

MEDICO-SURGICAL SUGGESTIONS

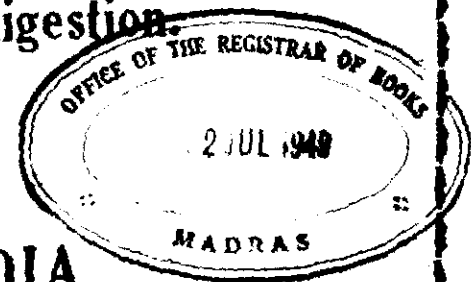
Vol. XVIII.

JUNE 1949.

No. 6.

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MEDICO-SURGICAL SUGGESTIONS

A MONTHLY JOURNAL OF PRACTICAL MEDICINE & SURGERY

Editor: Dr. P. R. Venkappaya

Established 1932

VOL. XVIII

JUNE 1949

NO. 6

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Annual Subscription: Rs. 5; Foreign: 10 sh. Single Copy: As. 8
Sample Copy for 4 As. Stamp.

Office of the Editor & Publisher: 2/337, Mint Street, Madras, India.
Phone: 4030

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KIDNEY STONES

S. P. WANCHOO, M.B., B.S., M.R.C.S., L.R.C.P.

Alwar

The subject of stones in the kidney has been taken up as the condition is much more common in U.P. and Rajputana than is believed by the average general practitioner. Whenever a patient complaining of renal colic or other symptoms pointing to renal stones comes to a practitioner he must not forget that his duty does not end by merely providing symptomatic relief to his patient. He must have his patient thoroughly investigated pathologically and radiologically to exclude the presence of stones or if present to have them properly treated.

SURGERY ANATOMY

Some cardinal points worth stressing are:

1. The right kidney is lower than the left.
2. The ureter lies posterior to renal vessels.
3. In front, the right kidney is in close relation to the ascending colon and duodenum and the left kidney to the descending colon.
4. The inferior vena cava is so near the right kidney that it is likely to be injured during removal of the kidney.
5. The kidney has two capsules, the outer fatty and the inner true capsule.

ETIOLOGY

The stones occur most commonly during the ages of 20 and 50 years. Both sexes are equally susceptible.

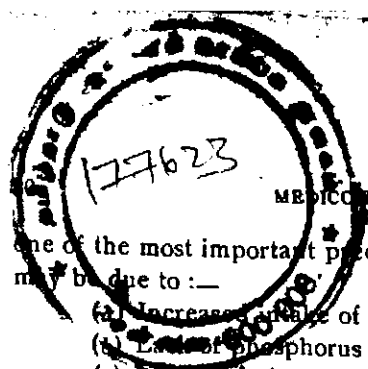
MODE OF FORMATION OF THE STONE

The urine contains a number of crystalline substances, which are held in supersaturated solution through the protective action of colloids such as mucin.

The formation of stone may result from:

- (a) Increased crystalloids excreted in the urine.
- (b) Diminution, qualitative or quantitative, in the supporting colloids.

INCREASE OF CRYSTALLOIDS IN THE URINE—An increase in the blood calcium with a consequent increased output of calcium in the urine is



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one of the most important predisposing causes. Increased blood calcium may be due to :—

- (a) Increased intake of calcium in the food ;
- (b) Lack of phosphorus in the diet ;
- (c) Increased absorption of calcium from the intestines, diet being normal ;
- (d) Withdrawal of calcium from the skeleton.

Increased intake of calcium in the food—The geographical incidence of urinary calculus is probably due in part to a local excess of calcium in the soil and water.

A map of urinary stone incidence drawn by McCarrison closely resembles the one of calcium distribution in India. The contrast is most vividly demonstrated in the following example :—

Dera Ghazi Khan on the right bank of the river Indus is rich in calcium. District Muzaffargarh facing Dera on the opposite bank is a calcium-poor area. The difference in the number of urinary stone cases in the two districts is great. Whereas calcium-rich Dera Ghazi Khan has an incidence of 76 per lakh of the population, calcium-poor Muzaffargarh has only 45 per lakh.

Lack of phosphorus in the diet—Less phosphorus in the diet means less concentration in the blood whereas phosphorus-calcium ratio must be maintained. To do that, the blood has to get rid of some of the calcium through the urine.

Increased absorption of calcium from the intestines—The diet being normal such increased absorption may be influenced by excessive administration of vitamin D.

Withdrawal of calcium from the skeleton—This is seen in the most severe form in osteitis fibrosa in which, as a result of parathyroid overaction, the whole skeleton is decalcified. In this disease, urinary calculus is a common complication. A similar withdrawal of calcium from the skeleton is seen to a lesser extent, in any chronic bone affection and even as a result of prolonged decubitus. Thus urinary calculus is not an uncommon complication, in tuberculosis of bones and joints and even fractures treated by prolonged recumbency. Recumbency causes a dependent position of the renal pelvis thereby preventing proper drainage.

DIMINUTION, QUALITATIVE OR QUANTITATIVE, OF SUPPORTING COLLOIDS—The solvent property of colloids is influenced by a number of factors :—

- (a) Any local lesion causing urinary stasis, predisposes to calculi which are common in malformations such as the horse-shoe kidney ;
- (b) Infection of the urine e.g., prostatitis, cystitis, etc.

CONSIDERATION OF OTHER FACTORS—1. **Salts**—Sodium chloride and sulphates have the property of preventing the formation of stones. This probably accounts for the fact that whales in their natural state do not

suffer from urinary stones ; and that in olden days the sailors, who used to eat mostly salted food were immune from stone formation.

2. **Hardness of water**—Temporary hardness of water is one of the most important causes of urinary stones.

3. **Deficiency of vitamins A and B**—Diets deficient in vitamins A and B encourage stone formation in two ways :—

1. By impairing epithelial nutrition of the kidneys
2. By decreasing the acidity of the urine, thereby precipitating calcium phosphate.

4. **Cereals**—Robert McCarrison tried to prove that certain cereals have definite correlation to stone formation—that rice eaters are less susceptible than wheat eaters. This is true if the low incidence in Bengal is compared with that of the Punjab. Against this theory also there is an interesting observation : The inhabitants of Manipur (Assam) are chiefly rice eaters and yet they have the same stone incidence as the people of the Punjab and West U.P. where people are mostly wheat eaters.

5. **Climate**—It has been contended by some urologists that high concentration of urine may be a factor in the high incidence of stone in the tropics.

Against this, again there is an interesting observation. The District of Nasik with its most pleasant climate has the same stone incidence as the District of Jacobabad which is the hottest spot in India. Parts of the Punjab, where the annual rainfall is less than 20 inches has the same incidence as the Manipur in Assam where the annual rainfall is more than 80 inches.

TYPES OF COMMON CALCULI

Stones may be primary or secondary.

Primary stones are those that arise in an apparently healthy urinary tract and are composed of substances normally present in the urine or as a result of metabolic disorders. They occur in acid urine and require no preformed nuclei. They are usually composed of oxalates, urates or uric acid.

Secondary stones are those that result from inflammation. Their formation requires a preformed nucleus which may be a primary stone, a foreign body, a clump of organisms or a mass of inflammatory exudate. They are formed in alkaline urine, since they are the result of liberation of ammonia from urea. They are invariably triple phosphates in composition.

Oxalate stone—After ingestion of food rich in oxalates they may be precipitated in the urine in crystalline form. Food rich in oxalates are spinach, tomatoes and asparagus. Strawberries are of ill repute in this respect but without reason, as their oxalate content is less than that of potatoes. Oxalate stones are very hard. They may be smooth and rounded or nodular and covered with sharp spicules. They irritate the

mucous membrane and excite an outpouring of lymph and blood which renders them dark brown or black.

Urate and uric acid stones—They are partly of exogenous origin from meat or other animal food and partly of endogenous origin from breaking down of tissues. They are hard but smooth, yellow or brown in colour and usually round or oval.

Phosphatic stones—They are soft and friable, grey or dirty brown in colour. Often they attain a large size and they form the majority of "staghorn calculus" of the kidney. Since they often arise from staphylococcal or streptococcal infection that resists treatment, recurrence after operation is common. Worry and mental strain may cause these stones on account of excretion of excessive phosphates in the urine of such patients.

PATHOLOGY

Stones may damage the kidney either directly by trauma or indirectly by obstructing the outflow of urine. The most frequent and damaging changes take place following obstruction, leading to dilatation of the ureter, pelvis and calices and in many cases resulting in pressure-destruction of the renal parenchyma. Small kidney stones are more likely to cause obstruction than large ones, because the former can move in such a way as to cause intermittent obstruction. Usually the first gross changes following retention is a gradual enlargement of the kidney which may retain most of the normal markings. As the retention increases, the kidney becomes lobulated and finally a distended thin-walled sac results, filled with a pale yellow fluid—the hydronephrotic kidney. Destructive changes progress much more rapidly when infection occurs by way of urinary passages or more often through the blood stream—the pyonephrotic kidney.

Pathologically there are two types of pyonephrotic kidneys :—(a) The kidney is thick-walled and contracted round about the stone. This type is more common in cases of incomplete obstruction, where the kidney is making a constant effort to expel the stone.

(b) In the second type the kidney is dilated bulbous or filled with fluid as in hydronephrosis, except that the fluid is thick greenish and foul-smelling. This type is more common when the obstruction is complete.

Stone and malignant disease—The majority of squamous-celled carcinomas of the renal pelvis are associated with pelvic stones. Squamous-celled growths are more likely to result from chronic irritation, which is provided in this case by the stone and it is more than likely, that the early removal of the stone, might have prevented the formation of the growth.

SYMPTOMS

Kidney stones may exist for years without causing symptoms. Symptomless stones are frequently discovered during an examination for other conditions or at autopsy. However, the majority of stones cause

fairly characteristic symptoms, which are pain, renal colic, hæmaturia passage of stones and anuria.

Pain—It is a fairly constant dull ache, localised to the kidney area, being most marked either in the back below the last rib or more rarely in the lower abdomen below the iliac crest which on the right side may simulate appendicitis. The pain may be increased by muscular exertion or sudden movements. The pain is due to distension of renal pelvis with urine from blocking of the pelvi-ureteral junction by stone.

Renal colic—It is one of the most characteristic symptoms. The colic is due to the effort of the kidney to get rid of the stone. The pain is usually severe and is described by the patient as "knife like" or "stabbing" in character and it usually "doubles him up". Coming on suddenly, it starts in the kidney region, radiates to the groin or the scrotum. The testes may be retracted by the cremaster muscle and may be extremely tender and remain so for sometime. Rarely it may radiate to the anterior and sometimes to the posterior aspect of the thigh. More rarely it may radiate to the shoulders, thus simulating gall-stones on the right side and angina pectoris on the left. For several days following the attack of colic there is a residual tenderness in the kidney area. Nausea or even vomiting occurs in severe attacks. There is a striking lack of constitutional symptoms in the uncomplicated cases. However, if the kidney is infected, the attacks of colics may be accompanied by chill and fever. The attack of colic terminates as suddenly as it begins. Renal colic is present in about 50 per cent of the cases having renal stones. On the other hand it may occur in conditions other than renal stones, e.g., in oxaluria and passage of blood clots in tumours of the kidney.

Passage of stones—The spontaneous passage of stones in the urine is an important objective symptom. The majority of these appear after an attack of colic, though sometimes they are passed without an attack.

Hæmaturia—Naked-eye blood in the urine is one of the symptoms that the patient may complain of. The fallacy is that the blood may be due to some other disease in the kidney or may come from some other organ of the urinary tract. The blood is rarely in sufficient amounts to affect the general health of the patient. The blood is increased after exercise.

Anuria—A sudden total anuria may be the first symptom of stone in the upper urinary tract. A common method of onset is rapid diminution and a final cessation of the urine.

PHYSICAL EXAMINATION

It is of little aid in the diagnosis of uncomplicated kidney stones. Nevertheless a careful physical examination should be carried out. There are two advantages :—

- (a) Other lesions simulating the symptoms of stones may be found.
- (b) Complicating conditions may be discovered :

(i) *Bimanual palpation of kidneys*—A kidney, which is unduly mobile or enlarged, will be grasped between the two hands. On the other hand, the kidney may be enlarged and yet not be palpable if it is wholly above the costal margin or obscured by the liver or a thick abdominal wall.

(ii) *Kidney pointing test*—The patient sits up; the examiner's index finger is pressed into the angle between the last rib and the erector spinæ muscle. Distinct tenderness points to some pathological condition in the kidney.

(iii) *Murphy's thumping test*—Put a hand flatly in the kidney region and thump it with the other fist. Distinct tenderness points to some pathology underneath.

(iv) *Laboratory Investigations*—Microscopic examination of the urine may show R.B.C. or pus cells

RED BLOOD CELLS. Red blood cells when present, are important in directing attention to the urinary tract in an otherwise normal case.

PUS CELLS. Pus cells when present, indicate infection plus stone. For obvious reasons one should insist upon a catheter specimen of urine in females.

ALBUMEN. Albumen in varying amounts would be present when R.B.C. or pus cells are present

BLOOD UREA EXAMINATION. It should be carried out in order to have a general idea of the total renal function.

X-RAY INVESTIGATIONS

Valuable aid in diagnosis is obtained by this examination.

Simple Radiography. Both antero-posterior and lateral films are necessary.

