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A MONTHLY JOURNAL OF PRACTICAL MEDICINE & SURGERY

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Established 1932

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

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SOME CLINICAL ASPECTS OF ECTOPIC GESTATION

By DR. MISS S. SUBBALAKSHMI, M.B.B.S., D.G.O.

Pregnancy and Labour are said to be physiological processes in the life of a married woman. Perhaps it was so in olden days but at present these are attended by such varied and serious complications that one wonders whether it can be considered as a normal physiological process. However even now there are several fortunate women who go through the course of pregnancy and labour without the slightest disturbance to their normal life.

Among the various complications of pregnancy one of the most serious ones is Ectopic Gestation. In the normal course of events a mature ovum is expelled from the ovary by rupture of the wall of the Graffian follicle and the ovum floats in the peritoneal cavity in the neighbourhood of the ovarian fimbria of the fallopian tube. There is a natural current of attraction for the ovum towards the abdominal ostium of the fallopian tube from where it is directed towards the uterine cavity because of the movements of the Celia of the fallopian tube as well as peristaltic movements. Somewhere near the uterine end of the tube more commonly in the Isthmial portion, the ovum is said to meet the Spermatozoan and the fertilized ovum is moved along the rest of the tube into the uterine cavity where the fertilized ovum gets lodged in the bed of decidua which is already prepared for the reception of the fertilized ovum.

Ectopic gestation is the term applied to the condition where such a fertilized ovum gets itself lodged in any other region except the uterine cavity. The location can be any where from the ovary up the uterine ostium and the resulting pregnancy is termed according to the region where it lodges.

- (1) When it develops in the ovary it is known as ovarian pregnancy.
- (2) When it develops in the general peritoneal cavity it is known as Primary abdominal pregnancy.
- (3) When it develops in the tube it is known as Tubal pregnancy and this is again divided according to the region of the tube involved:—
 - (a) Ampullar part.
 - (b) Isthmial part.
 - (c) Interstitial part.

(4) Sometimes the ovum gets access into a rudimentary part of the uterus and develops there outside the uterine cavity then it is known as a Cornual pregnancy.

The course of events varies according to the site of the developing ovum. The causation of the Ectopic gestation is any interference in the normal movement of the fertilized ovum.

(1) For an ovarian pregnancy to take place the fertilization should take place by the spermatozoan entering a mature graffian follicle before its rupture. This is very rare.

(2) Primary abdominal pregnancy occurs when the ovum is fertilized after it is let out of the graffian follicle and before it enters the fallopian tube. This is also very rare and when it occurs the fertilized ovum gets lodged in any of the abdominal organs as Intestines and even the Liver.

(3) Tubal pregnancy is the most common variety of the Ectopic gestations and the cause for the same is any obstruction along the course of the tube. The obstruction should not be complete but must be such as to allow the upward passage of the active spermatozoan but prevent the down-ward progress of the larger fertilized ovum. Such conditions are:—

(1) *Mild Salpingitis*:—This leads to the destruction of the Celia which are supposed to be necessary for the normal progress of the ovum from the abdominal to the uterine end of the tube. The movement of the Celia is supposed to set up a current and help the movement of the ovum towards the uterus. Further this mild inflammation causes swelling of the mucous membrane of the tube and thus narrow the tubal canal.

(2) Adhesions between the tube and the surrounding tissues may distort the tubal canal and cause obstruction to the passage of the fertilized ovum.

(3) Tumours within the tube wall or from other structure near by may cause obstruction by pressure and narrowing of the tubal canal.

(4) Malformations of the tube as Spiral twists in the tube or diverticula.

(5) A rudimentary tube closed at the uterine end may be entered by an ovum fertilized by a spermatozoan coming through the opposite tube.

(6) A very long tube. Here the ovum develops into the trophoblastic stage before it completes the passage through the unusually long tube.

(7) Unusual decidual reaction in the tube is also advanced as a cause of tubal pregnancy.

As already mentioned before the fertilized ovum may lodge itself in any portion of the tube as the ampulla, media, Isthmic or interstitial, but the course is the same in all cases. the trophoblasts producing cytolysis of the cells of the tube mucosa and the ovum then borrowing into the muscular wall of the tube in a way similar to that of pregnancy in the uterus. A full decidua cannot be formed as the tubal mucosa does not contain

