amytal—3 to 4 $\frac{1}{2}$ grains, or
2. Phenobarbital—3 grains.

If coma persists for twenty-four hours, the prognosis is dubious.

Chronic Alcoholism.—Chronic alcoholism is the state of those individuals whose drinking interferes with their normal activities, occupationally or socially. These patients fall into two groups:

1. The steady drinkers, or "addicts"; and
2. Those who drink only when on sprees. In this latter group psychological problems are dominant, and are benefitted by psychotherapy.

In chronic alcoholism the actual damage to the nervous system usually results from nutritional deficiencies, rather than from the toxic effect of the alcohol itself on the body tissues. There may be a serious vitamin deficiency because of the high caloric value of alcohol. Death may result from a polyneuritis or an acute psychosis.

Medical Treatment.—The main organic damage inflicted by alcohol on the human nervous system is the result of nutritional deficiencies, rather than from the alcohol itself. The immediate treatment requires that the

patient takes a diet well-balanced, and adequate in minerals, protein, and vitamins. Thiamin chloride is useful in doses of 5 to 10 milligrams daily.

Sedatives such as sodium bromide, gr. 15, or phenobarbital, gr. $\frac{1}{2}$ to 1, given three or four times daily may be useful.

Benzedrine, 10 milligrams, twice a day by mouth, produces a mild elation which is usually beneficial.

Psychological Treatment.—It is important to have a line of treatment mapped out, and the patient made ready to undertake it as soon as he is recovered from his acute symptoms. The importance of physical well-being as a fundamental step in promoting mental stability is one of the most basic principles to be applied to patients recovering from uncomplicated alcoholism. The condition of a chronic alcoholic is a mental illness. The pattern of drinking belongs to the realm of symptomatology. One of the chief errors in the past has been to consider the problem of drinking as an entity, without consideration of the patient's total personality. His thoughts, emotions, and reactions must form the material of therapy. The drinking as behavior may then be evaluated in its true significance, and usually as a symptom.

Prevention.—Preventive measures can be easily formulated, but they are difficult to apply. Education of the young may help in certain cases, but there is also the possibility that it may only serve to stress the fact that drinking is a socially approved form of behavior. A rational program of mental hygiene in childhood, along with the warmth of affection and the satisfactions and security of normal family life are the best safeguards against the development of alcoholism. The adjustment to reality, the building of character, and the maturing of a normal personality, are likely to result from these home conditions. The acceptance of life, of things, and of conditions as they are, and the fitting of one's self to them, are the best safeguards against a neurotic character in general, and alcoholism in particular.

Treatment.—The chief danger in selecting cases for treatment lies in the insincerity of the patients. Only from experience can the value of the patient's insight toward himself and the external world be judged. Excessive eagerness for treatment, and unusual co-operation by the patient in the beginning, are not always good signs. In general, the prospective patient must be evaluated in the same way that all neurotic individuals are appraised.

Occasionally the family is the greatest obstacle in the progress of treatment. Often its members must be educated, not only to the present condition, but to the more mature, and often more aggressive, attitude of the patient.

Whether to taper off, or stop drinking

suddenly, is a much mooted question. A slow reduction of alcohol permits the patient to determine his behavior with coercion. Other therapists feel that a complete halt in drinking is a major importance. Some substitute soft drinks or fruit juices.

The wise therapist will not scold or nag the patient, or comment on his condition in any way that suggests moral pressure.—*Journal of the M. Society of New Jersey.*

The Use of Urinary Antiseptics.—By OSWALD S. LOWSLEY, M.D., and WILLIAM E. FORSYTHE, JR., MD.

In the therapy of urinary infections, the following factors must be determined: (1) the type of infecting organism; (2) the presence or absence of faulty drainage; and (3) whether the renal function is adequate to convey the appropriate antiseptic to the desired point.

The infecting organism is usually identified by routine cultural methods, but Buchtel has shown that staining of the centrifuged sediment is far superior to blood agar culture with coccal infections, and almost as good as Endo's medium with bacillary infections.

Cases seen by the urologist are either the very severe or the chronic types of urinary infection; these require an immediate complete urologic investigation in order to determine the presence or absence of urinary obstruction. Corrective measures, if necessary, can thus be promptly instituted. Certainly any patient with urinary infection who has been treated for longer than one month with antiseptics (medical treatment), without clinical recovery, should have a complete cystoscopy with pyelography.

The renal function can usually be satisfactorily ascertained by blood urea nitrogen or non-protein nitrogen determinations. In border-line cases a phenolsulphonphthalein test may give added information.

Numerous drugs have been advocated as urinary antiseptics, but many have failed to stand the test of time. The following must be considered:

1. Water. In many cases water is an excellent antiseptic. Frequently patients will improve spontaneously when fluids are forced.

2. Oil of Santal. Though much less popular than formerly, this is still regarded as a useful drug for the treatment of gonorrhoea.

3. Hexylresorcinol (Caprokol). Some years ago Henline found that hexylresorcinol was a good antiseptic for coccal infections. Since the advent of our present antiseptics, however, it is now little used.

4. Pyridium, Serinium, Niazol (Neotropin), and other Azo Dyes. The dyes are good sedatives for irritation, but poor antiseptics.

5. Methylene Blue. We use this drug in many cases of urogenital tuberculosis, where

it often materially relieves the distressing bladder symptoms. On other urologic services it is used almost routinely for patients who have had transurethral resections. It frequently causes distressing gastro-intestinal symptoms, and, with decreased renal function, there may be marked renal irritation. The common dosage is 0.06 gm., 3 to 4 times daily.

6. Mercurochrome. Mercurochrome has not had widespread use. Recently, however, Emmett finds that 10 c.c. of a 1% solution, when given intravenously, acts as a good antipyretic in protracted cases of acute pyelonephritis. Furthermore reports fewer reactions when 1% mercurochrome is given in 50% glucose. Both authors report that other antiseptics must then be used to combat the infection.

7. Acroflavine. This drug gives excellent results when used locally in bladder and urethral infections, but it has not proven very satisfactory for oral administration.

8. Neoarsphenamine. This antiseptic is used specifically for resistant coccal infections. The usual dosage is 0.2 gm., given intravenously followed by 0.3 gm. in 5 to 7 days.

9. Alkalinization. Formerly it was thought that changing the reaction of the media from acid to alkaline, or *vice versa*, was of great value. We now feel that this is less effective than the use of antiseptics. Alkalinization is useful, however, in relieving some of the symptoms of acute cystitis and pyelonephritis. Among the more commonly used drugs are sodium bicarbonate, sodium citrate, and potassium acetate.

In severe cystitis from any cause, the following prescription (Kirwin's mixture) is very helpful:

Potassii citratis	...	dr. 6 (24 cc.)
Tinct. hyoscyami	...	oz. 1 (30 cc.)
Tinct. opii camphoratae	...	oz. 1 (30 cc.)
Elix. saw palmetto et santalwood q.s. ad.	...	oz. 4 (120 cc.)

Sig.: Dr. 2 (8 cc.) q. 4 hrs.

In less severe cases the following prescription is useful:

Tinct. hyoscyami	...	oz. 1 (30 cc.)
Potassii citratis	...	oz. 1 (30 cc.)
Aqua ad.	...	oz. 6 (180 cc.)

Sig.: Dr. 1 or 2 (4 or 8 cc.) q. 4 hrs. in water.