A.P. View.—After an efficient evacuation of the alimentary tract, the outline of a normal kidney should be visible, lying opposite the bodies of the 1st, 2nd and 3rd lumbar vertebræ and having an excursion of $1\frac{1}{2}$ to 2 inches in forced breathing. The right kidney is slightly lower than the left. When reading the films two points should be kept in mind:—(a) whether there is a general enlargement of the renal shadow and (b) whether there is any well-marked shadow, super-imposed in the renal area.

General Enlargement of the Renal Shadow. A good skiagram in a thin subject usually shows the outline of the kidney so plainly that one of them may be thought to be visibly enlarged. Marked enlargement may be due to congenital cystic kidney, hydronephrosis or pyonephrosis. The last two conditions have a bearing on the present subject, as they are sometimes the complication of a stone and their presence makes necessary a change in the line of treatment.

Presence of well-marked shadow superimposed on the renal area. If the shadow is triangular or branched, like the calices of the kidney,

the diagnosis of a stone is practically certain. Besides the presence of a stone, the size, number and exact location can be determined.

Lateral view.—A renal calculus gives a shadow superimposed upon the bodies of the lumbar vertebræ, unless the kidney is enlarged, when the shadow is displaced in front of the bodies.

Fallacies—(1) A shadow is thrown but it may not be due to stone in kidney.

(2) No shadow is thrown although a stone is present. When the shadow is not due to a stone in the kidney it may be due to:

1. Intestinal contents which cast a shadow on account of inefficient preparation of the patient, or if the patient has recently taken bismuth or magnesium salts. If in doubt, a second examination should be done after further purgation.

2. Calcification of abdominal or mesenteric lymph glands.—The shadow of a calcified lymph gland is usually mottled in appearance.

3. Gall stones.—They may give a shadow in the renal area on the right side. They are less dense and frequently multiple and faceted. In a lateral view the shadow of a gall-stone will occupy a much more anterior position. A gall-stone obstructed in the common bile duct may, however, throw a shadow opposite the body of the 1st or 2nd lumbar vertebra.

4. Calcified costal cartilage may throw a shadow.—The lateral view will differentiate at once.

5. Caseous masses in a tuberculous kidney.—The shadow is not as well defined as a calculus.

6. Calcareous area in a renal carcinoma.—The shadow is ill-defined. No shadow is thrown though a stone is present. This may be due to:

(a) Gas in the intestines.

(b) Stone lying in line with a rib.

(c) Presence of a non-opaque urate or uric acid stone.

Excretion Urography.—This is a very valuable examination in stone surgery. The advantages are:

1. Determines the comparative function of both the kidneys.
2. Demonstrates coincident disease in the affected kidney, which may preclude an operation or vary the type of operative procedure.
3. Determines the functional capacity and disease or abnormality in the opposite kidney.

4. Demonstrates the intra-renal pelvis. One knows where exactly to find a pelvic stone in such cases, thereby avoiding lot of unnecessary trouble during the operation.

5. In cases with negative X-ray findings, the study of renal function by urography will often give valuable information. Gross abnormality of function on the side of the kidney causing symptoms indicates a stone or some other disease, thereby pointing necessity of exploring the kidney by operation.

Distinguished urologists like Cabot are of the opinion that *visual estimates of kidney function by excretion urography is more accurate and satisfactory than the usual chemical tests of renal function.*

Cystoscopy and Ascending Pyelography.—These are not carried out by the author as a routine procedure because a proper excretion urography eliminates their need and is much less troublesome to the patient.

Diagnosis of calculus anuria.—Calculus anuria must be distinguished from anuria seen in hysterical patients and in the terminal stages of nephritis. The clinical picture of the patient, suffering from calculus anuria is quite different from that of nephritic uræmia although both conditions produce an excess of nitrogenous bodies in the blood. In contrast to the convulsive uræmic patient, the one with calculus anuria, in the early stages, is quite comfortable. His intellect is clear, œdema is slight or absent and gastro-intestinal symptoms are mild. The early state lasts about 5 to 7 days and on account of lack of symptoms is called "the tolerant stage." True uræmic symptoms follow later on. The lack of serious symptoms in the tolerant stage gives a false sense of security and the patient is allowed to get into an extremely hazardous condition, before it is recognised. It must not be forgotten, that anuria is always a serious condition and every effort must be made in arriving at an accurate and early diagnosis, so that proper treatment is planned and carried out before the final stage sets in. Hysterical cases may absolutely mimic calculus anuria and can be distinguished only by radiography. Where this evidence of stone is negative, hysteria is the evident diagnosis.

PROGNOSIS

There is a saying "A man is as old as his arteries." It should be amended and said "A man is as old as his arteries and his kidneys." The prognosis will therefore depend upon the amount of damage the stone has done to the kidneys.

TREATMENT

(a) Symptomatic (b) Curative (c) Treatment of causative condition like cervicitis, prostatitis, etc.

Symptomatic treatment.—It may be of (a) renal colic (b) calculus anuria.

Renal colic.—1. Hot water bottle; 2. Soap water enema; 3. Morphine and atropine subcutaneously in full dose, 4 hourly if necessary. In intractable cases morphia gr. 1/12 intravenously gives amazing relief. 4. Diuretics and barley water. 5. Antiphlogistine to the loins. 6. Hot hip bath at the onset aborts an attack in certain persons. 7. Cupping the loins. 8. Leeches.

Calculus anuria.—By ureteral catheterisation, displace the stone back into the pelvis. If that is not possible, attempt to pass the catheter up by the side of the obstruction and leave it there. This will give a breathing time to carry out other investigations. If ureteral catheterisation is not possible nephrectomy should not be delayed.

Curative treatment.—Some Vaidis and Hakims claim to have effected permanent relief by medicines in patients suffering from renal colics due to stones too large to be passed. It should be remembered, however, that colic is a symptom of life; when the kidney becomes dead, the colics would automatically stop. Thus by avoiding operation in such cases irrevocable harm can be done.

Treatment depends on whether the stone is unilateral or bilateral.

Unilateral stones.—For purpose of treatment these cases may be divided into three types. (a) Stones small enough to be passed. (b) Stones too large to pass. (c) Calculus pyonephrosis.

Small Stones.—If the stone is small enough to be passed, no treatment except diuretics and urinary antiseptics may be necessary. The decision for or against the operation, should be made upon the evidence of the amount of damage the stone is doing. Thus small stones lying quietly in the lower calyx, when not producing colic and unaccompanied by infection may be allowed to remain. However, these cases should be followed up by radiographs at six monthly intervals, to see, whether they are increasing in size. If the stone increases in size considerably, it should be removed. A stone in the infected pelvis is objectionable, and should it show no tendency to pass, it should be removed.

Stones too large to pass.—Such stones are from 1 cm. upwards in size. Advisability of removing the stone depends upon the age of the patient. In old people they are best left alone. Old people can live comfortably on a reduced amount of kidney tissue. The days of rigorous demands on the kidneys are over and attempts to increase the amount of functioning tissue may be unwise and hazardous. On the other hand in younger people, the stone must be removed whether causing symptoms or not, as its presence is incompatible with the continued integrity of the kidney. Later on, infection is bound to take place and the avoidance of the operation now, may mean the sacrifice of the kidney later.

Calculus pyonephrosis.—Such patients usually come to the surgeon in a fairly exhausted condition, as they had been victims of septic absorption for a long time. The undertaking of any serious operation in such cases would be unduly hazardous to the patient's life. Hence the first thing to do in such cases is to drain out the pus by a nephrostomy, scooping out any stones that come in the way. It is remarkable that after such drainage, the patients pick up enough strength in a short time to undergo any prolonged operation. However before undertaking a second operation, these cases must have fresh excretion urographs taken. It is amazing that mere nephrostomy sometimes permits us to revive some of these apparently functionless kidneys. However if the kidney is still functionless, it should be removed provided that the other kidney is in a satisfactory condition.

Bilateral stones.—Old people are best left alone. In younger persons the question of which kidney to tackle first is rather ticklish. The

general principle is that the kidney, which is the least affected should be taken up first, the reasons being—

1. If after operation, on the less diseased organ, the other kidney gets blocked, there is only slight impairment of renal function.
2. If the less diseased kidney is not operated upon first, it may cause obstruction, as it usually has smaller stones, which might easily get blocked due to increased compensatory activity of the kidney, following an operation on the diseased organ.
3. The less diseased kidney is the one likely to have caused the more recent trouble.

Depending on the health of the patient and usually 3 to 6 months after operation on the less diseased kidney, the other organ should be tackled and if necessary, removed.

Concomitant renal and ureteral calculi—Usually it is necessary to clear up the ureter before any surgical approach is made on the kidneys. The most satisfactory method is to remove the ureteral stone through a cystoscope. If that is not possible, then open operation would be needed.

1. If the ureteral stone is fairly high up on the same side as the kidney to be operated, then it can be pushed up into the pelvis and tackled through the kidney incision.

2. If the stone is well down, then it should be removed by extra-peritoneal lower abdominal route and this operation should precede the removal of stone from the kidney.

3. If the kidney is completely destroyed, mere removal of stone is useless. If the ureter above the stone is dilated, infected, and functionless, nephrectomy should be performed, removing the ureter to a point below the stone. On the other hand if the ureter is not dilated it is not necessary to remove the ureter with the contained stone during nephrectomy.

Operation—

Position of the patient—Lateral; some type of spinal support is essential.

Incision—The author uses the hockey-stick incision of Mayo. The lower part of the incision starts midway between the crest of the ileum and the last rib; it passes backwards almost parallel to the iliac crest until it crosses the border of the latissimus dorsi, where it turns upwards to end in the angle between the last rib and the spine. In cases where the 12th rib is rudimentary, this incision planned to pass close by the last rib which in this case is the 11th, is much higher and the pleura, which generally comes down below the 11th, may be injured. In these days, when some form of x-ray evidence is always utilised for diagnosis, there seems little excuse for overlooking a short or rudimentary 12th rib. Even then, if the pleura is injured, one should immediately close up the tear putting penicillin through a small catheter, which is taken away, after the tear has been completely sewn up. No harm usually results.

However such cases should be observed carefully for any signs of pleurisy or pneumothorax during the post-operative period.

The kidney is separated from its fatty capsule and freely mobilised by gently working with the index fingers over all its contours. On the right side, the last rib usually causes no obstruction in deliverance of the kidney. On the left side, as the kidney is placed higher, there may be difficulty. Cutting the last costo-vertebral ligament, usually permits the 12th rib to be pulled up well out of the incision.

The kidney having been delivered on the surface, must be held up. Two strips of small gauze sponges are passed under the poles, crossed on the sides of the kidney and held up by clamps by the assistant. The next stage of the operation will depend upon the site of the stone and whether or not the kidney has to be removed.

The following are the various operations, that are performed:—

1. Pelviolithotomy, i.e., the removal of a stone from the pelvis of the kidney.
2. Nephrolithotomy, i.e., removal of stone by incising the kidney cortex.
3. Combined pelvinephrolithotomy.
4. Resection of kidney.
5. Nephrectomy—It may be intracapsular or subcapsular.

Pelviolithotomy—Posterior pelviolithotomy is the operation of choice. Removal of stones through the pelvis does not destroy important structures; large vessels are not divided; and an accurate anatomical closure is possible. The operation is easily carried out and is rarely followed by immediate or late complications. Certain points are worth mentioning:—

1. When the pelvis is more accessible on the front, no hesitation need arise about opening it on this surface.

2. The overlying fatty tissue should be dissected away from the pelvis in a flap-like manner, whenever possible. This permits a more complete closure of the pelvis after removal of the stone.

3. A curved haemostat is used to search the pelvis and calyces for small stones. If the stone is not readily located, the incision may be enlarged for inserting the tip of the little finger, which explores the pelvis and calyces. It is not possible to enter the calyces, but pressing down on the overlying parenchyma, the contained stone may usually be felt.

4. Before closing the wound in the pelvis it is essential to demonstrate the freedom of the ureter from obstruction. This is done by passing a ureteral catheter down.

2. Several soft rubber tissue drains are inserted down to the region of the kidney pelvis. The first drain is removed on the 7th day and all drains by the 10th day.

Nephrolithotomy—At present with our accurate means of localisation of stones, nephrolithotomy is rarely indicated for uncomplicated stones in the pelvis and calyces. Occasionally in secondary operations, when the kidney is fixed, it is necessary to remove the stone by this method. Small incisions through the kidney parenchyma may be made quite easily and are not followed by undesirable sequelae. These sequelae are severe hæmorrhage, infection and destruction of a large part of the kidney.

tissue. The destruction may be greater than what would result from leaving the stone in the kidney.

Complications—Hæmorrhage and sepsis are the most common. It must not be forgotten that slight amount of bleeding occurs after all kidney operations, for 5 or 6 days. The urine is tinged with blood and no notice need be taken about it. When however the loss of blood is beginning to be felt, as shown by slowly rising pulse-rate, immediate action must be taken. First of all one should open up the wound and pack it. Then administer hæmoplastin and morphia. If the hæmorrhage does not stop, the kidney should be removed.

Combined pelvionephrolithotomy—In certain cases the stone is lodged in the calyx from which it is impossible to bring it to the pelvis, the communication between the pelvis and the calyx being too small. In such cases the combined operation is the one of choice. The pelvis is opened and the stone is located either with the finger or with a pair of forceps. It is then pressed upwards towards the cortex and a small incision made over it with a knife or pointed forceps. If there is infection, the incision in the cortex should be drained. If no infection is present it is closed, with several interrupted catgut sutures.