much interstitial cells. As the ovum grows it bulges the wall of the tube inwards occluding its lumen. The villi erode their way into the blood vessels and between the muscular fibres. The mucous membrane of the uterus is capable of a strong decidual reaction and acts as a barrier between the advancing chorionic villi of the developing ovum and the muscular wall. Further the uterine muscle is adapted to marked hypertrophy and stretching. On the other hand in the tube there is little or no decidua and the advancing villi rapidly eat their way into the muscular fibres and into the blood vessels. These blood vessels are large and the muscle of the tube is not so capable of hypertrophy and stretching. Hence in the tube the ovum acts like a rapidly growing destructive neoplasm. Some hypertrophy of the tube occurs in all cases and in rare cases the tube grows until term without rupture. Usually the hypertrophy of the muscle of the tube is insufficient to accommodate the egg and the muscle fibres at the site of the placenta are separated and destroyed by the erosive action of the placenta and a weak spot results. Any slight trauma or a strain causes a rupture at this site and bleeding takes place. If the rupture is on the free borders of the tube the bleeding takes place into the general peritoneal cavity; a hæmatocele forming in the pelvis. When the rupture takes place between the layers of the broad ligament a hæmatoma develops there. Rupture of the tube is the usual termination of an Isthmial and interstitial pregnancy and generally takes place in the second or third months. When the ovum is in the ampulla the gestation sac usually points in the direction of the abdominal ostium and a tubal abortion is the usual termination.

Clinical Course:—It is very rare for an Ectopic gestation to be without symptoms from the beginning. Several women give information that from the time of the cessation of the period there has been a dull ache in the lower abdomen. More often the history is that the patient missed a period and has the ordinary concomittant symptoms of early pregnancy; but soon complaints of pains in the lower abdomen especially in the affected side, cramp like pains due to the abal and uterine contractions. After a few weeks irregular bloody vaginal discharge appears which is usually mistaken for a sign of threatened abortion. External hæmorrhage usually indicates that the ovum has been disturbed from its site. On the occurrence of jarr, a strain or an examination, sometimes even without any notable event a sudden severe pain is felt on one side, the patient feels faint or dizzy and may vomit or have nausea. Symptoms of shock may appear and the shock may be due to the sudden destruction of the tube, irritation of the peritoneum by the extravasated blood, or by the great loss of blood. If this is not so severe as to cause loss of life, she gradually gets over it. The pains continue and sometimes, a uterine cast is expelled which gives the impression of having had a complete abortion.

If the first hæmorrhage is small, clotting occurs around the rupture and the blood is absorbed, the acute symptoms subside in a few days. Again because the clot is disturbed by movement of the women or the

blood pressure is raised the hæmorrhage recommences in a few hours or days, and the patient may die of anaemia from repeated hæmorrhages, or a sudden severe hæmorrhage.

The symptoms of rupture of the sac are pain on the affected side, sometimes excruciating and sudden, soon spreading all over the lower abdomen. Nausea, sometimes vomiting, sometimes diarrhoea plus evidence of hæmorrhage and shock. The striking pallor, pearly conjunctive, yawning and sighing, fast, small pulse and extreme weakness reveal the fact of blood loss. Internal examination when the blood is still fluid may not reveal anything but if one moves the Cervix carefully one can feel the uterus moving in a fluid medium. When the blood has clotted and hæmatocoele is forming a mass can be felt in the pouch of the Douglas. When the rupture has taken place into the broad ligament, a hæmatoma forming here, the pain is most intense because of the tearing asunder of the layers of the peritoneum. Internal examination will always disclose a firm mass on one side of the uterus. If the rupture or tubal abortion occurs more gradually the symptoms are proportionately less stormy and the true condition may not be discovered. The ovum usually dies when the rupture takes place. In some cases however if the placental site is not disturbed the ovum continues to grow. In such cases symptoms of peritoneal irritation such as pain, soreness, nausea, vomiting, diarrhoea or constipation, bladder disturbances, loss of strength etc., arise. The signs and symptoms of pregnancy continue, foetal movements are more pronounced and painful and the size of the abdominal tumor grows according to the period of pregnancy but may be asymmetrical. Sometimes it is median. At term a spurious labour sets in, the foetus dies and toxæmic symptoms usually set in as a slight fever, rapid pulse, anorexia, coated tongue, loss of weight etc. The patient may die of sepsis, of peritonitis, of exhaustion from prolonged suppuration, or the products of conception be gradually expelled through a fistula in to the bladder, the rectum, vagina, or abdominal wall. If injection of the sac does not take place, the foetus is transformed in to a lithopedion and may be carried on in the abdomen for many years.