10. Acidification. Many infections would readily clear up if the urine could be adequately acidified to a pH of 5.0 or less. Clinically this is difficult to do. Acidifiers include: Acid Sodium Phosphate, Ammonium Chloride or Nitrate, Sodium Benzoate, Calcium Chloride and Hydrochloric Acid. These drugs are used as adjuncts to Mandelic acid and methenamine.

11. Diet. The ketogenic diet has largely been replaced by newer methods of urinary antiseptics. The high acid ash diet is used

considerably as a supplemental agent, especially in cases of infection due to urea-splitting organisms, where it is difficult to obtain acidity.

12. **Methenamine.** Methenamine has continued to enjoy widespread popularity. The drug is excreted unchanged by the kidneys and becomes active in the urine through its conversion into Formaldehyde, which is the therapeutic agent. Hinman has shown that the splitting of Methenamine into Formaldehyde and Ammonia is a simple chemical process which can only take place in an acid urine. Hence the dosage must be sufficient and the acidity low enough for adequate conversion. The duration of the organism's exposure to the Formaldehyde is important; therefore, with polyuria the dosage must necessarily be large.

Methenamine is particularly useful in cases where medication must be given over long periods of time, as in cord bladder with residual urine. The drug has the advantage of being effective regardless of the kidney function. In office practice, many patients can tolerate methenamine and remain ambulatory, whereas with Mandelic Acid or Sulphanilamide they are unable to do so. We commonly give Methenamine in a dosage of 1.0 gm., 3 or 4 times daily, with suitable acidification.

13. **Mandelic Acid.** Mandelic Acid is especially effective against members of the B. coli group. The Streptococcus faecalis, which is not easily killed with Sulphanilamide, is more easily destroyed by Mandelic Acid.

Clinical study has shown that with a fluid intake limited to 1,200 cc. a dosage of 3 gm. every 4 hours will give a 1% urine concentration in 6 hours. It is necessary to keep the pH of the urine at 5.6 or less to obtain bactericidal action. Administration in the liquid form must be accompanied by a suitable acidifying agent to give the desired urine pH. Mandelic Acid may be given in powder form as either Calcium Mandelate or Sodium Mandelate. The required dosage remains the same. Administration of the drug in pill form seems to be accompanied by far fewer gastro-intestinal disturbances. Also, additional acidification is usually unnecessary.

Mandelic acid should be given for 1 week after the urine becomes sterile, but not longer than 3 weeks. After a rest period of several weeks, the course may be repeated if necessary. Frequent urinalysis should be done, as there may be renal damage in the form of nephritic changes. Liver impairment and increased blood pressure are also contraindications to the use of this drug.

14. **Sulphanilamide.** Sulphanilamide is at present one of the best known and most valuable drugs in the urologist's armamentarium. It has been found to be of value in eradicating infection caused by almost all of the usual organisms. Escherichia coli, Aerobacter aerogenes, Salmonella, Shigella, Strep-

tococcus haemolyticus, and the Gonococcus appear to respond best. Infections caused by the genus Proteus (the most severe urea-splitting organism), which were formerly the most difficult to eradicate, are now well handled with sulphanilamide. The response of staphylococcal infections is only fair, and streptococcus faecalis infections are relatively immune to the action of sulphanilamide. Luckily, these latter organisms yield to Mandelic Acid therapy.

Dosage.—We give the average patient 0.6 gm. (10 gr.) 4 times daily. Occasionally the initial dose may be larger. In patients with lowered renal function, the dose is lowered to 0.6 gm. 3 times daily, or even to 0.3 gm. 3 or 4 times daily. A simple dictum is never to give more than 1 gm. of the drug daily for each 10% of total phenolsulphonphthalein function. Carey suggests a dosage of 0.1 gm. per pound of body weight per 24 hours for infants, and half this dosage for children 10 to 12 years old.

All observers agree that saline cathartics should be avoided while sulphanilamide is being administered, as many reactions, several fatal, have been seen with this combination. Opinion seems divided as to whether other drugs should be discontinued during treatment with sulphanilamide.

We try to continue therapy with sulphanilamide for a period of 7 to 10 days, or even longer, if well tolerated. If indicated, we give a second course after a short rest period. Neoprontosil has proved to be effective in many infections, although at times not as much so as Sulphanilamide. Sulphapyridine does not appear to have a place in the field of urinary antiseptics.—*The General Practitioner.*

Diagnostic Value of the Xiphoid Sign.

The incidence and the diagnostic value of the xiphoid sign has been observed, according to Lyakhovitskiy, in their clinic for the last ten years. Observations were made on 600 patients presenting disease of the gallbladder and the bile ducts, gastroduodenal ulcer, cancer of the stomach, the esophagus and the colon and acute abdominal emergencies. The clinical observations were verified at operation in the great majority of cases. The xiphoid sign consists in the presence of maximum tenderness at the tip of the xiphoid process, particularly on upward pressure. This sign was always present in the disease of the gallbladder or the bile ducts. Anatomic studies carried out in their clinic point to a direct lymphogenous as well as indirect lymph node connection between the gallbladder and the group of lymph nodes situated behind the xiphoid process. The author believes that acute lymphangitis and lymphadenitis just posterior to the xiphoid is the cause of the tenderness. He considers this tenderness to be a pathognomonic sign of cholecystitis and cholelithiasis.—*J.A.M.A.*

Working Capacity of Diabetics.—Some interesting figures on the working capacity of diabetics have been given by the *Statistical Bulletin* of the Metropolitan Life Insurance Company. Of 653 patients between the ages of 20 and 65, who returned for treatment or check-up, it was found on questioning that 63 per cent of the men in the group were able to do full time work without important interruptions; another 27 per cent were able to work approximately two-thirds of the time, and another five per cent approximately one-third of the time. Only five per cent were disabled. For women these observations are less reliable, since most of them are middle-aged housewives attending to their households in activities not precisely defined within set time limits. However this may be, 46 per cent of the women in this broad age group reported little or no time lost from their usual activities; 34 per cent lost approximately one third of the time, and 14 per cent lost approximately two thirds of the time. Only six per cent were definitely disabled.

"Similar data are available for another group from the same Clinic composed of 605 diabetics whose disease began when they were under 40 and who had had their disease for at least 15 years. Of the patients in that group who were still under 40 years old, 90 per cent were able to work or lead a normal life. Among those who had passed the age of 40, 76 per cent were normally active. Moreover, 95 per cent of the patients reported themselves in good or fair health. Insulin played an important part in these results, for 92 per cent of the younger group and 71 per cent of the older group were taking insulin.

"How little their diabetes interferes with the working capacity of properly treated patients is shown by a study in an English clinic. The study related to 100 consecutive patients in varied occupations who had an average period of employment of five years since discovery of their diabetes. Of this group, only 15 per cent had any serious loss of time on account of illness traceable in any way to their diabetes. Thirty-nine per cent had lost no time whatever because of diabetes; 38 per cent had lost a brief period for a study of their insulin and dietary requirements at the beginning of treatment and eight per cent for subsequent study of the same kind. Furthermore 45 per cent of the group had lost no time for illnesses not related to diabetes. Of the 100 persons, 75 were men, 73 were between ages 14 and 40, and 83 used insulin regularly.

"Another measure of the normality of life of diabetics is set forth in a study of 60 patients of the Mayo Clinic. These persons of either school or working age were taking insulin and had been on a diabetic regimen for at least one year. Nearly three quarters of the patients continued at their previous employment and another ten, or 17 per cent, merely made some adjustment in their

working habits. Furthermore, 80 per cent were able to keep up their usual social or recreational activities."