Resection of the kidney—During the last decade the general tendency has been to be more conservative in operations on the kidney, as it is a sound surgical practice not to remove any tissue capable of functioning. Although the surgical technique is not yet sufficiently perfect to prevent the formation of sinuses, yet these when they occur, heal promptly. The important thing is that the stump of the kidney left behind must be assured of an adequate blood supply, before the vessels of the diseased part are clamped. Resection is of value, when destruction is confined to localised area of the sound tissue, where local fibrosis is generally present and therefore the hæmorrhage is not copious. After resection, two layers of sutures, inner and outer, are applied. They are supplemented by through and through interrupted sutures. The incision should then be covered with the flap made from adjacent fatty tissue. In certain cases, resection may be the only operation possible, the other kidney being functionless or removed previously.

Nephrectomy—It is indicated when destruction of the kidney is so complete that besides being of no value, it is a positive menace to the patient and when the condition of the patient demands rapid operative procedures.

Intra-capsular nephrectomy—The kidney is removed with its capsule. The following points are worth mentioning:—

1. The kidney is tightly adherent to the surrounding structures, and the peritoneum and pleura are likely to be injured. The accidents if recognised early and closed up, will rarely cause trouble.
2. In cases with a short pedicle, the approach is rendered easier by dividing the ureter at a point below the kidney and freeing it up to the

pelvis. This enables the operator to separate the pelvis from the vessels, thus diminishing the size of the pedicle.

3. The vascular pedicle is freed as much as possible by the removal of fatty tissue and fibrous bands.

4. To ensure safety the pedicle is doubly or triply ligated with stout chromicized catgut in a double strand.

5. Soft rubber tissue drains are left as usual and taken out after 3 to 5 days.

Subcapsular Nephrectomy—In some cases the fatty capsule of the kidney is so thoroughly adherent to the surrounding tissues on one side and the true capsule on the other, that its removal is practically impossible. This is specially true if some operation had been performed previously. Under such circumstances, one has to remove the kidney without its true capsule. After opening the capsule it is separated from the kidney by blunt dissection and folded down over the pedicle. The base of the kidney is now felt as a thickened mass, which includes the pedicle. It is extremely difficult to clamp such a mass. The danger is that the clamp might cut through the mass and bleeding takes place behind it. However in these extremely destroyed kidneys, the blood supply is usually poor and only moderate pressure is required to control bleeding. If bleeding is not controlled the artery forceps can be left for 48 hours and then taken off. A subcapsular operation leaves behind a thickened and partially infected fatty capsule, which prolongs drainage and leaves sinuses. They usually close up after some time. It must be understood that this operation is not one of election but is usually forced on the surgeon as one of necessity.

Accidents—1. Opening of the pleural cavity—This has already been dealt with.

2. Injury to the intestines—Only three portions of the intestines are likely to be injured. On the left side the descending colon; on the right side the ascending colon and 2nd part of the duodenum. If recognised at once, the tear should be stitched up and recovery is the rule.

Complications—Paralytic ileus is fairly common after kidney operation and should be anticipated and dealt with at once.

Mortality—It is highest in nephrolithotomies and lowest in pelvionephrolithotomies—nephrectomies are in the middle.

Recurrence—In most cases the period of stone formation is limited; when the stone-forming period (30 to 50 years) has passed stones are not likely to recur, following their complete removal.

The rate of recurrence is 24% after nephrolithotomies, 12% after pelvionephrolithotomies, 6% after pelvionephrolithotomies.

Recurrence is most marked after nephrolithotomies as in some cases fragments of stones are left behind at the time of operation. Although recurrence is sometimes unpreventable, the following instructions to operated cases, when they leave the hospital, are of value:—

1. Take plenty of table-salt especially during the summer.

2. Avoid taking oxalate forming articles like spinach, tomatoes, etc.
3. Avoid mental strain and worry.
4. Take plenty of water to flush the kidneys.
5. Avoid too much of meat and other protein foods, especially kidney, liver and brain.
6. During any illness requiring prolonged recumbency, the patient should supplement his diet with vitamins A and B.

In conclusion it may be mentioned that any surgeon tackling stones in the kidney should be prepared to do a nephrectomy at a very short notice. Removal of kidney stones howsoever skilfully done is sometimes followed by severe bleeding, which can only be controlled by its removal. Nephrectomy in such cases carry a very high mortality but there are occasions, when both the patient and the surgeon may have to face the risk.

The abyss is worth a leap however wide

When life, sweet life, lies on the other side *

* A paper read at the U.P. Provincial Medical Conference.

(*Journal I.M.A. March 1949.*)

Extracts.

THE MYSTERY OF THE EOSINOPHIL.

An increase in circulating eosinophils is a feature of number of disorders which otherwise appear to have little in common. There are groups of conditions, such as allergic diseases of all kinds, parasitic infestations, and cutaneous eruptions, in which we can at least say that sensitization, a metazoan parasite, or a visible skin disease links the group together. But outside these categories come a number of other conditions which appear to have nothing to do with three main groups. One of these is lymphadenoma: enlargement of lymph glands with eosinophilia nearly always leads to the diagnosis of that disease. The eosinophilia may be very marked indeed and extend to 50 per cent or more of the total leucocytes, themselves abnormally increased. Some have felt that this implies an allergic background, and attempts apparently unsuccessful, have been made to prove sensitization by intradermal inoculation of lymphadenomatous material. It is probable that in this disease the eosinophilia in the blood is the result of an overflow from the eosinophil deposits in the affected lymph glands, and that it is, therefore, analogous to the lymphocytosis in lymphatic leukaemia. Eosinophilic leukaemia may be considered as a disorder linking the true eukemias and lymphadenoma, and lymphadenoma should be looked upon as one of many possible forms of malignancy in an organ with many functions and an eventful embryonic career.

Sometimes however, eosinophilia with enlargement of lymph glands occurs in serum sickness and may be confusing. The presence of heterophilic antibodies to sheep red cells differentiates the two conditions—the test for these is so unpredictable and apparently irrational that it recalls some of the methods of mediæval medicine in its more esoteric phases.

* Allergic eosinophilia is most variable in its appearance. Many patients with severe asthma have no eosinophilia; on the other hand,

there may be marked eosinophilia in patients who react acutely for the first time to certain drugs or foodstuffs.

Symptomless eosinophilia is most often due to metazoan parasites, and in certain parts of the world where helminth infestation is universal eosinophilia is equally common. In the tropical belt of Africa infestation by *Filaria perstans* is both symptomless and practically universal, at least in some areas, and the eosinophils may amount to 70 per cent or more of the circulating leucocytes. It should be remembered that amoebiasis does not cause eosinophilia—protozoa never evoke a response which is essentially metazoan. For some time to come helminth infestation must continue to be carefully excluded in adult males with eosinophilia, particularly in those who, interned in Japanese prison camps, so commonly contracted hookworm and *Strongyloides* infestation.

A further condition commonly associated with eosinophilia is periarthritis nodosa. This disease is to day recognized to be more common than was once believed, and a proportion of the cases recover. Unless a biopsy is possible on a skin nodule the diagnosis of the condition must always be a guess; but eosinophilia is commonly encountered, and where albuminuria, fever, and eosinophilia are found together this disease must at least be considered. The contemporary view is that the condition is allergic, and the eosinophilia certainly gives this some support.

Of recent years there have been separated certain other conditions, all rare, in which eosinophilia is present in tissues or circulating blood and where some authorities have thought it possible to define clinical entities. One such condition is eosinophilic granuloma of skin, detailed studies of which have recently been published (WELDMAN—*Arch. Dermat. Syph.* 55: 155, 1947). Clinically the disease is stated to be chronic and usually self limited condition in which doughy, firm, reddish-brown tumours form in the skin. The diagnosis is essentially a laboratory one, since eosinophilia of the order of 50 per cent is present in the circulating blood and also in the actual lesions. The condition is strikingly similar histologically to periarthritis nodosa, since the lesions occur in relation to small blood vessels and perivascular tissue. Allergy has also been confirmed in some cases: for example, a *Trichophyton* was grown from the feet of a patient, and trichophyton extracts gave positive intradermal reactions.

A much disputed eosinophilic disorder of the lungs was described by Löfller in 1932, and a similar condition, commonest apparently in India, is known as "tropical" eosinophilia. A survey of the latter condition has recently been made by Joseph (*Indian M. Gaz.* 81: 512, 1946), who considers the two disorders distinct. But in certain cases such as that described by Perlingiero and Gyorgy (*Am. J. Child. Dis.*, 73: 84, 1947) infestation with roundworms has been present. Indeed, so many types of worms pass through the lungs at one stage of their life cycle that pulmonary symptoms due to their presence are inevitable. Very definite proof that a parasitic infestation is absent must be demanded before accepting these disorders as new entities. The discovery of mites in the sputum of patients must be accepted with abundant reserve. Entomologists tell us that their peace of mind is constantly being undermined by reports of mites in sputum, urine, or faeces. The truth is that mites are everywhere and easily fall into containers later filled with pathological material.

Eosinophilic granuloma of bone is a much more distinct entity. It was first described by Finzi in 1929, and something under fifty cases

have been recorded. It is now generally agreed that the condition is one stage in the development of a disturbance of lipid metabolism, and that the tamely named and Schuller-Christian disease is essentially the same disorder in an earlier stage. Other conditions in which tissue or blood eosinophilia may be present are numerous, but in most of them the eosinophilia is erratic and of most uncertain significance. In the whole gastro intestinal tract, for example, acute inflammation is often eosinophilic; in widespread secondary malignant deposits blood eosinophilia has been recorded, but is not the rule; eosinophilia in blood and tissues occurs in some cases of radium sickness; and on occasion eosinophilic pleural effusions are found which appear to have no common aetiology or prognostic significance.

There is in fact, no apparent link between all the varied conditions in which eosinophils are a prominent feature. But it is worth remembering that ignorance about the function of all other leucocytes, except polymorphs, is as great. No one has suggested what function a basophil cell or a monocyte may be expected to carry out. Lymphocytes amount to 40 per cent of circulating cells, yet few haematologists would like to be dogmatic about their purpose. If the eosinophil is a mystery, it is least in good company — *Brit M. J.* 1,989, 1948.



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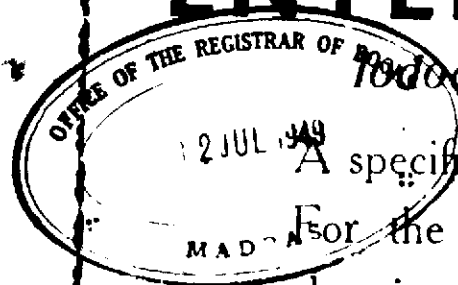
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Editor: Dr. P. R. Venkappaya

Established 1932

VOL. XVIII

MAY 1949

NO. 5

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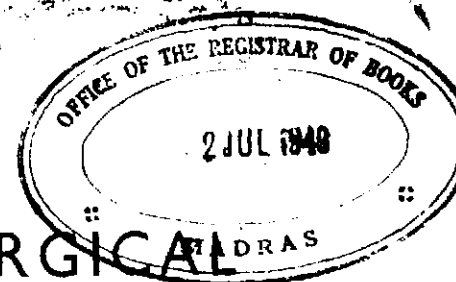
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Office of the Editor & Publisher; 2/337, Mint Street, Madras, India.
Phone: 4030.

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVIII

MAY 1949

No. 5

A GENERAL REVIEW OF NITROUS OXIDE ANAESTHESIA*

LELAND O. LEARNED, M.D.

Salt Lake City, Utah.

Nitrous oxide was discovered by Joseph Priestley between 1772 and 1776 during his experiments on air. He marvelled at its property of supporting the flame of a candle coupled with its ability in pure form to kill animal life.

In 1798 the Pneumatic Institute was founded by Dr. Thomas Beddoes near Bristol for the treatment of consumption and other lung conditions by the inhalation of gases. A laboratory assistant there became celebrated by publishing his observations on nitrous oxide in 1800 which to this day are considered a classic. This was Humphrey Davy who wrote, "On April 11, 1799, I made the first inspiration of pure nitrous oxide. It passed into the bronchia without stimulating the glottis, and produced no uneasy feeling in the lungs . . . In cutting . . . (a wisdom tooth) I experienced . . . great pain. I breathed nitrous oxide. The pain always diminished after the first four or five inspirations; the thrilling came on as usual, and uneasiness was for a few minutes swallowed up in pleasure. . . . Modification of the powers of nitrous oxide by mixture of the gas with oxygen or common air will probably enable the most delicate to respire it without danger . . . As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place." Davy's remarkable work notwithstanding, half a century of pain was still to be endured until the eventual introduction of nitrous oxide in 1844.

An itinerant chemist named Gardner Quincy Colton was delivering a series of lectures on chemistry. As a means of brightening up the duller portions he would administer nitrous oxide to members of the audience. Colton's demonstration at Hartford, Connecticut, on December 10, 1844, was a notable one, for it was there that Horace Wells, the dentist, witnessed a volunteer under the effects of the gas injure his leg

*From the Department of Anaesthesiology, University of Utah School of Medicine. Presented before a meeting of the Utah State Society of Anaesthesiologists, Jan. 22, 1948.

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sufficiently to draw blood although he had no recollection of sustaining the injury or the incident.