Diagnosis

1. *Before Rupture* :—It is very rare to get cases coming for examination before rupture. In almost all cases the patient gives a history of previous pelvic inflammation, puerperal or gonorrhœal, and a long period of sterility elapses before the aberrant conception. When a woman in the reproductive period after some irregularity of the menses such as going over her time by a few days or a scanty flow complains of Cramping pains in the lower abdomen, mostly unilateral with irregular uterine discharge, the suspicion of ectopic pregnancy is aroused. On internal examination, a unilateral pulsatile, very tender swelling is palpated. The uterus is often slightly enlarged. The tumour has to be differentiated from thickened tube, a small ovarian cyst which has undergone a twist etc. The tenderness on palpation is much more marked

in the case of a tubal pregnancy than the other conditions. A thickened tube due to inflammation may be differentiated by means of a blood smear examination which may show an increase of the leucocytes.

2. *After Rupture* :—If the woman gives a history of having missed a period, and then suddenly an excruciating pelvic pain occurs with dizziness, faintness or collapse the diagnosis is almost certain, and is confirmed by finding extra uterine tumour, or sometimes the discharge of a uterine cast. When the development of the symptoms are not so alarming but gradual the condition will have to be differentiated from an ordinary abortion. In both we get symptoms of early pregnancy and later uterine discharge with pain in the lower abdomen.

1. In abortion the uterus will be enlarged corresponding to the period of amenorrhœa, whereas in an Ectopic although the uterus is enlarged it will not be corresponding to the period of amenorrhœa except in the rare cases where an intra uterine pregnancy coexists with a tubal pregnancy.

2. In abortion the onset of abortive symptom is quiet, with gradually increasing and regular pains in the lower abdomen resembling labour. In Ectopic the onset is stormy with irregular and colicky pains sometimes few and excruciating localised on one side. One definite descriptive term given by the patients in these parts in the cases of Ectopic is clearly diagnostic. They give the term as "Panju Keral" perhaps meaning the radiating nature of the pain. In every case where the patient described the pain as such the condition was certain to be Ectopic gestation.

3. External hæmorrhage is profuse or moderate with clots in cases of abortion whereas in Ectopic the hæmorrhage is usually slight and is dark. In a few cases that come to this hospital the hæmorrhage was rather profuse.

4. In the case of abortion the symptoms of hæmorrhage are proportionate to the visible blood loss whereas in the case of Ectopic it is out of proportion to the visible blood loss.

5. In the case of abortion matter discharged in the vaginal discharge contains foetal parts whereas in the other nothing is seen or only a decidual cast with no villi.

In the case of a Pelvic Haematocoele :—When the blood is fluid it may not be felt as a separate mass. It will give a false impression as if the uterus is enlarged to such an extent, but the cervix is not so soft as in the case of a uterine pregnancy and if the cervix is carefully and slowly moved up and down it will give a feeling as if it is in a fluid medium. When the diagnosis is not clear a needle passed into the posterior pouch will clinch the diagnosis. When the blood has clotted a mass will be felt. With the history of an abortion usually given by the patient this condition, will have to be differentiated for a pelvic inflammatory mass. A blood smear examination or again a needle in the posterior pouch will give the diagnosis.

When the woman comes with an extra uterine pregnancy at or on nearly full term the condition is not easily diagnosed at first. When they come with a history of having gone over time, suspicion is aroused. Many cases give a history of having had slight labour pains after which the foetal movements stopped. When we investigate the causes for the retention of the foetus beyond term we may get at the diagnosis.

When however the woman is seen when the foetus is still alive unless a very careful examination is made the condition may be overlooked. The points which arouse suspicion that it is not a normal pregnancy are:—

1. Abnormal presentations. These are much more common in extra uterine than in intra uterine pregnancies.
2. Foetal parts felt very superficially over the abdomen.
3. The whole foetus being present much higher in the abdomen than usual.
4. The foetal movements are felt to be very painful by the patient.

With the presence of these symptoms if the woman is questioned carefully, some abnormality in the course of the pregnancy will be forthcoming. Internal examination usually reveals the uterus to be small and pushed to one side by the abdominal tumour. When the developing ovum encroaches upon the uterine wall as in the case of interstitial pregnancy or pregnancy in a rudimentary form, the uterus may be much enlarged but a sound passed into the uterus will reveal the cavity to be empty.

Treatment.

There is no expectant treatment for growing ectopic gestation. In the presence of threatening symptoms one should not waste time on a fine differential diagnosis. If the diagnosis is made before rupture of the sac or during a tubal abortion the indication is to remove the ovum by Laprotomy. Under such circumstances the operation is very easy resembling an ordinary salphingectomy.