Physicians who struggled with diabetes before the advent of insulin cannot fail to be impressed with these favorable figures. The poor diabetic of the preinsulin days fought a losing battle to keep midway between starvation and coma. Denied most of the good things of life, all but the very mild cases constantly lost weight and strength and the ability to earn a livelihood until an intercurrent affection ended life. Generally, the average length of life from the beginning of the disease did not exceed five years and during this short span there was a constantly increasing invalidism.

That today 63 per cent of a large group can do full-time work without important interruptions is a great tribute to Banting and his memorable discovery. The picture still is not perfect and much knowledge of diabetes must still be gained before mankind is completely relieved of great menace to its health. To quote further from the *Statistical Bulletin*: "Admittedly, these records of well being and working capacity are not as good as in persons in normal health. A definite norm for purposes of comparison is not available but there can be little doubt that the full success attainable has not yet been reached. The figures cited give eloquent testimony of the excellent results already obtained."

"There is good reason to expect continued improvement in the prognosis of diabetic patients, for progress is constantly being made along many lines bearing directly or indirectly on their welfare. Intensive research is actively being carried on regarding the underlying endocrine relationships involved in diabetes, and the experimental work in the artificial production of diabetes by pituitary injections may be found to give a clue to a new type of therapy. At the same time, efforts are continuing to improve the forms of insulin now available. The idea in view is to produce one whose action may approximate even more closely than the best form now available, the action of the insulin normally produced in adequate quantity in the pancreas of normal individuals. Efforts are being made in many parts of the country to improve the general level of treatment of diabetics with the facilities now available. By intensive post-graduate medical education, older physicians whose formal education in diabetes goes back to pre-insulin days, are being made acquainted with up-to-date methods of treatment. Meanwhile, the younger physicians, whose training includes these newer methods, are forming an increasing proportion of the total number in practice.

"The modern aim in the treatment of diabetes, namely to restore them and keep them as useful and productive citizens in the community, is thus on the way to being

more and more nearly realized. Both doctors and diabetics themselves can help in attaining the goal. Every diabetic maintained at work is not only himself the gainer, but

thereby establishes a reputation which helps to overcome the prejudice of employers against giving jobs to diabetics."—*Medical World*.

Surgery

Management of Facial Paralysis by Physical Measures.

Newman and his co-workers state that the treatment of facial paralysis is dependent on its various etiologic factors, on the question of whether the paralysis is of central or peripheral origin, and on the site of the lesion. They managed thirty cases by the use of physical therapeutic measures. The ages of the patients ranged between 6 and 79 years, average 37. With the onset of an acute refrigerans type of facial paralysis iodides in saturated solution of potassium or syrup of hydropic acid are indicated for their general alterative action. Analgesics are valuable. Saline laxatives are used during the acute stage of inflammation for their possible detergent effect. The physical measures applicable during the acute phase of the refrigerant palsies are directed toward the reduction of the inflammatory exudate and toward keeping the denervated muscles in position of physiologic rest. Decongestion at the stylomastoid foramen can be accomplished by cantharides plasters, hot moist applications, radiant heat, negative galvanism and conventional or short wave diathermy. The frequency of application is indicated by the pain and the tolerance of the tissues. To prevent muscles from stretching they are supported by attaching two Y bands of adhesive tape at the zygomatic bone and temporal region. Positive galvanism is especially efficacious for the relief of pain. With the subsidence of the acute symptoms within eight to ten days, testing for reaction of degeneration is instituted. When no reaction of degeneration is present, recovery can be expected in from two to eight weeks. If a sufficient amount of recovery is not obtained after six months of rigorous physical therapeutic measures, surgery is to be considered. Active treatment now consists of heat, massage, voluntary exercise and electrical stimulation (with interrupted galvanic, sinusoidal and faradic currents). Diathermy or radiant heat is applied to the paralyzed side of the face for from fifteen to thirty minutes. Another method of promoting a circulatory response consists of the common ion transfer 0.5 per cent acetyl-beta-methylcholine hydrochloride. From 15 to 20 milliamperes of the galvanic current for twenty minutes is adequate. Negative galvanism for its heating effect can be applied for thirty minutes over the stylomastoid foramen. The strength of current should be just less than the amount required to cause a contraction of the muscles on the unaffected side. On the first day three contractions over the motor points are sufficient, and on subsequent days the number of contractions is increased but always kept within

the fatigue range of the muscle. After one or two weeks the slow sine wave is substituted, from twenty to thirty contractions per minute being used. When the faradic current can be tolerated, it should replace the sine wave current. Gentle stroking massage which follows stimulation preserves muscular tone. Exercise of the facial muscles is carried out in front of a mirror every day. The etiologic agent must always be removed before physical measures are instituted. Seventeen of the thirty cases followed exposure, six middle ear disease, one dental manipulation, one trauma associated with an automobile accident, two head colds, one mumps, one an operation on the eighth nerve for vertigo, one a postpartum infection and two mastoidectomy. In the seventeen cases of exposure paralysis, a partial reaction of degeneration or no reaction of degeneration was present after ten days. Eight of these patients received only heat, massage and exercise, while the remainder received electrical stimulation as well.—J. A. M. A.

Minor Injuries to the Fingers.—D. M. Carter discusses a few of the commoner and more important types of injuries to the fingers in *Guy's Hospital Gazette* (May 19, 1940).

The following types of injuries will be considered:—(a) Simple crushes, cuts and lacerations, (b) Fractures of the phalanges and the metacarpal heads, (c) Interphalangeal sprains and subluxations.

(a) Crushes of the fingers, especially of the tips, often give rise to a painful bulbous extremity which may take a long time to heal. Hemorrhage should be controlled by firm compression over the points of bleeding. After the wound has been cleansed the contour of the digit should be reformed and a plaster accurately applied to the whole finger. It may be necessary to pass one or two turns around the wrist to stop the plaster from coming off. By this means the patient is enabled to use the remainder of the extremity, which will not be rendered useless and functionless by prolonged immobility. The plaster forms a limiting membrane to the entire digit; this greatly facilitates epithelization and healing.

If the nail be nearly avulsed from its bed or if a hematoma has formed beneath, it is most expedient to remove it at once.

It is not uncommon to find that quite large areas of skin have been completely flayed from one or more digits. For these cases an immediate pinch graft from the

deltoid region placed over the raw area and the whole incorporated in a plaster finger stall gives excellent results. When the plaster is removed there may be perfect healing with a digit of normal contour which rapidly resumes its function. Very often, however, these cases "are dressed" for many weeks, become infected and permanently stiff. They are the cause of prolonged disability, and not uncommonly come to amputation.

Crushes of the terminal phalanges with or without bony injuries are often associated with the condition of mallet finger, which is a rupture of the strip of the extensor tendon going to the base of the terminal phalanx. A plaster is applied in the same way, but should be moulded so that there is hyperextension of the terminal phalangeal joint, the other phalangeal joints and the metacarpophalangeal joint being slightly flexed. In this way the two ends of the divided tendon are approximated and join. This is a far better method of treating mallet finger than the rather uncomfortable and cumbersome procedure of strapping the finger into the palm. Even an old-standing case may be treated in this way.

The following is an interesting condition that may follow a blow on the end of the finger. Although no fracture, dislocation or laceration has occurred, the patient is left with a painful, swollen, stiff and slightly deformed finger, which may be present for months. X-ray shows nothing, and the condition is probably due to severe bruising of the bone with the formation of a subperiosteal hematoma. If left alone and not pumped and massaged the condition always gradually rights itself. The correct treatment, therefore, is to do nothing but reassure the patient that all will be well in a few months.