The following morning Wells invited Colton to his office to administer the gas to him. He had one of his teeth extracted without pain. Writing for the Nitrous Oxide Centennial, Ralph M. Waters states, "Wells made the mistake that remains a common one to this day. He over-emphasized the importance of the drug rather than of a thorough knowledge of its effects and of skill in its administration. Colton, who had experience and therefore possessed considerable knowledge of nitrous oxide and skill in giving it, went on with his lecture tour never suggesting by word or deed that he ought to share in the credit for the first administration of surgical anaesthesia. He was emphatic in latter years that the idea belonged entirely to Wells. The more familiar one becomes with the then who claimed a share in the honor of being the discoverer of anaesthesia, the more certain one is that Gardner Q. Colton was as deserving as any."

In 1868 Colton organized the famous Colton Dental Association, and by 1868, 40,000 nitrous oxide anaesthesias had been given by this group. In 1868 Clover was the chief protagonist for nitrous oxide in England. He devised new inhalers and first described the use of nitrous oxide as an induction agent before the administration of ether. In the same year E. Andrews of Chicago proposed the use of oxygen with nitrous oxide for non-asphyxial anaesthesia. Ten years later Paul Bert read before the Academy of Sciences in Paris his famous paper on the use of nitrous oxide-oxygen under increased pressure. He declared that to obtain surgical anaesthesia nitrous oxide must have a partial pressure equivalent to one atmosphere (760 mm. Hg), and to avoid anoxemia oxygen must be at the same tension under which it exists in air (156 mm.). To fulfil both of these requirements he proposed that an 85 per cent nitrous oxide—15 per cent mixture be administered at a pressure of one and one-quarter atmospheres in accordance with Dalton's Law of Solubility of Mixed Gases. He used a pressure chamber to accomplish this. Having used this method of anaesthesia on animals and humans, he wrote enthusiastic accounts. Bert's criteria for surgical anaesthesia must have been quite different from the current ones, for his results have not been substantiated by present day workers using even greater pressure (Brown, Lucas and Henderson).

Further progress in nitrous oxide anaesthesia since Andrews' introduction of oxygen has been in the development of gas apparatus. In 1910 a new stimulus was given to nitrous oxide anaesthesia by Crile's "Anoci-Association" principle in which local infiltration and nitrous oxide inhalation anaesthesia were combined to aid in the realization of the so-called "shockless" operation.

Chemical and Physical Properties.

Nitrous oxide is prepared commercially by the thermal decomposition of ammonium nitrate. The gas is scrubbed to remove acids and alkalies,

compressed by stages to prevent decomposition from excessive heat and to remove non-liquefiable gases such as nitrogen and oxygen, and treated with iron filings to remove the toxic higher oxides of nitrogen. It is marketed in steel cylinders as a liquid under pressure.

It is a sweetish colourless gas, stable under ordinary conditions, and highly soluble in water, alcohol, and fats. Although non-inflammable, nitrous oxide readily yields its oxygen to support combustion; in this respect it is equally dangerous as oxygen itself in the presence of combustible chemicals. In this connection serious explosions have occurred during the administration of nitrous oxide-ether mixtures. It is stable in the presence of soda lime. Nitrous oxide is the only inorganic gas used as an anaesthetic agent.

Pharmacology.

Nitrous oxide is highly soluble in blood but does not combine with hemoglobin. Chemically inert in the body, it is excreted unchanged very rapidly by way of the lungs, a small amount also passing through the skin. Although nitrous oxide supports active combustion, the oxygen in its molecule is unavailable for tissue consumption. With the exception of the nervous system the tissues of the body are not affected by the gas. Any alterations in the tissues, the metabolism, or the vital functions are due to accompanying anoxia and not to nitrous oxide per se. Dogs anaesthetized continuously for three days recovered as readily as if anaesthetized only a few minutes and without ill effects.

The exact mode of action of nitrous oxide is unknown. That it does possess anaesthetic properties which are independent of anoxemia is incontrovertible. Asphyxiant gases such as helium and nitrogen when given in such concentrations as 90 per cent with 10 per cent oxygen fail to produce anaesthesia, whereas nitrous oxide in concentrations of 80 per cent or lower frequently does. Much lower concentrations of nitrous oxide produce unquestionable analgesia. Various animal experiments further substantiate the depressant effect upon the gas upon the nervous system. If given with adequate oxygen, nitrous oxide has the widest margin of safety of any known anaesthetic agent.

Guedel classifies nitrous oxide as a "15 per cent potent anaesthetic agent," meaning that in the presence of adequate oxygen and under ideal conditions of basal reflex irritability it is capable of producing first plane surgical anaesthesia and no more. However, satisfactory surgical anaesthesia is seldom achieved under these circumstances. It is the consensus that true surgical anaesthesia with nitrous oxide does not exist without some measure of anoxemia. Hence in order to obtain satisfactory anaesthesia, nitrous oxide must be supplemented by more potent agents or by anoxia. Based on this fact are essentially two ways of administering nitrous oxide for surgical anaesthesia.

Methods of Administration

The McKesson-Clement view point employs varying degrees of anoxia to compensate for the lack of potency of nitrous oxide. These

authors declare that it is the only inhalation agent that may be used with safe degrees of oxygen deficiency because it does not depress the protective mechanism of the body whereas other inhalation agents have toxic and depressing action on the medullary and other centers including the carotid sinus. They state further that hence cyanosis and hypoxia are dangerous when associated with ether, cyclopropane, or chloroform because the normal protective mechanism of the body functions either inefficiently or not at all. According to this method of giving nitrous oxide the surgical stage of anaesthesia is subdivided into a light plane, a normal or surgical plane, and a profound plane, the signs of which are those produced by variations in the oxygen concentration.

It is apparent that the light plane of McKesson-Clement is really not surgical anaesthesia at all according to Guedel's scheme, that the profound plane consists of the manifestations of acute asphyxia, and that the normal plane corresponds to Guedel's plane one or two with superimposed anoxia.

Clement stresses the importance of the time factor. Satisfactory anaesthesia is dependent on tissue saturation with the anaesthetic substance. Only a few inspirations of pure nitrous oxide are sufficient to replace the oxygen in the blood. A much longer time is required to displace the nitrogen and oxygen in the tissues. To shorten this to the minimum, secondary saturation is utilized.

The induction of anaesthesia with 100 per cent nitrous oxide comprises a primary saturation. The first sign of oxygen lack is an increased respiratory rate. Oxygen is added in that percentage which allows efficient respiration and avoids deep narcosis. A gradual saturation of the tissues is thus effected and any desired plane of anaesthesia accomplished. Secondary saturation was accidentally discovered by McKesson who observed that a patient in profound anaesthesia could be rapidly resuscitated with pure oxygen, following which occurred a period of apnea attended by complete muscular relaxation. The mechanism of this phenomenon lacks explanation. Clement states, "a secondary saturation requires an intimate knowledge of the signs of anaesthesia, a disregard of cyanosis, and an apparatus capable of delivering oxygen under pressure for resuscitation if necessary." The technic consists of a sudden return of the mixture at any time during the anaesthetic to 100 per cent nitrous oxide followed by the administration of oxygen to counteract the excess and to produce relaxation. The saturation may be partial or complete. To produce partial secondary saturation the nitrous oxide per cent is suddenly increased anywhere up to 96 or 100 per cent. When evidence of deep anaesthesia appears, one or two breaths of a mixture containing from 25 to 50 per cent oxygen is given. This procedure is repeated until the desired level is obtained.

Complete secondary saturation is achieved by the administration of pure nitrous oxide until the patient is on the verge of respiratory arrest, followed by one or two breaths of pure oxygen. The nitrous oxide is

then maintained at 90 per cent. Partial differs from complete saturation only in the depth of anaesthesia produced before the administration of oxygen. They both accomplish the same result except that complete saturation is more drastic and acts more quickly.

In accordance with newer concepts in physiology the modern school of nitrous oxide anaesthesia places foremost the need for adequate oxygen intake at all times, this never being reduced below 20 per cent. The weakness of nitrous oxide is compensated for by the use of heavy premedication, by combination with regional anaesthesia, or by fortification with more potent agents.

It is well known that certain types of individuals are resistant to nitrous oxide-oxygen anaesthesia. They are alcoholics, drug addicts, hysterics, children, robust or obese persons, or any one with an elevated metabolic rate from any cause. However, the advantages of nitrous oxide-oxygen anaesthesia can be given, these patients with the aid of the aforementioned means. Although no detailed account of all of the various ways of combining nitrous oxide with other agents will be attempted, a few of the currently used technics are worthy of mention.

Sodium pentothal and nitrous oxide-oxygen anaesthesia is an ideal example of combined anaesthesia. Barbiturates are potent hypnotics, but possess virtually no analgesic properties. Nitrous oxide is a good analgesic agent. The total dosage of pentothal during an operation is considerably reduced by nitrous oxide, thus there is less likelihood of prolonged post-anaesthetic depression.

Nitrous oxide-ether-oxygen mixtures have long been a favorite anesthetic combination. The nitrous oxide makes for a pleasant induction; the ether adds the necessary potency to provide good surgical anaesthesia. Heavy pre-anaesthetic sedation with opiates and barbiturates is sometimes all that is needed to render nitrous oxide-oxygen anaesthesia satisfactory without further supplementation.

Cyclopropane is a currently popular supplementary agent, used either continuously or intermittently with nitrous oxide-oxygen mixtures. Rectal tribromethanol is another method of enhancing nitrous oxide, but is now being rapidly supplanted by the more conveniently administered sodium pentothal. Both of these supplements are to be preferred to the inflammable ones in the presence of ignition sources.

Crile for many years combined nitrous oxide-oxygen with local infiltration with gratifying results. It can also be used to supplement spinal and other regional nerve blocking procedures. Curare has opened new vistas for the proponents of nitrous oxide, for any degree of muscle relaxation can be provided during nitrous oxide anaesthesia.

It is unfortunate that such a useful agent as nitrous oxide has been unjustly criticized because of its misuse. However, it is coming once again into its own, thanks to more rational technics of administration.

Untoward Effects of Nitrous Oxide Anaesthesia.

The overwhelming preponderance of anaesthesiologists censure as totally unphysiological and hazardous the use of anoxia as a supplement for nitrous oxide. The contingent dangers of anoxemia during nitrous oxide anaesthesia have been cited by Courville, Caine, Eastman, and others. The classical monograph of Courville merits emphasis.

Patients manifesting cerebral lesions following nitrous oxide anaesthesia have been classified by this author into five clinical groups. 1. Sudden death on the operating table. 2. Delayed exitus. 3. Prolonged survival periods. 4. Recovery with residual cortical and lenticular damage. 5. Transitory mental and emotional changes. The pathologic findings in the brain depend upon the severity of the anoxic insult and the time interval between this and death. They vary from simple engorgement with petechial hemorrhages through patchy necrosis on up to extensive degeneration of the cerebral cortex and lenticular nuclei.

In cases surviving a number of hours or days death is preceded by deepening coma and hyperthermia. Symptoms following cerebral anoxemia may consist of mental and emotional aberrations, convulsions and other motor abnormalities, and visual disturbances, usually blindness of varying degrees. Any or all of these may be transitory or permanent. It is to be clearly understood that damage to the brain is not due to any toxic property of nitrous oxide, but is entirely the result of anoxemia.

Next to the brain, the heart is the organ most sensitive to anoxia. Under nitrous oxide anaesthesia patients with coronary artery or myocardial disease may develop acute coronary insufficiency from anoxemia without the warning of angina. Impaired cardio-respiratory function due to anoxia may lead to atelectasis, pulmonary edema or cardiac failure. Thus Haldane epitomizes, "Anoxia not only stops the machine, but wrecks the machinery."

To preclude the use of anoxia by anesthetists it has been advocated by Rovenstine and Barach that only cylinders of 80 per cent nitrous oxide—20 per cent oxygen be made available, comparable to medicinal helium—oxygen mixture.

Advantages of Nitrous Oxide-Oxygen Anaesthesia.

1. Rapid induction and emergence. Nitrous oxide is virtually eliminated from the blood in two minutes; no trace can be deducted after five. Patients react quickly even after long procedures.
2. It is non-irritating and has a pleasant odour, this quality alone making it valuable for inducing ether anaesthesia.
3. Nitrous oxide is non-toxic and provides the widest margin of safety of any of the systematic anaesthetic agents.
4. Minimal undesirable after effects such as nausea and vomiting.
5. Non-inflammability. This is a major safety factor which allows its use in the presence of cautery and other sources of ignition.

6. Used in combination with other agents, nitrous oxide materially reduces their total dosage, obviating excessive postanaesthetic depression.

7. A state of analgesia is most readily obtained with nitrous oxide. This is of value in dental work, for pains during the first stage of labor, and for special procedures such as thoracoplasties during which the patient retains his cough reflex to bring up secretions. This property also is useful for supplementing inadequate and waning regional nerve blocks.

Disadvantages.

All of its disadvantages are due to the very property that renders it safe, namely, its lack of potency. On this account it is unsatisfactory for deep anaesthesia where extreme muscular relaxation is required unless it is properly supplemented.

Large concentrations of oxygen cannot be successfully used with it, hence it is interdicted in many conditions in which anoxemia from any cause already exists or in which anoxemia may develop as from severe shock or hemorrhage. This fact was recognized by Humphery Davy a century and a half ago.