A tubal rupture and a tubal abortion is not possible to be differentiated before Laprotomy. When the symptoms are less alarming and gradual an abortion may be surmised rather than rupture. The best treatment is to do a Laprotomy on diagnosis and remove the ovum and blood clots from the peritoneum. Salphingectomy should also be done even if the ovum has escaped through the abdominal ostium. I have no hesitation in advocating this treatment since it is marvellous to see the patients improving after the operation although they look so hopeless before the operation. If the patient is under shock it is better to allow a few hours before the operation so that she will get over it unless the pulse rate shows that steady hæmorrhage is going on inside. In these cases nothing is to be gained by delay in the operation, where as there is some chance in doing the operation immediately.

When the case is met where the child is viable and is an abdominal pregnancy, the pregnancy is allowed to go to term and a Laprotomy is

done before the calculated expected date so that the child may be saved. In such cases the operation advocated is a Laprotomy and removal of the child leaving the placenta undisturbed to be dealt with later so as to avoid excessive hæmorrhage. In cases where the foetus is long dead Laprotomy is done and the secondary sac removed from the surrounding tissues. This is a very difficult process since the sac is very often firmly adherent to the intestines and its removal may result in damage to the intestinal wall. In such cases it is advised to remove the sac as far as possible and leave the rest for gradual absorption than risk damage to the other viscera.

The Miscellany August 1948.



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B.C.G. VACCINE

DR. N. ROY, M.B., D.T.M.

"The Ministry of Health in the Government of India after careful consideration of the question in all its aspects have come to the conclusion that vaccination with B.C.G. will be cheap and effective method of reducing the incidence of tuberculosis which is assuming epidemic proportions in this country. . . ."

"The World Health Organisation has very kindly agreed to send a B.C.G. Demonstration Team to India. The object of the visit is not only to popularise B.C.G. vaccination but also to show to the authorities concerned, the process of manufacture of the vaccine and the technique of administration. The W.H.O. Team is expected to work in India for a period of 4 months. It is the intention of Government to continue and expand the B.C.G. programme after the W.H.O. has left, so that the benefit of vaccination might be brought to as many people as possible throughout India", said Lt-col. R. Vishwanathan, Advisor on Tuberculosis, Government of India in a broadcast from Delhi Station of A. I. R. on 5-5-48.

So it will be meet and proper for us to ascertain the present position of B.C.G. in the light of the experience gained with regard to it in other parts of the world.

The fancy to control tuberculosis by such simple measures as vaccination fired the imagination of many eminent scientists. Many of them had met with classical failures which have built up great pillars of success. The immunisation of children by turtle bacillus by F. F. Friedman and the recent observations by A.Q. Wells on the vole bacillus are instances in point. But certainly it was not in store for Dr. Koch, the famous German bacteriologist to realise the hope at first held out by his so many tuberculin. The French bacteriologist Calmette and Guérin obtained a virulent tubercle bacillus with the antigenic property retained in it. They cultured virulent bovine tubercle bacillus in a medium of potato soaked with ox bile and 5 per cent glycerine for 18 years in 230 transplants and got the B.C.G. vaccine. It can be maintained in ordinary media with transfer to bile media after 10 subcultures. Calmette's idea was that the invulnerability of pathogenic tubercle bacillus lay in the lipoid coating which could be held in solution or colloid suspension in the bile. Calmette and his followers vaccinated a large number of children and from time to time published statistics which proved the harmlessness and efficiency of his vaccine which became known as B.C.G. or Bacille Calmette Guérin. Then Scheel in Trysil vaccinated 1,300 persons. They were followed up and there was less morbidity in the group. About this time there occurred the Lübeck disaster, in which 72 out of 251 vaccinated infants died of tuberculosis. It was ascribed to contamination with virulent strains of *Mycobacterium tuberculosis*. But the possibility that there was some flaw in the culture technique and the organisms thereby gained virulence cannot be ruled out, in the light of

studies of Gildemeister and others on the dissociation of the turtle bacillus, tubercle bacillus, frog tubercle bacillus and avian and bovine tubercle bacillus, into S & R types. Petroff, in this connection, thinks that the bile potato medium used for culture of B.C.G. has effected artificial selection of R forms which is more stable and saprophytic at the expense of form which is parasitic and more liable and has been suppressed by the low pH of the medium. Therefore, the B. C. G. vaccine can undergo variation and regain virulence. But this test tube possibilities pales into academic insignificance if the organisms remain fixed in the vaccinated individual which again has not been proved to be otherwise in a large number of observations throughout the world. This is also why the whole technique of B.C.G. vaccination should be thorough and accurate and cannot be commercialised.