(b) **Fractures.**—Only three of the commonest types of fracture of the digits will be mentioned. These are:—1. Crushed and comminuted fractures of the terminal phalanx. 2. Fractures of the shaft of the proximal phalanx. 3. Fractures of the metacarpal heads.

They may be simple or compound.

1. Compound finger injuries should be treated by immediate operation. A quotation from Watson-Jones may help to demonstrate their importance: "An open fracture of a phalanx is no less worthy of the skill of an expert than an open fracture of the femur, and there is often little difference in the economic value of successful treatment."

As in all compound fractures, the wound should be excised and, if possible, sutured; cat-gut where possible should be avoided for the same reasons that it should not be used in the control of hemorrhage. If the wound is large, skin grafts may be employed, but small areas can be left open. The whole digit is then placed in a plaster in the same

manner as for simple lacerations. Any deformity in the bone should, of course, be reduced and maintained in the corrected position by a plaster cast.

A severely crushed and contaminated finger may require amputation. In the case of the thumb this advice shall on no account be followed, as the problem is a different one. Any part of the thumb should be conserved if possible, for, even if stiff, it does not get in the way as in the case of the fingers, and, even if its terminal joint be rigid, it can still oppose and grip with the other mobile fingers. If an amputation has to be done it should be as conservative as possible. If it is not possible to fashion flaps, the end can be left raw and the stump skin-grafted and fixed in plaster.

2. **Fractures of the proximal phalanges.**—Fractures of the proximal phalanges account for half of the bony injuries to the fingers. There is usually a characteristic displacement with a forward angulation about the middle of the shaft of the bone. This deformity is produced by the action of the interossei and lumbricals, which flex the proximal and extend the distal fragments, thus producing a forward convexity.

This deformity should be overcome by traction and by flexing the distal fragment into line with the proximal one. The corrected position should be maintained by a forearm plaster cast with an extension incorporating the affected digit so that the metacarpophalangeal joint is flexed to 45 degrees and the proximal inter-phalangeal joint to 90 degrees.

If the fracture is unstable it may be necessary to use pulp traction, the line of action running from the pulp (with the finger in the position already described) to the second fixed point, which is to the plaster just in front of the wrist, traction being maintained by an elastic band.

After three weeks the plaster should be removed. All the other fingers should be actively exercised throughout the period of immobilisation.

3. **Fractures of the metacarpal heads.** These are generally produced by blows on the end of the knuckle. Again the deformity is characteristic, the head of the metacarpal being tilted forwards, thus producing a backward angulation at the end of the bone. Reduction is usually not difficult.

The metacarpophalangeal joint should be flexed and the head of the metacarpal bone pushed back into position by a thrust in the long axis of the proximal phalanx. The corrected position should be maintained by a dorsal forearm slab extending to the metacarpal heads, with a dorsal extension of the plaster over the affected digit. This is maintained in right-angled flexion at the metacarpophalangeal joint, the inter-phalangeal joints being likewise fixed. The plaster

may be removed after three weeks and active exercises commenced.

(c) *Inter-phalangeal sprains and dislocations*:—Of equally serious importance in injuries of the fingers are interphalangeal sprains and dislocations. A persistently painful joint often results from these injuries. The joint capsule is often torn, there is oedema, haemorrhage, swelling and the formation of much periarticular adhesions. It is essential to reduce this oedema and adhesion-formation in order that a normal range of movement can be obtained. The joint should be rested in a plaster finger stall in a position of slight flexion. By this means swelling is reduced to a minimum and adhesions are avoided. This plaster should be maintained from two to three weeks. On no account should the joint be pummelled about, stretched, or attempts made to overcome stiffness by force, for the swelling and adhesions are only aggravated. The worst possible complication of an interphalangeal

sprain is massage and passive exercises. After three weeks' rest the patient should be able to overcome stiffness by his own effort. If the traumatic exudate has been allowed to subside, he will recover his full range of movement, even though this may take a long time. However, if attempts are made to hurry up this recovery, a full range of movement will be delayed and may never be re-established.

The same plan of treatment is followed in dislocations; these are reduced by traction and by flexion of the distal phalanx on the proximal one of the joints dislocated. Attempts to hasten recovery by stretching and pulling should be vigorously avoided. This warning applies equally to the stiff finger produced by fracture, and the only method of hastening recovery is active exercise. Heat, diathermy and wax baths are sometimes of assistance if available.—*The General Practitioner*.

Obstetrics and Gynaecology

Relief of Pain During Labour.—In *New England Journal of Medicine* (Nov., 1939) JOHN ROCK discusses a number of points on obstetrics. We extract that part dealing with anaesthesia and analgesia.

Chloroform and ether alone were boons in their time; nitrous oxide was a welcome addition. Novocain has its special uses. Morphine and scopolamine, at a price, showed how comfortable labour could be made. Now the barbiturates and paraldehyde take an honoured place among these merciful agents. They are all potentially dangerous, to be sure, but so is digitalis, and even ethyl alcohol.

The degree and the safety of obstetric analgesia with the agents at hand critically depend on the ability of the attending physician to perceive the peculiarities of each patient, as well as those of her obstetrical condition and of the quality of her labour, and to apply these agents accordingly. Furthermore, it is clear that the exigencies of such procedures, both maternal and foetal, justify their use only in thoroughly equipped hospitals. Bad results under other conditions call not for repudiation of analgesia, but rather for improvement of these conditions.

The experience in many clinics during the last decade currently presents these conclusions:—

1. Morphine, 1/6th gr., or pantopon, 1/3rd gr., enhanced by scopolamine, 1/200 to 1/100 gr., repeated alone or together, as necessary, at intervals of 3 to 4 hours, is helpful during the first stage of primiparous labour. Morphine or pantopon must not be given unless one is reasonably sure that delivery will not occur within 4 hours,

because of their depressant effect on the foetal respiratory centre. They are therefore not often useful during the second stage of labour or for multiparas.

2. Barbiturates are more safely given by mouth or by rectum than intravenously, although their action is thereby slightly delayed. Pentobarbital and Sodium Amytal are the popular forms, and of these the former acts more quickly and in smaller doses. From 4 to 6 gr. is given, preferably with scopolamine, 1/200 to 1/100 gr., when contractions are well established, and if possible before they become acutely distressing. Pentobarbital, 1½ to 3 gr., is repeated at intervals of 3 or more hours, or as the patient becomes wakeful; scopolamine, 1/200 gr., is given every 3 or more hours if she is rational. Barbiturates given by mouth are not dependable if the stomach contains much recently ingested food. Complete narcosis with barbiturates must not be induced by any route if the stomach contains food, for vomitus is often expelled with difficulty, a fact which makes inhalation of food particles easily possible.

3. In addition to the barbiturates and scopolamine, in order to allay undue restlessness, paraldehyde in doses of 4 to 8 cc. may be given by rectum with 30 or 60 cc. of ether in an equal amount of olive or cottonseed (not mineral) oil, once or twice toward the end of the first stage.

4. Nitrous oxide and oxygen, in proportions of 1.0:1 or 1.5:1, are given during the second stage, and a modicum of ether is added, if necessary, for delivery.