Summary.

A general review of nitrous oxide has been attempted with special reference to its history, physical and chemical properties, pharmacology, methods of administration, advantages and disadvantages, with a brief description of the untoward effects resulting from anoxia during nitrous oxide anaesthesia.

Conclusions.

Administered with sufficient oxygen, nitrous oxide is the safest general anaesthetic available. If its limitations are acknowledged and the substance used accordingly, nitrous oxide is a most valuable entity in the realm of anaesthesia.

(Rocky Mountain Medical Journal, March 1949.)

ANTE-NATAL CASE.

S. N. GARDE *

Ballentyne, the father of ante-natal care, mentioned the following as the benefits that should be expected from ante-natal care:—

- (1) The removal of anxiety and dread from the minds of expectant, parturient and puerperal patients.
- (2) The removal of much discomfort amounting in many cases to suffering.
- (3) The early and much more satisfactory treatment which can be given to the dangerous complications of pregnancy such as toxæmia, syphilis or heart disease.
- (4) The still birth rate will be at once lessened.

* From the Department of Obstetrics and Gynecology, Bai Yamunabai Nair Hospital, Bombay.

(5) One may confidently look for a fall in the maternal death rate, due to such obstetric complications as sepsis, hæmorrhage, embolism and the like and to the operative interference they call for.

Ante-natal care if properly and conscientiously followed would achieve these benefits.

DIAGNOSIS OF EARLY PREGNANCY

It would not be out of place to discuss briefly the diagnosis of early pregnancy.

Amenorrhœa, morning sickness, frequency of micturition are the earliest symptoms of pregnancy. Breast signs, violet discoloration of the vulva, increased moisture and discoloration of the vagina, softening and discoloration of the cervix, enlargement of the uterus and Hegar's sign, felt bimanually, are the earliest signs of pregnancy. The signs of early pregnancy need not be discussed, except that in the obese and multiparus patients it is indeed difficult to appreciate the slight enlargement of the uterus. The symptoms on the other hand need to be discussed briefly as they might occur without pregnancy.

Amenorrhœa is usually the earliest symptom. Amenorrhœa coming on in a woman of child bearing age, who has been regular before, highly suggestive of pregnancy. The other possibilities are, a unmarried girl exposed to the risk of pregnancy, a married person who strongly desires a child and cannot get one, mental shock, change of climate and surroundings and rarely general conditions e. g. pulmonary tuberculosis.

Morning sickness: Most pregnant women experience sickness; only a few never have it. Usually it starts by the 6th week and disappears by the 14th. Women who fear pregnancy or greatly desire it, may get morning sickness without being pregnant. Vomiting of course can occur due to associated conditions and they must be always kept in mind.

Frequency of Micturition: In early pregnancy, frequency of micturition may occur due to the exaggeration of the ante flexion of the uterus resulting in irritability of the bladder. Urinary infection also causing day and night frequency must be excluded.

No single sign or symptom mentioned above is diagnostic of early pregnancy. Collectively of course they are very useful in making a diagnosis of early pregnancy. X-Rays before the 16th week are useless. The only reliable way of making a certain diagnosis of early pregnancy is by means of one of the three hormone tests for pregnancy, the Aschheim-Zondek (mouse), the Friedman's (rabbit) or the Hogben (African toad) tests. In places where there are no facilities for doing these tests, three injections of Prostigmin (Roche) dose 1 to 2 c. c, daily will serve as a useful test. If the period does not come after two days of the last injection it is suggestive of pregnancy. This is correct in 60% of cases. Gillifen and Gregg proposed an intradermal test with antiutrin (Parke Davis & Co.—Chorionic gonadotropic hormone). The basis of the test is that the pregnant woman would not be sensitive to the gonadotropic

substance found in pregnancy-urine. The test is worth trying provided it is realised that the test is unreliable.

EXAMINATION OF THE PATIENT

It must be emphasized that routine ante-natal care begins as soon as the diagnosis of pregnancy is made. It is unfortunately a common, and yet erroneous belief that the ante-natal care begins at the 7th month. Most patients, and even some practitioners believe that the pregnant woman has to go for registration at the 7th month and then for delivery.

The examination must be thorough and orderly. The history is taken first, then a general medical examination, and then obstetrical examination and lastly the investigations.

HISTORY

The history includes the family history, personal history, history of present pregnancy, menstrual history and previous obstetric history in multiparæ.

Family History: Enquire regarding the conditions that are likely to affect child bearing, particularly multiple pregnancies, pulmonary tuberculosis, and high blood pressure.

Personal History: Enquire into the history of the patient having suffered from measles, chicken pox, small pox, whooping cough, diphtheria and rickets in childhood, sore throats, heart or kidney diseases, tuberculosis, appendicitis and any operations, in adolescence. Most of these conditions damage the kidneys (toxæmia), others affect labour and a few the puerperium.

Present Pregnancy: Enquire particularly about morning sickness, bleeding (warning hæmorrhage), constipation, breathlessness, sleeplessness, cramps, pain and discharge.

Past Obstetric History: Enquire into how many full time deliveries she had. Ask for the ages of the oldest child and the youngest. Carefully go into the history of past pregnancies, labours and puerperium. Enquire into the weights of the infants at birth. Take a detailed history of any abortions she has had, particularly the month at which she had the abortion, whether there was any post-abortion sepsis and whether she could ascribe them to any particular cause.

GENERAL MEDICAL EXAMINATION

At the first examination take the height and weight and then go over the various systems. Note the general state of nutrition and the condition of the teeth, tongue and throat. The breasts should be examined and their state of development and the condition of the nipples noted. The mucous membranes are examined for anæmia, the feet and the legs for œdema and deformities (rickets). Note if there is a male distribution of the hair as it might indicate a male type of pelvis.

Weighing: The patient should be weighed at each visit. To be of real value the weighing machine must be accurate and the patient as far as possible wear the same clothes. Cummings who investigated 1000 pregnant women found the total average gain of 25 lbs. during pregnancy,

the monthly gains in weight being, 0,1,4,4,5,5,8,8, lbs. It is a good working rule to consider that more than 5 lbs. gain in any month or a sudden gain at any time, is an abnormal increase in weight. And an abnormal increase in weight is often the earliest sign of pre-eclamptic toxæmia.

Blood Pressure: This must be recorded at each visit. A rise of blood pressure is often the earliest sign of toxæmia. Browne considers a systolic pressure above 120 mm. of Hg. and the diastolic above 80 as raised. Many authorities consider this as an unduly severe standard. To support the correctness of his contention he has quoted the work of Robinson and Brucer and his own vast experience.

Examination of Urine: Routinely the urine is examined for albumin and sugar. If albumin is detected a catheter specimen should be taken to exclude the possibility of contamination from the vaginal discharge. Albuminuria is usually a late sign of pre-eclamptic toxæmia, oedema or raised blood pressure preceding. Rarely it might be the first sign. If sugar is detected, it is most likely to be lactose. To differentiate between glucose and lactose the osazone test is employed. It is however important to take the blood sugar curve and exclude the possibility of diabetes. If there is a suspicion of urinary infection, which is not uncommon, an examination for pus cells will have to be made; more than 5-6 pus cells per field is very suggestive.

ROUTINE OBSTETRICAL EXAMINATION

This includes estimating the probable date of delivery, pelvic menstruation, abdominal palpation and vaginal examination.

Estimating the probable date of delivery. The most reliable way is to calculate from the date of the last menstrual period. Add 7 days to the 1st day of the last period and either count forward 9 months or backwards 3 months. Of course the simplest way is to refer to an obstetric table. In taking the history of the last menstrual period, always ask whether the period was normal. It is not uncommon for a woman to have a scanty period in spite of pregnancy. It is wise therefore to enquire into the last two normal periods to avoid an error in the calculation of the probable date of delivery. An error of 15 days either ways in the expected date of delivery is considered normal. The less reliable methods of estimating the expected date of delivery are based on (1) the fundal height (2) the date of quickening (3) the X-Ray pictures (Roberts or Hastings Ince methods).

Pelvic Menstruation: Bourne and Williams state: "That the external measurements should really be regarded as valueless." Dohrn has well said that the physician who neglects pelvimetry is comparable to one who attempts to treat pulmonary diseases without the aid of auscultation and percussion. I am in entire agreement with this statement. In a primigravida or a multipara with bad obstetric history the following measurements should be taken routinely (1) interspinous (2) intercrural (3) the external conjugate. These measurements give a rough idea of the inlet. It is equally important to measure the transverse diameter of

the outlet and palpate the pubic bone and note the pubic arch. To correctly know the type and the capacity of the pelvis, X-Ray pelvimetry is invaluable.

Abdominal Palpation In the earlier months of pregnancy the abdomen is mainly palpated to see that the fundal height corresponds to the duration of amenorrhœa (pregnancy). It is quite unnecessary prior to the 32nd week of pregnancy to worry about the presentation, still less about the position. It is common for the presentation and the position to vary before this time. If at 32nd week a malpresentation is found we must try and discover the cause. The causes of malpresentation are (1) contracted pelvis (2) placenta prævia (3) twins (4) multiparity (5) hydramnios (6) pelvic tumours.

The commonest malpresentation that one encounters is the Breech. The best time to perform the external cephalic version is 34th to 36th week. It is easier to perform the version at the 34th week than 35th, the dangers being (1) premature rupture of the membranes with onset of labour (2) prolapse and entanglement of the cord (3) separation of the placenta (traumatic accidental hæmorrhage) (4) rarely, rupture of the uterus. Fortunately most of the dangers can be avoided by gentle manipulation and avoidance of anaesthesia. Because of the possibility of premature onset of labour some authorities prefer postponing the version to 36th week so that even if the woman should go into labour the child has a good chance of survival.

The second point is to determine the position, whether anterior or posterior. So far there is no evidence to show that by means of posture or the Buist pads we can change an occipito-posterior position to an anterior. Buist pads do help to change an occipito-lateral to an anterior position. But just these cases need no help as they invariably rotate forward. In addition it must be realised that the Buist pads cause physical discomfort and mental anxiety which more than offsets any possible advantage they may possess.

The last, but not the least, one has to ascertain the relation of presenting part to the brim. In a primigravida the head is normally engaged by the 37th week. If the head is not engaged by this time we must ascertain the reason for it. In 20 per cent of cases no cause can be discovered for the non-engagement. The common causes of non-engagement of the head are (1) contracted pelvis (2) occipito-posterior position (3) placenta prævia (4) multiple pregnancy (5) hydramnios (6) pelvic tumours (7) and a loaded colon.

It is outside the scope of this article to discuss each of these conditions. But it would not be irrelevant to discuss briefly cephalo-pelvic disproportion. To estimate the degree of disproportion is one of the most difficult problems in obstetrics. Radiology does help. Conclusions based purely on radiological findings give a more gloomy picture than is the case. Radiological help, therefore, must supplement our clinical

judgment. The method commonly used to estimate the degree of disproportion is Munro-Kerr's modification of Muellers method. For the last 8 years I have been using Chassar Moir's method of estimating disproportion by external manipulation. An assistant is asked to exert pressure on the funds of the uterus by means of his forearm. The accoucher then grasps the head with his left hand and pushes it downwards and backwards into the pelvis. Then he places the index and the middle fingers of the right hand on the upper border of the symphysis to estimate the degree of overlap. It may be found (1) That the head can be made to enter the pelvis. This means there is no disproportion and the woman would deliver normally or at the worst with forceps (2) that the head overlaps so much that the parietal bone overhangs the anterior surface of the symphysis. Vaginal delivery in such a case is not possible and a caesarean section must be chosen as the treatment.

It is admitted that Chassar Moir's is a crude method of assessing disproportion. However, I have found the method very useful and it certainly has the advantage of simplicity.

Without fear of contradiction it may be stated that premature induction of labour must not be used in the treatment of disproportion in a primigravida. Multigravida, of course, are a different problem. We have the previous obstetric history to guide us. Here in suitable cases premature induction of labour could be usefully employed and a caesarean avoided.

Vaginal Examination:—It is always wise to do a vaginal examination at the first visit. The great advantage is we can discover pelvic tumours without symptoms early. If discovered these could be dealt with more conveniently at this early time. Another advantage of an internal examination is that gives us a better idea of the capacity of the pelvis than what we get from the external measurements.

INVESTIGATIONS

X-Rays:—X-Rays are used in cases where there is a doubt about the presentation or there is a suspicion of foetal abnormalities, for pelvimetry and cephalometry. In some clinics abroad X-Ray pelvimetry is done routinely on all primigravida. It is a good idea. If it is not possible to do it routinely, it should certainly be carried out if the following conditions exist:—(1) short stature (2) evidence of rickets (3) evidence to suggest an android pelvis (4) floating head in a primi-gravida at the 37th week (5) history of previous difficult labours in a multipara or the child dying soon after delivery.

Two views should be taken, an antero-posterior and a lateral. The lateral is the more useful one in cephalo-pelvic disproportion. It also gives a better idea of the outlet. But the antero-posterior gives a better idea of the architecture of the pelvis and of the foetus. Cephalometry is not developed to the same extent as pelvimetry. It is useful in estimating the extent of cephalopelvic disproportion and in estimating the maturity of the child. It has already been stated that conclusion based

solely on radiology tend to be more pessimistic than is the case. Radiology should supplement clinical judgment and not replace it. It is important that the obstetrician and the radiologist should work in co-operation. For foetal deformities and doubtful presentation a plain antero-posterior X-Ray would be best.

Routine Screening of the Chest:—A strong plea is made for doing this routinely. The incidence of pulmonary tuberculosis in pregnancy is the same in general population. The figures for Britain are 1 in 200. Mass radiology has demonstrated that pulmonary tuberculosis can exist without symptoms. The incidence of tuberculosis is much higher in our country. Dr. C. S. Patel, considers 1.60 as fair estimate for Bombay Presidency. It can be taken as the figure for the whole country. With such a high incidence it is indeed very desirable to do routine screening of the chest.

Blood Examination:—The red blood cells must be counted and hæmoglobin estimated at the first visit. It is particularly important to do this in our country where the incidence of anæmia is so high. Wassermann reaction or the Kahn's test is done routinely. As it is difficult to do so in private practice, it must be done where the history is suggestive, i.e., history of premature labours, macerated foetus and still births. Syphilis is rarely a cause of abortions.

Vaginal Discharge:—Normally in pregnancy there is an increase in the vaginal discharge. If the discharge is profuse, purulent or irritating or if the patient should complain of it, the discharge must be examined microscopically and also by gram staining. The common causes of Leucorrhœa in pregnancy are (1) fungus infection (2) gonorrhœa (3) syphilis. Gonorrhœa should be treated with penicillin and sulphonamides, syphilis with penicillin, arsenicals and bismuth. Fungus which forms the largest group must be treated with application of 2 per cent gentian violet frequently. Apart from the annoyance the discharge causes to the patient, it must be treated because quite often this vaginal discharge causes ophthalmia neonatorum and occasionally thrush.

Frequency of Examination: The patient should be seen every month from the time of the first visit till the 30th week. Every fortnight from the 30th week till the 36th week and then every week until delivery.

ADVICE

Diet: Professor F. J. Browne in his admirable book, ante-natal and post-natal care has discussed this point in great detail. The following is his summary:—(1) Provided the diet has been mixed and generous one no appreciable increase in its quantity is necessary in pregnancy. (2) At least half the protein should come from animal sources, viz., meat, milk and eggs. (3) Care should be taken that sufficient calcium and phosphorus are provided for the proper formation of the foetal skeleton and teeth. The best source of these is milk, of which at least 2 pints should be taken daily. This may include that taken in junkets, custard, etc. Other less important sources of calcium and phosphorus are oatmeal, whole-meal

bread, fruits, vegetables and green salads. (4) To provide the small quantities of iodine necessary sea fish should be eaten twice weekly. Fish liver oil also contains it in large amount and is good substitute if taken daily. (5) The diet should contain a plentiful supply of all vitamins. To ensure this the fresh green vegetables and salads, including lettuce, spinach, cabbage, brussels, sprouts or green peas, tomatoes, carrots, potatoes, fresh ripe fruit, and dairy produce eggs, milk, butter and cheese should be eaten daily. Liver should be eaten once weekly. (6) Because of the prevalence of rickets and dental carries vitamin D is probably by far the most important of all the vitamins in pregnancy and lactation, for it is needed to ensure the utilisation of calcium and phosphorus, and their deposition in the developing bones and teeth of the foetus. Its distribution in food stuffs is very limited for only egg yolk contains any considerable amount of it. It is advisable, therefore, to give 2 tea-spoonfuls of cod-liver oil, or an equivalent quantity of halibut liver oil, daily. (7) The diet should contain sufficient roughage to prevent constipation. In addition to that in fruit, vegetables and meat, whole-meal bread and oatmeal porridge (eaten with milk at breakfast) are useful and effective.

Dietary Supplements: The people's League of Health and the Toronto experiments have amply proved the value of dietary supplements. The demands of all the vitamins are increased in pregnancy. There are numerous proprietary multi-vitamin preparations on the market. Any one of these preparations must be given throughout the pregnancy and puerperium. In prescribing a multi-vitamin preparation, one with 9000 (I.U) of A and 340 (I.U) of D is suitable. Iron is best administered as a ferrous salt. The dose will largely depend on the percentage of haemoglobin. Iron is better tolerated when taken with milk than with water. Taking iron with milk is particularly advised for those patients who cannot tolerate it. Calcium (1.2gms) should be given throughout the pregnancy. It could be profitably stopped in the last 8 weeks of pregnancy.

Care of the Breast: Breasts must be prepared for sucking. If nipples are retreated an effort must be made to draw them out by rolling them between the thumb and the fingers. The nipples should be kept clean by daily washing them with soap and water. The patient should be instructed to apply cold cream and Eau de Cologne to the nipples once a month. She should be advised against compressing the breasts. If the breasts are pendulous a comfortable support should be advised.

Marital Intercourse: Marital intercourse should be completely avoided in the last 8 months of pregnancy. There is reason to believe that there is higher incidence of puerperal infection amongst women who have intercourse in the last 8 months. There is also room for suspicion that it might lead to premature rupture of the membranes with onset of labour. If there is history of abortions it should be forbidden throughout the entire pregnancy.

Exercise: Walks in the open air are the best forms of exercise. It is difficult to standardise how long the patient should walk. That depends on each individual. The golden rule is to stop short of fatigue. There is no reason to stop the household duties. These can be carried on till the end of pregnancy. But if the patient is doing hard manual work such as working in mills, she should stop working at least 6 weeks before term. All violent exercises should be avoided during the last 6 months but if there is history of previous abortions they are best avoided from the beginning.

Sleep: The pregnant woman should have at least 8 hours sleep every night. It is also desirable to have a couple of hours rest in the afternoon. As far as possible it is best to avoid drugs. Natural means like walks in the open air, a bath at night or a cup of Horlicks or Ovaltine would help much in inducing sleep.

Constipation: This is quite common during pregnancy. It is probably due to the action of Progesterin on the involuntary muscle of the intestines and the pressure as a result of growing uterus. As far as possible it should be treated by the use of proper diet and exercise. Many cases, however, require the aid of drugs. Strong purgatives should be avoided. The best drugs to use are phenolphthalein, milk of magnesia, cascara and senna. Liquid paraffin should be avoided on the theoretical grounds that it might deprive the patient of fat soluble vitamins by dissolving them.

Travelling: Much will depend upon the comfort with which one can travel. It is difficult to make general statements. Each case must be judged individually. If there is history of abortions it is best to avoid long or uncomfortable journeys. In any case it is best to avoid travelling in the last four weeks of pregnancy. Sea and air travel definitely carry more risk than land. Apart from the danger of miscarriage or premature onset of labour, it is good to keep in mind the awkwardness of the situation in case the delivery should occur during the journey.

The Teeth: Ideally every pregnant woman should see her Dentist at least twice. Elective dental work should be postponed till after the delivery. But there is no reason at all to postpone urgent work.

Re-Assurance:—A good obstetrician must spare all the time that is required to allay the numerous anxieties the patients manage to collect. The doctor must encourage the patient to come to him for the problems that confront them, instead of getting them solved by their relatives and friends. The patient must be made to feel that no problem she has, is frivolous or ridiculous. At each visit it is good to tell the patient that all is well. Small explanations about the various examinations the doctor does are always welcome by the patient. If during routine examination some abnormality is discovered, it is wise not to tell the patient but to inform some responsible member of the family. It is important that when the woman goes into labour she is fit both physically and psychologically. A doctor seriously interested in obstetrics will learn much from Dr. Grantley Dick Reads book "Natural child birth". He has made

many useful suggestions as regards the psychological bringing up of the pregnant woman.

(Indian Journal of Medical Sciences, April 1949).

Correspondence.

The Editor

Medico Surgical Suggestions, 2/287 Mint Street, Madras.

Dear Sir,

In July of last year you favoured me with the hospitality of your correspondence columns to announce certain changes in dosage of 'Paludrine'. Consequent on these changes in dosage it has become convenient to make available to the Medical Profession two new sizes of 'Paludrine' tablets. The availability of these new tablets is being announced this month in the medical press, but I shall be glad of the privilege of using once again, your correspondence columns to inform the Medical Profession of the reason for introducing the new sized tablets.

The matter will be better understood, if I first recapitulate briefly the recommendations with regard to 'Paludrine' dosages:

(1) For protection against malignant tertian and suppression of benign tertian malaria—0.8 gm. once weekly, or 0.1 gm. twice a week at 3 and 4 day intervals.

(2) For radical cure of malignant tertian malaria 0.8 gm. twice daily for 10 days.

(3) In benign tertian malaria, the greatest hope of a radical cure with 'Paludrine' is offered by the dosage regime of 0.3 gm. daily until the fever subsides, and then 0.3 gm. once a week or 0.1 gm. twice weekly at three and four day intervals for about 6 months.

(4) For "clinical" cure of all types of malaria 0.3 gm. daily until the fever subsides.

(5) For children over ten, the dosage for adults is indicated both for treatment and prophylaxis. Children under ten should be dosed according to age and size, but the minimum given to any child, however young, need not be less than 0.025 gm.

It is clear from the dosage schedules enumerated above that the most convenient dosage unit of 'paludrine' is 0.3 gm. for adults and 0.025 gm. for young children. Tablets containing these quantities of 'Paludrine' hydrochloride have therefore been made available to the Medical Profession.

Yours faithfully,

J. M. MUNGAVIN.

(J. M. MUNGAVIN, M. B., B. Ch. (CANTAB))

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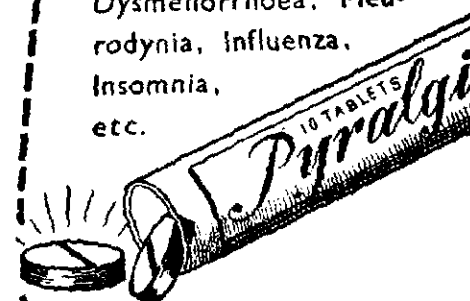
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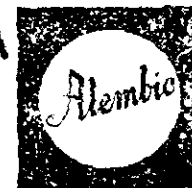
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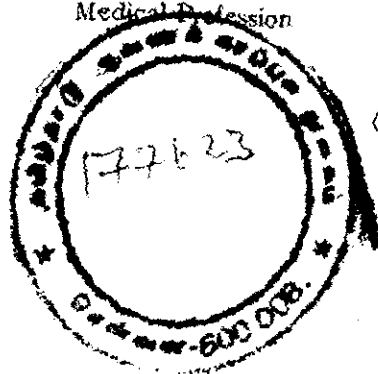


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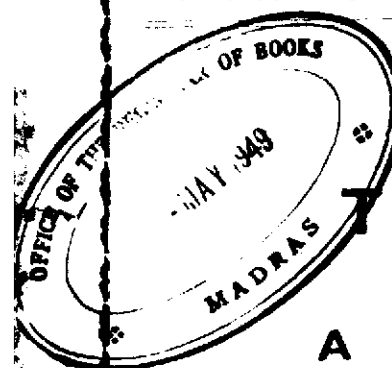
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A MONTHLY JOURNAL OF PRACTICAL MEDICINE & SURGERY

Editor: Dr. P. R. Venkappaya

Established 1932

VOL. XVIII

APRIL 1949

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Sample Copy for 4 As. Stamps.

Office of the Editor & Publisher; 2/337, Mint Street, Madras, India.

Phone: 4030.

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVIII

APRIL 1949

No. 4

EXPERIMENTS WITH FLOCCULATED INSULIN LEADING TO CHEMOTHERAPY OF CANCER WITH PHOSPHOTUNGSTIC ACID- H_2O_2 PREPARATIONS

H. N. MUKHERJEE, B.Sc., M.B., D.I.C. (LOND.)

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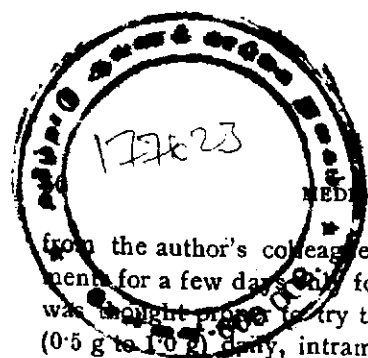
With the idea of protecting insulin against enzyme action the author was first led to experiment with precipitated or flocculated insulin (Mukherjee, 1930).

In connection with the author's work with precipitated insulin phosphotungstates (Mukherjee, 1935, 1936) it was found that phosphotungstates, molybdates, vanadates, and many allied substances have hypoglycaemic, oxidising actions. The oxidising actions of phosphotungstates and molybdates etc., simulate the action of oxidising enzymes. From a consideration of these properties the author was led to try the effect of these substances in cancer and a preliminary report was published in the *Calcutta Medical Journal* (1936) with a subsequent brief reference in the *Biochemical Journal* (Mukherjee, 1936). In these earlier experiments patients suffering from cancer were usually given 2 c.c. of 20 per cent solution of sodium tungstate subcutaneously thrice a week for a fortnight and the following changes were observed:—

1. Marked diminution or even disappearance of pain.
2. Decrease of discharge.
3. Some decrease in size of the growth.

In later work (it may be mentioned in passing that the author is engaged in this work for over 12 years) using sodium tungstate in bigger amounts (0.5 g to 1.0 g) subcutaneously similar results were obtained. Sodium phosphotungstate and sodium phosphomolybdate were also used in some cases of cancer and also in sarcoma. Sodium metavanadate was tried with caution on one patient (with sarcoma) in very minute (2 mg.) doses subcutaneously for a short period and was then stopped for fear of toxic action.