5. For obvious reasons the patient must never be without competent, continuous supervision.

6. The rare patient whose cardiorespiratory system is unduly sensitive to barbiturates and who therefore develops pulmonary oedema, must be promptly supplied with oxygen by tent or mask.

7. The newborn baby, after barbiturates and scopolamine have been used, may not at once cry or even breathe deeply. He may be stimulated, but very gently, as by rubbing or patting on the back, pinching the toes, or immersing the buttocks momentarily in cold liquid. All babies should be drained, and the mucus in the pharynx should be aspirated.—(G.P.)

Recent Advances in Hormone Therapy.

In an article on this subject in the *Canadian Medical Association Journal* (June, 1940) W. N. Kemp begins by calling attention to some of the newer views regarding the clinical application of biological principles.

The first of these is the principle of the potentiation of dosage division. This principle is widely utilized by commercial houses in the biological standardization of gonadotrophic hormones. A rat, or a mouse, or a rabbit is given twice or thrice daily injections of the gonadotrope under assay for three days, and a certain standard effect upon the gonads or the vagina is noted by means of which the unitage of the product in question is computed. Then, with a degree of indifference to the marked disparity between biological effects in animals and therapeutic attempts in human beings which is truly remarkable, the product is passed on to the physician with the usual recommendation that it be injected into the patient twice or thrice weekly! This utterly unscientific recommendation is apparently based on the supposed resistance of patients to receiving treatment more often than three times weekly. Probably there is something to be said for this supposed resistance to frequent injections, but it seems only reasonable to point out to physicians, and through them to patients, that the more frequent the injections, the more efficacious is the treatment and the shorter is its duration where a definite growth stimulating effect is the therapeutic objective as in the treatment of uterine hypoplasia, etc. Unfortunately, like many another medical habit the Monday, Wednesday and Friday concept of gonadotrope administration has become firmly fixed in the minds of commercial houses and medical practitioners as well.

Probably of equal or even greater importance to the above principle of dosage division in therapeutic significance is the knowledge of which hormone should be used for each desired specific gonadotrophic, oestrogenic or progestational effect. For example, chorionic gonadotrophin should seldom, if ever, be used in the first half of the menstrual cycle to produce a gonadal effect; on the other hand, pituitary or equine

gonadotrophin, when indicated, should almost always be used in the first phase of the menstrual cycle. The two latter gonadotropes, being preponderantly follicle-stimulating in their action, should be administered before the time of ovulation, while chorionic gonadotrophin should be used in the second half of the cycle for the purpose of stimulating the development and continuity of the corpus luteum after ovulation has already occurred. Of course, this therapeutic limitation for chorionic gonadotrophin does not apply to the treatment of metrorrhagia; here the immediate control of uterine haemorrhage a specific and empirical function of chorionic gonadotrophin, is the main desideratum of treatment.

Thirdly, comes the question of the proper timing of the administration of the gonadotrope or oestrogen or other hormone, particularly in relation to the events of the menstrual cycle, or, in a broader sense, to events of the whole female reproductive period. For example, in treating a patient for deficiency of the luteal phase, as for the purpose of stimulating corpus luteum function in a woman being treated for functional sterility, it is important not only to use chorionic gonadotrophin, but to defer its administration until the 18th day of the cycle in order to obviate any possibility of producing atretic follicles in the ovary and thus nullifying the other preceding and essential function of the ovary—the maturation and extrusion of a ripened ovum.

The last but by no means the least important principle to which attention is directed is the question of the use of none other than properly standardized hormones marketed by reputable firms. In this regard it is interesting to note that Hawkenson has recently reported that out of a total of 27 so-called oestrogenic hormones on the American market examined by him only 6 were standardized and only 6 were of appreciable oestrogenic potency.

THE ANTERIOR PITUITARY GLAND.—The growth-promoting "complex" of the anterior lobe of the hypophysis ("complex" because it probably consists of several hormonal elements or factors), first reported by Evans and recently improved by Collip, has been shown to be of great practical value in the treatment of patients showing skeletal growth retardation. Not only are "frank" "pituitary dwarfs" benefited by the administration of this hormone but many undersized children can be advantageously raised to a normal growth level by the judicious use of Collip's growth "complex."

The only other anterior pituitary hormone to which any practical value can be attached at the present time is "anterior pituitary gonadotrophin", or, as Collip called it, "gonadotrophic factor." Parenthetically, it might be said that the three principal gonadostimulating hormones (gonadotropes or gonadotrophins) have been respectively termed: "anterior pituitary gonadotrophin"

(produced from the anterior lobes of cattle); "chorionic gonadotrophin" (produced from pregnancy urine), and "equine or pregnant mares' gonadotrophin" (produced from the serum of pregnant mares).

Chorionic gonadotrophin or A. P. L.—Chorionic gonadotrophin or, as Collip originally named it, A.P.L. (anterior pituitary-like hormone), is definitely of clinical value, the report of the Council of the American Medical Association to the contrary notwithstanding, for the treatment of menometrorrhagia, hypogonadism, or Frohlich's syndrome, deficiency of corpus luteum activity, and for the treatment of cryptorchidism, impotence or hypogonadism in males.

OTHER ENDOCRINE PRODUCTS.—The use of endocrine products is pre-eminent for the control of functional uterine haemorrhage, chorionic gonadotrophin, progesterone, and thyroid extract being particularly prominent in this field. Although the exact rationale of action of chorionic gonadotrophin has not yet been forthcoming that defect in no way detracts from its clinical value in the treatment of functional uterine haemorrhage. Lissner has for years emphasized the importance of thyroid extract in the treatment of menorrhagia, calling attention to the fact that irregular uterine haemorrhage may itself be the presenting symptom of hypothyroidism, particularly in adolescents. Recently Shute, Mason and others have re-emphasized this correlation between thyroid hypofunction and irregular functional uterine haemorrhage.

Metropathia haemorrhagica.—This condition, known also as endometrial hyperplasia or cystic hyperplasia of the endometrium, is caused by a too prolonged oestrogenic action without the natural interruption and endometrial debridement which accompanies normal corpus luteum function through the ordinary mechanism of menstruation. These patients almost invariably have follicular cysts of the ovary, or ovaries, and invariably are "without benefit" of corpus luteum function. While, in many instances, these patients can be symptomatically controlled by the judicious use of chorionic gonadotrophin, the most effective treatment yet to be devised for the systematic control of this condition is the so-called "medical curettage" of J. S. L. Browne, of Montreal. He has suggested, following a preliminary surgical curettage of the uterus, that endometrial denudation be regularly induced by the periodic administration of progesterone, 5 mg. on alternate days for 4 injections. By this means a "medical curettage" can be induced at 4, 5, or 6 week intervals according to the judgment of the physician. In this manner regular periods of uterine bleeding are periodically induced which cannot, for all practical purposes, be distinguished from natural menstruation. Thus the "irregularly irregular" haemorrhage of the metropathia patient is systematically brought under control.

Pregnandiol.—Sodium pregnandiol glucuronide or "pregnandiol," as has been shown by Browne and Venning, is the excretion product of progestin or progesterone. These workers have formulated a valuable practical method of isolating and measuring this substance in the urine and, together with Henry, have shown the practical value of this test in evaluating (1) the occurrence of ovulation; (2) the adequacy or otherwise of the luteal phase of corpus luteum function, and (3) the imminence or otherwise of abortion.