It was then considered worthwhile to concentrate on phosphotungstic acids. As it has been the usual custom to get the inoperable cancer cases



from the author's colleagues in the surgical and gynaecological departments for a few days. Only for studying the effect of these preparations, it was thought proper to try the effect of bigger doses of sodium tungstate (0.5 g to 1.0 g daily, intramuscularly and also intravenously in patients usually of 40 kg. to 60 kg. body-weight. Patients taking sodium tungstate and also sodium phosphotungstate intramuscularly daily for a fortnight or more did not show any untoward symptom. Phosphotungstic acid suitably buffered (in 0.5 g to 1.0 g doses) intramuscularly daily was also tried in some cases. Hydrogen peroxide solution (1.0 c.c.) was also given intramuscularly in a few.

By this time some of the author's colleagues in the surgical and gynaecological wards were convinced that some of these injections allay the pain of cancer in most cases and possibly cause some slight decrease in size in a few cases. Naturally on applying to them the author used to get two groups of cases (1) operable malignant cases with pain where the surgeon was waiting for biopsy report and other examination reports necessary before an operation, and (2) inoperable cases rejected also by the radiologist or in given up cases with recurrence after operation and radiological treatment. In both of these groups of patients the author could try the effect of these injections at most for a fortnight with similar results as that mentioned before, i.e., though there was agreement about the relief of pain—about regression of the tumour opinion varied.

With the idea of obtaining a more potent preparation a number of phosphotungstate derivatives were tried. Sodium salt of a phosphotungstic acidthioglycolic acid complex prepared in the laboratory was then tried in cancer. This sodium salt solution (pH—5 approximately) has a deep blue colour which is discharged on treatment with hydrogen peroxide solution (Peroxyl—May & Baker Ltd.) added in-sufficient amount. The blue colour reappears after a short time when the solution can be again rendered colourless with further additions of H_2O_2 solution. The process can be repeated for a number of times. It appears that this complex compound can take up and also give up oxygen easily.

As the main reason for using these substances in cancer depends on their oxidising and other properties the author was next induced to experiment with phosphotungstic acid dissolved in hydrogen peroxide solution. When phospho-24-tungstic acid is dissolved in hydrogen peroxide solution a yellow colour develops due to the formation of a complex compound.

On boiling for sometime or on evaporating on a water bath the yellow colour is discharged with liberation of oxygen. The yellow colour is also discharged with liberation of oxygen, on treatment with strong alkalis.

As in the present paper the action of this yellow phosphotungstic acid- H_2O_2 preparation on cancer will be considered the method of preparation is described below.

Method of Preparation

50 g of phospho-24-tungstic acid (Merck & Co.) was placed in a glass beaker and was then dissolved in about 50 c.c. of hydrogen peroxide solution (Peroxyl—12 vols. May & Baker Ltd.) by stirring with a glass rod. The total volume was ultimately made up to 100 c.c. with further addition of hydrogen peroxide.

This 50 per cent solution of phosphotungstic acid in hydrogen peroxide was kept in a glass bottle. After a few days a slight insoluble sediment settled at the bottom. The supernatant fluid was then clear and bright yellow in colour and was carefully pipetted off (if necessary filtered) without disturbing the sediment at the bottom. The solution liberated oxygen vigorously if shaken. When one c.c. of this yellow solution was added to a solution of blood in a test tube there was no frothing showing that there was very little free H_2O_2 . The solution was strongly acid in reaction and contained 0.5 g of phosphotungstic acid per c.c. Henceforth this preparation will be referred to as preparation Y in this paper.

Buffers

As the Preparation Y is strongly acid and alkalis degrade it, various buffers were tried to reduce the acidity. Sodium lactate was considered a suitable buffer but it was soon found that mixed with sodium lactate the yellow compound was degraded. Ultimately the author had to rely on 20 per cent solution of sodium tungstic in water as buffer.

When 1.0 c.c. of Preparation Y was mixed with 1.0 c.c. of 20 per cent solution of sodium tungstate the pH of the resulting mixture was 4.5 (about). This pH was considered suitable for administering the material by injection.

Dose and Method of Administration

The average body-weight of the patients with cancer on whom Preparation Y was tried was about 50 kg. (40 kg.-60 kg). 1 c.c. of Preparation Y (0.5 g of Phosphotungstic acid) buffered with 1 c.c. of 20 per cent sodium tungstate (0.2 g of sodium tungstate) was considered a safe dose to be injected daily for a prolonged period. In some cases twice this dose once daily or by two injections morning and evening was given without any ill effect.

Preparation Y and the 20 per cent sodium tungstate solution were kept separately in different bottles or sealed glass ampoules. Preparation Y required no sterilisation. The sodium tungstate solution was sterilised by boiling before being put into glass ampoules. Just before use 1 c.c. (or more when necessary) of Preparation Y was mixed in an all-glass syringe with an equal volume of 20 per cent sodium tungstate solution for immediate injection into the patient. Unnecessary delay in giving the injection after mixing with the buffer in the syringe may degrade the preparation.

Preparation Y was first tried intravenously on a female patient with inoperable scirrhus cancer of the right breast with involvement of axillary

glands and brawny oedema of right arm associated with severe pain over right breast and right arm.

2 c.c. of Preparation Y was buffered with 2 c.c. of 20 per cent sodium tungstate and was injected intravenously daily for six days by which time pain was completely relieved. After another 10 intravenous injections of the same strength daily the brawny oedema of the right arm completely disappeared. But the intravenous injections caused nausea and marked anorexia. In fact, the first patient to take this Preparation Y intravenously bore it very well. It was tried on four other patients intravenously,—two with cancer and two with sarcoma. They could not take more than six injections. All had nausea, vomiting and anorexia. So the intravenous administration had to be given up in favour of intramuscular injection. The intramuscular injections are painful but if the Preparation Y is properly buffered and the injections are given with a fine sharp needle in the gluteal region patients do not complain.

Effect on Cancer

Preparation Y was tried intramuscularly in 1 c.c. to 1.5 c.c. dose daily buffered with sodium tungstate in 8 inoperable cases of cancer (2 female patients with squamous celled carcinoma of cervix uteri; 2 male patients with squamous celled carcinoma of the penis; 4 female patients with cancer of the breast—2 with scirrhous cancer and 2 with adeno-carcinoma).

The author obtained consistent good results in these cases as mentioned below.

1. With Preparation Y administered intramuscularly daily the pain of cancer in most cases was completely relieved after one to six injections (1 to 6 days).

2. If the injections were continued daily, then after about 18 injections (about 18 days) definite improvement of ulcers, diminution in size of growths were observed. Fungating masses and the brawny oedema in affected arms also disappeared by this time.

DISCUSSION

With Preparation Y administered as described above definite improvement as evidenced by relief of pain, healing of ulcers and definite diminution in size of growths were observed in many cases of cancer. Its effect was found to be more potent than that of the allied substances previously used by the author.

The introduction of Preparation Y into the body amounted to the introduction of a catalytic oxidising complex into the system, and it is expected that the use of Preparation Y or similar preparations of phosphomolybdic acids etc., in experimental animal cancer may help in the proper understanding of the metabolism of cancer cells. Moreover as phosphotungstic acids etc., react with many substances of biochemical importance in the living system their trial in cancer is indicated.* It is

* A complex phosphotungstic acid-phosphomolybdic acid— H_2O_8 preparation is now being tried in cancer and the results will be reported in another communication.

also expected that with further research along this line patent preparations may be produced for chemotherapy of cancer.

The cancer patients on whom these investigations were carried out were usually poor patients in free beds. It was not found possible to carry on these investigations for more than 4 weeks in any one of them for the following reason. As the cases were inoperable cancer cases it is very difficult for the surgeons in charge of the ward to keep beds occupied by incurable cases when there is a tremendous rush for new admission. The author thankfully admits, however, that even this comparatively short time has been of much help in studying the effect of these preparations on cancer. With proper facilities investigations over a longer period will be carried out. In two patients it has been possible to continue the injections for nearly six weeks. The patients remained free from pain with a feeling of well-being. The growths and ulcers remained inhibited with apparent slight further regression.

The cancer patients mentioned in this paper were all properly diagnosed as cancer cases clinically by the surgeon in charge and also by biopsy.

No toxic effect whatsoever was observed in these patients following the use of this preparation intramuscularly as described above.

SUMMARY

1. A Phosphotungstic acid- H_2O_8 preparation is described which appears to have consistent definite beneficial effect in cancer.

2. This preparation in suitable doses when administered intramuscularly (also intravenously) daily for about a week relieves the pain of cancer. After continued daily injections for two to three weeks definite decrease in size of growths and ulcers is observed. Fungating masses and the brawny oedema of affected arms disappear and exudation from ulcer is decreased. The patients remain free from pain with a feeling of comfort.

3. For a proper understanding of the metabolism of cancer cells and also for chemotherapy of cancer further research along the line indicated in the paper is suggested.

ACKNOWLEDGMENT

The author's thanks are due to Dr. Sobodh Datta, F.R.C.S. (EDIN.), Professor of Surgery and to Dr. Satinath Bagchi, M.Sc., M.B., M.O. (CAL.), Professor of Gynaecology and Obstetrics of this Institution for permission to try the effect of this preparation in cancer patients under their charge. Thanks are also due to Dr. U. N. Banerjee, M.B., Visiting Surgeon, Gynaecology & Obstetrics Department and to Dr. U. Mukherjee, M.B., M.S. (CAL.), Visiting Surgeon, Surgical Department.

(Journal I. M. A. Jan. 1994)

FOOD REQUIREMENTS IN PREGNANCY AND LACTATION

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The efficient performance of the function of reproduction is closely associated with nutritional state of the reproducing female. This is clearly recognised by the farmer when feeding his cows, sheep and pigs and much of its success as a farmer is dependent upon his application of this knowledge.

The reproducing females require, in addition to the dietary constituents (adequate in quantity and variety) necessary for her own bodily maintenance, supplementary quantities many food stuffs in order to nourish her offspring both in utero and at the breast. The question of how intimately successful reproduction in the human being is associated with nutritional factors has not yet received the attention it deserves. Consideration of maternal mortality and morbidity, of abortion, miscarriages, and stillbirths, of neonatal and infantile mortality, has, it seems to me, been orientated too closely to the pathological and infective processes which may be the terminal factor in obstetric disaster, and too little to the fundamental factors of nutrition which may prove to be the precursors of the morbid condition just referred to. There is much basal truth in the suggestion made by Dame Louise Mc Ilroy in 1935 that the solution of the problem of maternal mortality and morbidity lies in the kitchen rather than in the laboratory or hospital ward. There are those who have advocated a restricted intake of food during pregnancy in order that the birth weight of the child may be kept low and so ensure easy delivery. The balance of evidence, however, appears to indicate that birth weight is uninfluenced by restrictions of diet that are likely to be submitted to by the expectant mother. Further, there appears to be little reliable evidence to support the contention that excessive eating by the mother results in the production of over-weight infant, whatever effect it may have on the maternal Organism. Nor is it certain that food restriction during pregnancy reduced the incidence of toxæmias; for there now is evidence supporting the view that it is food restrictions of deficiencies that are potent can a factors in the production of the toxæmias which we have tried to avoid by cutting down the quantity of food eaten.

It appears to me that the mere determination in grammes and milligrammes of the minimal requirements of the pregnant woman for the proximate principles of satisfactory diet is of academic rather than of practical importance; for as deficiencies seem to be of more consequence than excesses there must be in the field application of laboratory findings a factor of safety introduced which, in the daily routine of marketing and cooking has of necessity to be somewhat generous. The idea that special diets are essential for the reproductive phase of female activity does not coincide with physiological dicta. If the diet of a woman of

reproductive age, requires, during pregnancy additions not merely quantitative in nature it is indicative, not that she needs new substances for the purpose of gestation, but that her previous diet was inadequate.

The quantity of food eaten, expressed in mere calories, is of little practical importance. Gross shortage of calories, except among a very small section of the impoverished, is rarely encountered. A deficient caloric intake can be easily and cheaply corrected by the addition of cereals and/or sugar, and little anxiety need be felt on this score. The unfortunate factor is that if the caloric intake is mainly derived from carbohydrate sources these substances may bulk too largely in the total intake and may by substitution, reduce below the safety level the ingestion of foods containing protein, minerals, and vitamins. Here is real danger of this among women who exist at a low income level.

There is a lack of reliable data as to the optional intake of fat during pregnancy. It is probably that the kind of fat eaten is of more importance than the quantity, and the varying value of fats from different sources lies not so much in their chemical composition as in the extent to which they act as vehicles for various vitamins. Linoleic acid, however (a constituent of some fats), does seem to have special qualities.

There has been much controversy as to the roll of protein during pregnancy. Many practising obstetricians advocate a low protein intake in order to avoid toxæmias. I suggest that this attitude be examined with care. The League of Nations Technical Committee recommends two grammes of protein per kilo of body weight. Those who advise a diet containing a large quantity of milk do not seem to realize that they are recommending large quantities of protein and in a form in which there is no loss from cooking such as occurs as flesh proteins. Terroine, mainly on theoretical grounds, is an advocate for a low protein diet at all ages, but the recent work of McCance and Widdowson on the losses of protein during the preparation and cooking of food points to the advisability of a safety factor in consumption much greater than theoretical considerations warrant. Analysis of the food intake of the poorer sections of the community shows that the amount of protein is often very very low, and is even precariously near the maintenance level of the mother herself. Some native races, notably the Eskimo, consume enormous quantities of protein, and apparently without ill effect.