Progesterone.—Progesterone is the crystalline synthetic form of progestin (corpus luteum hormone), and is available commercially for clinical use. The most important therapeutic applications of progesterone involve (1) the induction of "medical curettages" after the manner of BROWNE (described above); (2) the emergency control of uterine haemorrhage; (3) the prophylactic treatment of habitual abortion and the actual treatment of threatened abortion, and (4) the control of after-pains. It is to be noted also that BROWNE'S technique can be used to advantage in regularizing the irregular menstrual cycles commonly seen in adolescence, possibly using doses of progesterone considerably less than those required in the treatment of adults for metropathia haemorrhagica.

Oestrogens.—Oestrogen is a general term given to substances exerting oestrogenic properties, viz., having the ability to produce oestrus in immature or gonadectomized animals. There are three natural oestrogens (1) oestriol (emmenine, theolol, tri-hydroxy-oestrin); (2) oestrone (oestrin, theelin, keto-hydroxyoestrin), and (3) oestradiol (dihydroxyoestrin, di-folliculin, etc.). Only the first of these, oestriol, is sufficiently active *per os* for practical use. The most powerful oestrogen yet to be produced synthetically is Dodd and Robertson's well-known "diethylstilboestrol." This substance is about three times as active oestrogenically as oestrone, and, in addition, has the great practical virtue of being for all practical purposes as active following oral administration as after parenteral injection. Indeed, so powerful is this synthetic oestrogen that the incidence of nausea and other untoward symptoms which have commonly followed its use has been probably incorrectly ascribed to toxic influences. In my experience diethylstilboestrol produces toxic manifestations only when it is administered in "single overdoses," i.e., in too large single doses, such as 1 or 2 mg. If the total daily dose is divided into several 0.25 mg. doses, and particularly if each tablet or capsule is coated so that it will only slowly disintegrate in the intestine itself, little or no nausea or other untoward symptoms follows its administration. I hasten to add, however, that this statement is not to be interpreted as expressing the view that continued ingestion of a potent

oestrogen such as diethylstilboestrol is in the ultimate best interests of the patient.

The principal indications for the administration of oestrogens are, as one would expect, conditions of oestrogenic deficiency. Of these the commonest is the climacteric which results from abrupt and almost total ovarian insufficiency, whether natural or artificially induced. At this physiological epoch where hot flushes are the *deus ex machina* of treatment, diethylstilboestrol is the most effective agent for the immediate control of symptoms. For this purpose, i.e., the control of the hot flushes, very few patients require more than 2 mg. of diethylstilboestrol a day, and many obtain comfort on a daily dosage of 1 mg. or less provided only that the daily dose is divided into several doses distributed over the whole 24 hours.

If, as occasionally happens, a patient presents herself before the symptoms of the climacteric have become severe and while she is still menstruating, undoubtedly Collip's emmenin is the oestrogen of choice. In patients who are seen early and who are adequately treated with divided doses of emmenin, the severe symptoms of the climacteric can be prevented and they can gradually and without untoward symptoms be let down to the lower oestrogenic level upon which it is their future lot to live.

Another form of treatment for the menopausal syndrome which shows considerable promise is the sub-cutaneous implantation of pellets of an oestrogen such as oestrone. This therapeutic principle which was first described by Parkes and Deansley has been recently revived in a very practical form by Jacoby and Der Brucke. By their technique pellets of oestropo can easily be implanted in the subcutaneous tissues where they will give a continuous oestrogenic effect and relieve the untoward symptoms of the climacteric for periods ranging from 2 to 16 weeks.

Schneider, Hawkinson, and others have called attention to a type of female patients undoubtedly suffering from partial ovarian deficiency many years before the menopause. These women are reported to be greatly benefited by the frequent daily administration of a standardized and orally active oestrogen such as emmenin.

Uterine and genital hypoplasia can now be adequately treated at a not-too-great cost to the patient by utilizing the new synthetic oestrogen, diethylstilboestrol. By the judicious and well-planned use of this substance, amenorrhoea, whether primary or secondary, can be successfully and inexpensively treated. In patients in whom the amenorrhoea is primary, or where it is associated with genital hypoplasia, it is usually advisable to follow the "substitutional therapy" of diethylstilboestrol with "functional therapy," involving the use of pituitary or equine gonadotrophin in courses for two weeks, followed by injections of chorionic gonadotro-

phin to stimulate the corpus luteum to produce the second or luteal phase of the cycle.

Androgens.—Androgen is a generic term applied generally to what used to be termed "male-sex hormones." Androsterone, one of the early male-sex hormones, has been succeeded by the more potent testosterone, the brain child of Ruzsika. Undoubtedly the synthesis of testosterone marks a notable achievement in biological chemistry. The propionate of testosterone is now commercially available, and is quite capable of developing male secondary sex characteristics and libido and potentia in eunuchs, provided only large and long-continued dosage regimens are followed. MCCULLAGH has reported one such eunuchoid adolescent who, after approximately 3,200 mg. of testosterone, bloomed into real virile manhood. Unfortunately, like other forms of purely substitutional therapy, testosterone administration must be continued indefinitely in these cases to prevent relapse to the eunuchoid condition.

Testosterone propionate has been recommended, and indeed has been used, for many other and varied conditions in both males and even in females. Here the point of wonder is not that it will produce the "pituitary inhibition," etc., which is claimed for it, but that it is used for this purpose when other more suitable and less hazardous forms of endocrine treatment are available.

THE ADRENAL GLAND.—The pharmacodynamic action of epinephrine, the active secretion of the chromaffin cells of the adrenal medulla, is too well known to require consideration here. Rather would it seem more apropos briefly to discuss the therapeutic possibilities of the adrenal cortex and its secretion or secretions, it being supposed that there are others in addition to cortin.

Addison's disease.—As was expected, cortin and its more recent synthetic counterparts, desoxycorticosterone and the other adrenal steroids, are of distinct value in the treatment of this well known but comparatively rare disease. Thorn has recently shown that the subcutaneous implantation of pellets of desoxycorticosterone acetate are of great value in the treatment of this disease. However, it is interesting to note that, judging from recent reports presented at the Twelfth Annual Meeting of the Central Society for Clinical Research, desoxycorticosterone lacks something which the natural adrenal secretion, cortin, contains. In the opinion of the writer this missing something is most probably ascorbic acid or vitamin C, a substance which was first found in the adrenal cortex by Szent-Gyorgyi. In addition to substitutional treatment with natural cortin or synthetic adrenal steroids large quantities of Sodium Chloride are, of course, required by Addisonian patients to compensate for the great loss of Chlorides which is so characteristic of clinical and experimental corticoadrenal insufficiency.

The vomiting of pregnancy :—In 1931, I ventured to make a number of "educated guesses"; among others that the vomiting of pregnancy as well as the syndrome occurring in infancy known as status lymphaticus (the so-called "thymus syndrome") were both clinical manifestations of temporary cortico-adrenal deficiency. The writer's own work, which was confirmed by FREEMAN and MELICK in 1936, and recently by KOTZ and KAUFMAN, would seem to prove the almost specific action of adrenal cortical hormone (or hormones) for the prevention and treatment of the common syndrome of nausea and vomiting so often associated with the first trimester of pregnancy. It would appear that "cures" for the vomiting of pregnancy have for so many years been the "Wolf! Wolf!" of practical medical practice that it takes a long time for a really effective form of therapy to receive general trial! Nor is this to be wondered at.

Status lymphaticus, or the "thymic syndrome," continues to account for many sudden deaths in infants particularly in the Pacific north-west. In the interim the writer's early hypothesis has not been confirmed or denied, save only by KINSMAN, who reported marked improvement in 8 children suffering from the so-called "breath-holding" spells which are generally regarded in Vancouver, B. C., as a sub-clinical form of status lymphaticus, or, as some would term it, the "thymic syndrome." After treatment with desiccated adrenal cortex by mouth the patients reported by KINSMAN, previously ineffectively treated by irradiation of the thymus area, were rendered symptom-free.

In addition to the two clinical syndromes above mentioned the writer has also ventured to suggest that the administration of adrenal cortical secretion or glandular substance is indicated in the treatment of severe burns, acute toxemias, and cyclic vomiting. Evidence is gradually accumulating which suggests that several of these hypothetical arrows have not been so wide of the mark and perhaps deserve further clinical study. Of one thing, I am convinced, and that is that the adrenal cortical hormone (or hormones) or its allied synthetic steroids requires the co-administration of ascorbic acid in order to obtain its full beneficial effect in prophylaxis or treatment.

Vitamin E :—EINARSON and RINGSTED have suggested from their experimental studies that the muscular dystrophies and amyotrophic lateral sclerosis in human beings may be related to vitamin E deficiency. BICKNELL, following up the animal experiments of EINARSON and RINGSTED by a small series of clinical therapeutic trials, is of the opinion that, "The results of giving vitamin E for muscular dystrophy and amyotrophic lateral sclerosis support the contention that these are deficiency diseases and curable."—*The General Practitioner*.

Testosterone Propionate for Uterine bleeding.

The Mazers list the advantages of testosterone therapy for the treatment of premenopausal dysfunctional uterine bleeding as follows: (1) It obviates the need of applying radium or the use of X-rays, which is usually followed by severe climacteric symptoms. (2) It does not cause sudden and permanent amenorrhea. (3) It does not require hospitalization and is therefore readily accepted by most patients. The Mazers find that smaller doses, a total of from 50 to 200 mg. given over a month, are effective and do not evoke masculinizing changes. Testosterone propionate relieves "dysfunctional uterine bleeding in about 50 per cent of the patients who submit to a month's treatment. The modus operandi of the smaller doses in controlling uterine bleeding of the dysfunctional type is either through the ability of the product to neutralize the continuous action of estrogen on the müllerian tract or through inhibition of the unknown endometrial bleeding factor. Regardless of dosage, it cannot rejuvenate aging ovaries or stimulate the ovaries of younger women to biphasic activity; therefore its influence on dysfunctional uterine bleeding is temporary but long enough to permit natural readjustment to take place. Failure of readjustment results in recurrences. The authors treated sixty-four women, forty-eight of premenopausal age and sixteen younger women, with testosterone propionate in sesame oil given intramuscularly every other day for one month. Forty-four women received a total of from 50 to 200 mg. and twenty from 300 to 600 mg. Thirty-five preliminary curettages were performed as an office procedure to eliminate malignant growths. The remaining women refused to submit to a curettage. A cure was considered to have been effected if the abnormal uterine bleeding ceased during the month of treatment and did not recur for at least three months after its withdrawal. The follow-up period ranged from three to nineteen months with an average of 7.6 months. Forty-two of the sixty-four patients (66 per cent) were cured and twenty-two (34 per cent) were not or were only temporarily improved. Twenty-seven, or 77 per cent, of the thirty-five women who were curetted remained well during the follow-up period, whereas only fifteen of the twenty-nine non-curetted patients remained well for this length of time. This indicates that in 25 per cent curettage alone arrested the dysfunctional uterine bleeding for a period of three or more months, at least long enough for the endocrine imbalance to adjust itself. This is in accord with the authors' experience with eighty-two error-rhagic women who had received no other treatment than curettage. Larger doses of testosterone did not yield better results; fourteen noncuretted patients received the larger doses with a cure in seven, and fifteen noncuretted patients received the smaller doses with a cure in eight. Seven of the forty-two cured patients had recurrences of uterine bleeding in less than six

months after withdrawal of treatment. There were no constitutional ill effects among the sixty-four treated patients. Four patients conceived within one to ten months after withdrawal of treatment. Three of them were delivered of normal infants and one had an induced abortion. The climacteric symptoms complained of by some patients were not influenced even by the large doses employed.—J. A. M. A.

PROCEEDINGS OF SOCIETIES, ASSOCIATIONS, ETC.

The Krishna District Medical Association, Masulipatam.

(The Krishna District Branch of the Indian Medical Association).

At the monthly meeting held on Saturday the 21st December 1940 at Masulipatam in the Local Town Hall, presided over by Dr. M. Seshacharyulu, L. M. S., Masulipatam, the papers on the following subjects by the Doctors noted against them were read and discussed :—

(1) A case of Acute Nephritis treated with Sulphanilamide—By Dr. K. Kuppuswamy, M.B.B.S., Masulipatam.

(2) Physiology of Human Desires—By Dr. Y. S. Chowdary, L.M.P., Mudinepalli.

(3) Causes of Chest Pain—By Dr. N. Rama Rao, L.M.P., Gollapalli.

(4) An Interesting Case of the Stone in the Bladder and

(5) A Case of Ruptured Uterus—By Dr. M. V. Subbarao, L.M.P., Resident Medical Officer, Govt. Headquarters Hospital, Masulipatam.

MEDICAL NEWS

The Secretary of the Indian Chemical Manufacturers' Association, Calcutta has sent us the following for publication :—

The necessity of according to the manufacturers of chemical and pharmaceutical products, the facility to have a clinical trial of their products in the hospitals under the control of Government and local bodies, has been stressed in the course of a communication addressed by the Indian Chemical Manufacturers' Association to all the Provincial Governments and major Indian States. It is pointed out that this facility is available in foreign countries and it has considerably helped in making the products manufactured in those countries getting proper market and popularity, whereas the absence of the same in India forms one of the greatest handicaps to the industry. Recently the Medical Research Association in the U. K. in

conjunction with Government Departments and the Association of British Manufacturers arranged clinical trials of several important synthetic remedies previously obtained from abroad but now being manufactured in Great Britain, in order to ensure that these drugs of British manufacture were equivalent to the corresponding imported products. The Chemical Association states that several drugs and proprietary remedies identical to those coming from Germany and other foreign countries are now being manufactured in India and the manufacturers are in a position to prepare many more also but the absence of the facility of clinical test makes it difficult to convince the medical profession and the buyers about the products of Indian manufacture being equally efficacious as the corresponding foreign medicines, which are looked upon as standard. The facility of clinical trial in India would make it possible for many foreign medicines to be replaced by indigenous ones thus helping the chemical and pharmaceutical industry in this country.

As a result of the efforts of Indian Chemical Manufacturers' Association, Calcutta, the Government of India has decided to exempt Benzol used in the manufacture of medical preparations from excise duty. The Government of India levied an excise duty of as. 10. per gallon (subsequently increased to as. 12.) on Benzol on the ground that it can be used as motor spirit as a substitute for petrol. The Indian Chemical Manufacturers' Association had pointed out to the Government that Benzol was used as solvent in the manufacture of Alkaloid preparations, but on account of the excise duty, the Alkaloids prepared in India could not stand in competition with the imported Alkaloids in normal times. The step now taken by the Government of India would enable utilisation of large quantity of Benzol manufactured in coke oven plants which was till now going to waste. It would also give impetus to the manufacture of Alkaloid preparations in this country.