Mineral Requirements.

Minerals constitute an essential part of the dietary of pregnant women and, certainly among the poor, deficiencies in these substances are not uncommon. Anæmia is very often present in those with restricted income, and the degree of anæmia seems to be progressive, the multipara showing greater degrees of it than the primigravida. The requirements of the female of the reproductive age in regard to iron, are because of monthly depletion, greater than those of men of comparable ages, and with a habitual diet barely sufficient to maintain the iron

requirements of a man, the anæmia of the women is progressively increased with age. The association of anæmia with gastric hyperacidity may not be unconnected with some of the nausea and vomiting commonly observed. The number of milligrammes of iron needed to maintain a positive balance of this mineral in the body has been determined, but dietetically is not of importance in that if the deficiency is made good by pharmaceutical preparations the daily dosage must be much greater than the theoretical requirements; if the iron is given in food-stuffs which contain it naturally the amount given should also be in excess because of the variable content of iron. As there is no evidence that excess of iron can be harmful the actual quantity prescribed may be large.

The daily requirements of the women for calcium have, like those for iron been determined with considerable theoretical accuracy but in practice the needs seem to be greater than estimated by laboratory methods. There has been a fear that excess of calcium may render the foetal head less susceptible to moulding during its passage to the outer world, but reliable evidence on this point is lacking. Clinically it does appear to be recognised that the imperfectly calcified head of the premature infant suffers damage during birth more readily than does the brain within a fully developed skull. Ease of delivery may thus be gained at the expense of damage to the infant's brain, and even to its chance of survival. The usual diet of many women of the poor classes is substantially deficient in calcium, and I have found that this shortage is imperfectly correct by the addition of a pint of milk a day to the diet. Clinically this is manifested by the occurrence of painful muscular cramps and perhaps of tumultuous movement of the foetus, even when the woman is getting the calcium in a pint of milk in addition to that contained in her ordinary diet. The administration of one of the preparations of calcium in such cases relieves the pain and discomforts of calcium shortage with dramatic suddenness.

Mineral shortage is, like vitamin shortage, rarely a single deficiency. When one particular mineral is ingested in insufficient quantity it is odds on their minerals or vitamins being also present in the diet in inadequate quantities.

Functions and action of Vitamins.

The question of the sufficiency of vitamins during pregnancy is extremely complex, and here again it seems that the only way to safety lies in ensuring that a margin be provided. The ill effects of hypervitaminosis are unlikely to be manifested unless colossal doses are administered.

The association between minerals and vitamins is not yet completely worked out, though much valuable research is being done in this respect. The routine administration to all pregnant women, at any rate women of the poorer classes, of vitamins A & D is becoming more and more popular, and although carefully controlled experiments on the

subject have been few it does seem that the incidence of puerperal pyrexia, and even of puerperal fever, may be diminished by this means. Certainly women living at or near the poverty line are unanimous as to the increased sense of well-being when these two vitamins are supplied.

The functions and actions of the B group of vitamins and of wheat-germ oil (Vitamin E) are extremely complex and as yet incompletely understood. For about five years I have made extensive use of wheat-germ oil, and it undoubtedly does prove effective in the prevention of many abortions, miscarriages, and premature births; and in some cases of pregnancy albuminuria its beneficial effects are rapidly apparent.

Those who have followed the interesting experiment carried out in South Wales under the direction of Lady (Rhys) Williams, in which the diet of expectant mother has been very materially increased in regard to protein and the B group of vitamins among other supplements such milk must have been impressed with the results. In brief, the results are that in about seven thousand expectant mothers whose diet has been substantially increased, the death rate, particularly from sepsis, is only a small fraction of that among about fourteen thousand women not so helped. If the results so far obtained during a relatively short time are continued it would appear as if the nutritional factor in maternal mortality is of the utmost importance and provides the key to the solution of a great social problem.

Relation of Nutrition to Lactation.

Space does not permit of consideration of other necessary dietary constituents or of more than a passing mention of the relation of nutrition to lactation. So far as breast feeding is concerned we have much to learn from the dairy farmer, whose living is dependent upon milk production. He knows well that protein is the key to successful lactation though of course other dietary constituents, and particularly the minerals, play their part. Application of the practice of the dairy farmer to the nursing mother is usually successful. No woman, any more than a cow, can produce milk without adequate consumption of protein. A pint of human milk contains approximately twelve grammes of protein, and this protein can only be derived from the protein in the mother's diet. But the human body is not a perfect biochemical factory, and the nursing mother requires, for each pint of breast milk produced, approximately twenty-four grammes of good quality protein in her diet in addition to her own bodily requirements of protein. Application of this simple arithmetical sum has done more in my own experience to promote successful breast feeding than any other measure or combination of measures.

Conclusion

The subject for discussion to-day is a large and its ramification so numerous that I have been able to indicate only a very few of the problems with which we are daily brought into contact. It seems to me that the addition of various preparations of minerals and vitamins to a deficient diet is a pharmaceutically correct procedure, but ought not be necessary:

neither should supplements to the diet. The food eaten should contain a sufficiency of all numerous substances requisite for reproduction and lactation, and there is some reason to this that the natural products may be better than those prepared by artificial means. Further, it is probable that the natural food contains substances one cannot yet define them which, though necessary for the maintenance of health, have not yet been separated or recognized in the laboratory. Unfortunately economic considerations enter into the solution of the problems.

One may perhaps summarize the position by stating that the most satisfactory diet for the nursing and pregnant mother is one which contains the greatest possible variety of food in adequate quantities.

(*The Indian Medical Review Feb. 1949.*)

Extracts.

EDEMA OF THE LUNGS.

By: A. L. BARACH, M.D.,

Etiology: 1. Heart disease. Left ventricle insufficiency is a definite cause of edema of the lungs which may occur suddenly during the course of coronary artery thrombosis, hypertension and aortic regurgitation. It is less common in aortic and mitral stenosis. Pathogenesis of pulmonary edema in heart disease is:—

1. *Mechanical.* 2. *Anoxic.* 3. *Neurogenic.*

1. *Mechanical:* During sleep plasma volume increases in the lungs and this is favoured by the recumbent posture which allows a freer entrance of blood into the right heart. Passive congestion of lungs due to left ventricle insufficiency may also be the cause.

2. *Anoxic:* Vital capacity of the lungs decreases on recumbent posture and also there is diminished ventilation during sleep. These produce anoxia which increases capillary permeability in the lungs.

3. *Neurogenic.* Relief of symptoms in pulmonary edema by morphine or sedatives indicate some neurogenic factor at work as well.

2. *Changes in capillary permeability.* Pulmonary edema resulting from changes in capillary permeability is seen in the following diseases:—

1. *Pneumonia, lobar or broncho.* Inflammation in the lungs, toxæmia, anoxia and neurogenic stimuli of the central nervous system play the part in causing edema of the lungs.

2. *Peripheral circulatory failure.* In shock sudden pulmonary edema may occur. Severe tissue anoxia increases in the capillary permeability and along with this neurogenic factors may also be present.

3. *Irritant gas poisoning such as phosgene and nitric acid fumes.*

4. *Nephritis.*

5. *Edema of lungs may follow tracheotomy and removal of pleural fluid.*

6. *Use of morphine in severe intractable asthma or pneumonia.* In intractable asthma or pneumonia the respirations are obstructed and intrapleural pressure is positive during expiration which hinders the entrance of blood into the right heart. Morphine decreases the effort of breathing and so positive intrapleural pressure is lowered. This as well as anoxia will cause pulmonary edema.

Treatment: Positive pressure respiration with oxygen is the ideal thing in pulmonary edema due to increased capillary permeability. The patient is kept in absolute bed rest and continuous positive pressure administered by a special apparatus. The pressures generally should range from 3-8 cm. of water. When pulmonary edema has cleared the pressure is reduced by 1 cm. of pressure every 2-4 hours until atmospheric pressure is reached. Oxygen mixture used should contain from 80-50% oxygen.

In patients with right heart disease or peripheral failure, in drowning cases, post operative anesthesia and gas poisoning cases intermittent positive pressure interferes with the return of blood to the right heart.

In halation of the nebulised solution of 1% neosyneprine, 1 in 100 epinephrine are useful in pulmonary edema from inhalation of irritant gases. Aminophylline orally or parenterally is also useful, especially in cardiac cases.

Morphine is useful in acute paroxysmal dyspnea occurring during the course of heart disease. Phenobarbital and papavarine may also be used. Aminophylline alone by mouth or in combination with phenobarbital is very useful. It may be given by intramuscular injection or rectally in doses of 0.5 gm. In pulmonary edema after tracheotomy for laryngeal obstruction a special tracheotomy tube projecting $\frac{1}{4}$ " from the neck is used. A Y shaped tube is connected to it. To one end is attached an inspiratory valve that allows free inspiration and to the other expiratory valve for breathing under positive pressure of 5 cm. of water.

Oxygen helps pulmonary edema as it cures anoxia also but pure oxygen is harmful as it is irritant. At the most it should be 70%.

(Sept. 1948 p. 27-32).

(Abstracted from the *American Practitioner.*)

INTRAVENOUS 'PALUDERINE' (PROGUANIL).

By R. N. CHAUDHURI AND CHAKRAVARTI.

The authors used 'Paludrine' acetate in 5-ml. ampoules each containing 100 mg. of the drug. The drug was tried in the following cases:—

1. Malignant malaria. High fever 105 F. 25 mg. of 'Paludrine' acetate was given intravenously. Second day the fever was almost normal but shot up again next day. For five days it continued at 104.5 F. and spleen was palpable on the ninth day and temperature still higher. At the stage 50 mg. of the drug was given intravenously, twice daily for 2 days. The fever was controlled in 60 hours and the blood was free from parasites in 48 hours. The patient was watched for 8 months without any recurrence of fever.

Case 2. Benign tertian temperature 106 F. 50 mg. of 'Paludrine' was injected intravenously and one tablet 100 mg. was given thrice a day for five days. Temperature became normal and blood was free from parasites after 48 hours.

Case 3. Benign tertian with palpable spleen. 100 mg. of 'Paludrine' was injected three times at four hours intervals. The temperature became normal in 24 hours and blood free from parasites in 72 hours.

Case 4. Malignant tertian, 10 days duration. Toxic and dehydrated and semiconscious. Spleen was palpable. 'Paludrine' 100 mg. was given intravenously at 4 hours interval for 4 doses. The patient became conscious on the following day and temperature became normal after 32 hours and blood free from parasites after 48 hours.

Case 5. Benign tertian, unconscious. Was given one intravenous injection of 100 mg. 'Paludrine' and 2 tablets of the drug by nasal tube thrice daily for five days. The one injection of 100 mg. was given daily for two days. The temperature became normal but unconsciousness remained. But slowly regained consciousness in 10 days. Malignant tertian parasites were also detected so this was a mixed infection.

Case 6. High continuous fever for three days, with intense headache and frequent vomiting. Spleen palpable general condition weak. Blood showed malignant tertian rings. An intravenous injection of 200 mg. of 'Paludrine' was given followed by two more injection of 100 mg. each at four hours. Temperature become normal 8 days after the injection. Blood was negative on the second day.

Case 7. Remittent fever and frequent vomiting about a week's duration spleen palpable. Malignant infection, was given intravenous injection of 300 mg. 'Paludrine' on the third day he became afebrile and blood was negative for malarial parasites.

Case 8. Mixed infection with Benign tertian and malignant malaria spleen palpable, temperature 105 F. He was given one intravenous injection of 'Paludrine' 400 mg. followed by 100 mg. of the drug thrice daily orally for three days. The temperature became normal and the blood became free from parasites.

Case 9. Malignant malaria, spleen palpable, conscious but dazed with intense headache and frequent vomiting. 'Paludrine' intravenously in a dose of 400 mg. was given. During injection vasomotor reactions as hot sensation over the body were felt. There was some pain in the vein injected also but these passed away. Temperature became normal after 56 hours and the blood was free from parasites in 28 hours.

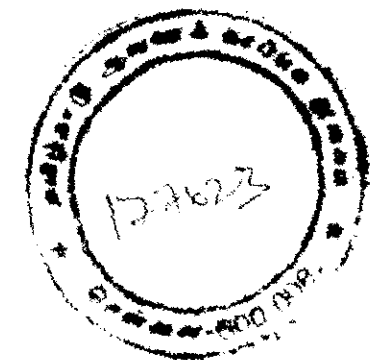
Case 10. Malignant malaria, fever and vomiting for 2 days. Weak condition. Spleen was palpable. 'Paludrine' was given intravenously in doses of 400 mg. followed by one 100 mg. tablet twice daily for four days. The temperature became normal after 26 hours.

Case 11. High continuous fever and vomiting for three days. Semi-conscious, malignant infection. Two injections of 100 mg. of the drug was given 4 hours apart. The patient died.

"Paludrine" in a dose of 200-400 mg. given intravenously had no bad effects and the temperature was controlled in 2-3 days.

Abstracted from the B. M. J.

(Jan. 15, 1949 p. 91-93)



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Printed by Mr. S. Sundaresan, L.P.T., for the C.C.P. Works, Ltd., 1/17, Mount Rd., Madras.