NOTICE

Dextrose Therapy in Every-day Practice :

A survey of the Literature, 1900—1936, on the Experimental and Clinical Studies Applicable to Medicine and Surgery—By E. Martin, Sc. D., pp. 451, with 44 illustrations Published by Messrs. Paul B. Hoeber, London and New York. Price \$ 3.

We have been informed by Messrs. Corn Products Co. Ltd., P. B. 994, Bombay, that they are in a position to offer a limited number of copies of the above valuable publication for the benefit of the medical profession at the concessional price of Rs. 8 per copy, post free. We hope our readers will take advantage of this unique offer and secure their copies at an early date.

NEW PREPARATIONS AND INVENTIONS

Multin 'Shino'.—Manufactured by Shionogi & Co. Ltd. Osaka, (Japan) contains a mixture of albuminous bodies lipoids, and fats. Its immediate effect is to stimulate the reticulo-endothelial system to greater activity and thereby increase the protective and resistant powers of the body in a very effective but mild way. This action is well demonstrated by the fact that the temperature comes down by "lysis" and a rather rapid convalescence is achieved. It is extremely well tolerated and will never bring about any unpleasant reactions. Therefore and on account of its composition—"Multin" cannot be compared with the common protein shock producing milk preparations which, besides shock, also cause a sudden rise of temperature, which is hardly desirable.

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BOOKS RECEIVED

INFANT FEEDING—By Alan Moncrieff, M.D., F.R.C.P. Published by Messrs. Edward Arnold & Co., 41 & 43, Maddox Street, London, W. 1, Price, 1s. 6d. net.

MODERN DRUGS IN GENERAL PRACTICE—By Ethel Browning, M.D., CH. B., Published by Messrs. Edward Arnold & Co., 41 & 43, Maddox Street, London, W. 1, Price, 10s. 6d. net.

LECTURES ON DISEASES OF CHILDREN—By Sir Robert Hutchison, M.D., L.L.D., F.R.C.P., Bart., and Alan Moncrieff, M.D., F.R.C.P. Eighth edition, 1940. Published by Messrs. Edward Arnold & Co., 41 & 43, Maddox Street, London, W. 1, Price, 21s. net.

AIDS TO OPHTHALMOLOGY—By N. Bishop Harman, M.A., M.B. (Cantab.) F.R.C.S., Eng., Hon. L.L.D., Ninth edition, revised by P. M. C. G. Moffatt, M.D., (Lond.), M.R.C.P., F.R.C.S., Eng. D.O.M.S., 1940. Published by Bailliere, Tindall and Cox., 7 & 8, Henrietta Street, London, W. C. 2., Price, 4s. 6d.

AIDS TO PSYCHOLOGY—By J. W. Ewen, M.R.C.P., Edin., D.P.M. Second edition, 1940. Bailliere, Tindall and Cox, 7 & 8, Henrietta Street, London, W. C. 2., Price, 3s. 6d.

THE 1940 YEAR-BOOK OF PUBLIC HEALTH—By J. G. Geiger, M.D., Director of Public Health, City and County of San Francisco. Published by Year Book Publishers, Chicago.

INTRODUCTION TO BIOCHEMISTRY—By W. R. Fearon, M.A., SC. D., M.B., F.I.C., Second edition. Published by Messrs. William Heinemann, (Medical Books), Ltd., 99, Great Russell Street, London, W. C. 1., Price, 17s. 6d. net.

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"INFECTIOUS DISEASES"

Special Issue of the Antiseptic—Feb. 1941.

The first special issue of the Antiseptic during 1941 on the above subject will be published on the 15th of next month. Subjects for the second and third special issues to be brought out in June and Oct. 1941 will be announced later on. Every attempt will be made to make these special issues as useful to the general practitioner as the previous ones.

Past Special Issues of the Antiseptic.

Silver Jubilee Number	1929	*University Extension Board Lectures—May 1936
Eye, Ear, Nose & Throat Number	1930	Tropical Diseases Number Part I
Radium and Radiology	1931	do do Part II
Obstetrics and Gynaecology	1932	*Tuberculosis Number
*University Extension Board Lectures—March & April	1933	Skin Diseases
Venereal Diseases Number	"	*Diseases of the Heart
*University Extension Board Lectures—Feb. and March	1934	*Surgical Emergencies
*Special Annual Numbers—May & June	"	Modern Treatment of Diseases
Pediatrics Number	Oct.	*Diseases of Women
University Extension Board Lectures—Feb., March & April	1935	Ophthalmology in General Practice
*Special Annual Number	"	*Diseases of Gastro-intestinal Tract
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		*Respiratory Diseases—Part I
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Copies of only those marked with an asterisk are available

Opinions of Medical Journals about some of the Special Issues.

Burma Medical Times, on Tropical Diseases Number—"An up-to-date compendium on Tropical Diseases which deserves to be in the library of every medical man in the tropics."

Indian and Eastern Chemist, on 'Modern Treatment of Diseases'—"Publishers are to be congratulated on the production of an issue of exceptional interest. Contributors to this much enlarged Number include physicians and surgeons of national reputation."

Indian Journal of Ophthalmology, on Diabetes Number—"It is a handy reference book on the subject dealing with the diagnosis, treatment and other practical problems of diabetes."

Indian Journal of Pharmacy—Diabetes has been discussed from various view points and every reader is sure to benefit by the wealth of information it supplies."

Indian Medical Journal, on Tropical Diseases Numbers—"Thorough, brilliant and useful. They deal about important tropical diseases."—on Diabetes Number—"This is a special Number dealing exhaustively with Diabetes."

Journal of Andhra Medical Association, on Genito-Urinary Diseases—"Most of the articles are of a practical nature and make instructive as well as interesting reading."

Journal of Stanley Medical College, on Skin Diseases—"Contains very informative articles by various writers from different parts of India."

Medical Digest, on Tropical Diseases, Tuberculosis and Skin Diseases—"are in keeping with the high traditions of the Journal, containing as they do, articles on the subjects from the

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Patna Journal of Medicine, on Diseases of the Heart—"The authors have here dealt with various common maladies of Heart and have suggested quite impressively the various lines of treatment."

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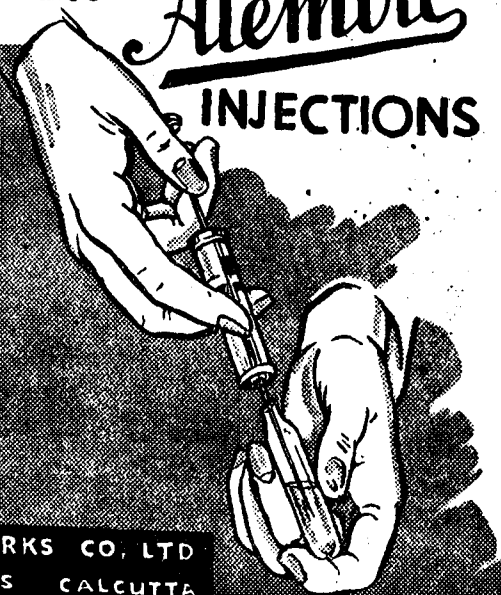
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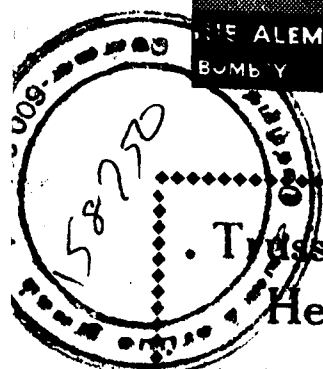
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