Though Lübeck catastrophe caused a setback to further progress of B.C.G. vaccination in greater portion of the European continent, it has since got a firm foothold in the Scandinavian countries. Heimbeck in the Ullevaal communal hospital in Norway made the following observation among probationer nurses. The course for the nurses there is for 3 years with a period of service in the T. B. ward with 300 to 400 beds. From 1924-33, 722 nurses were examined with Pirquet test; 226 were negative and 496 were positive reactors; 94 among the negative and 24 among the positive group developed tuberculosis; 10 per cent in the negative group died.

From 1927, Heimbeck began to use B.C.G. (by subcutaneous route) in negative reactors; 164 nurses became positive and only 3 developed tuberculosis; 94 nurses remained negative and 22 nurses from this group developed tuberculosis. An investigation among medical students of 3 categories such as—(1) Pirquet negative and not vaccinated with B.C.G., (2) Vaccinated with B.C.G., and (3) Pirquet positive revealed an incidence of tuberculous disease of (1) 4.3 per cent, (2) 1.2 per cent and (3) 7 per cent respectively. Up to 1937, Norwegian statistics revealed that tuberculous morbidity in the vaccinated group is 2.6 per cent as against 17.1 per cent in the unvaccinated.

For the present, I shall leave the Scandinavian field and take the American work by Joseph D. Aronson, Egma.1. Pan and Robert M. Saylor, which is a very thorough investigation. In 1926, Dr. W. H. Park of New York City Board of Health Laboratory received a culture from Prof. Calmette, Pasteur Institute, Paris. A subculture from the above was kept at the Henry Phipps Institute, Philadelphia, under the lock and formed the strain 817 and was used for vaccinating 1,058 children. It is needless to say that the place in the Phipps Institute is not used for any other studies in bacteriology or pathology and the equipment and supplies used there for the study are new and strictly limited to the maintenance of the culture and preparation of the vaccine. After 10 subcultures at intervals of 2 weeks in a medium of potato soaked in veal infusion broth they were grown for 3 generations on potato soaked

in beefbile containing 5 per cent glycerine broths. The strain was also cultured in a synthetic medium called Souton's medium.

The strain 575 was received by one of the workers in January, 1938, from Prof. Guerin, Pasteur Institute, Paris. They were also cultured as above. In potato medium the same cultural characteristics as strain 317 were present. 512 children received this vaccine.

The tests for a virulence of the B.C.G. strains were done at intervals as follows:—30 mgm. of the cultures were injected into the peritoneal cavity of normal guineapigs. After 3-4 months of observation, the animal was killed and necropsied. No evidence of generalised tuberculosis was ever found.

The test for estimating the protective value of B.C.G. against reinfection in the animals was done as follows:—5 mgm. of B.C.G. was injected subcutaneously in normal guineapigs; 6 weeks later, they were infected with 100 virulent bovine tubercle bacillus intratracheally or with .001 to .01 mgm of a virulent human tubercle bacillus subcutaneously. The same amount of injection by one of the two routes was given to two groups of unvaccinated guineapigs. B.C.G. vaccinated animals infected intratracheally with virulent bovine bacillus show fibrous or fibrocaseous hilar lymph glands and a small number of fibrous or fibrocaseous tubercles, in the internal organs, but no microscopically demonstrable tubercle bacilli. Among the unvaccinated control animals the hilar glands were caseous with caseous foci in the internal organs and microscopically demonstrable numerous tubercle bacillus. In the vaccinated guineapigs infected subcutaneously with virulent human tubercle bacilli, slight tuberculous changes of the internal organs with the regional lymph glands showing thin milky fluid in the centre were seen. In the control animals, similarly infected extensive caseation of the lymph glands and internal organ were seen.

After the above tests were thus found satisfactory, B.C.G. vaccine was prepared in the following manner. The stock cultures and new laboratory equipments and chemicals were transported to as near the field of operation as possible so that a fresh supply of vaccine can be ensured. This itinerant laboratory was housed preferably in a school building. No sputum or material contaminated with or any culture of any bacteria was allowed in the place. 10 preparations of subcultures from above 2 strains were made in the synthetic Souton's medium and 3 preparations were made from the strain 317 on potato soaked in veal infusion broth. The subcultures were grown at 38°C from 7-30 days. The bacillary mass was collected over several layers of sterile filter paper to drain off excess of fluid. This mass was then ground in a sterile glass flask containing stainless steel balls about 4 mm. in diameter and required amount of sterile salt solution was added to give it the final shape of the vaccine.

This vaccine was tested now for any contamination by inoculating 2 c.c. of it into Dunham tubes containing 1 per cent glucose broth. If this test was negative, sterile, the vials filled with B.C.G. vaccine were packed

into a vacuum jar containing ice and was used mostly within first 12 hours or at most 3 days. The following technique was adopted for vaccination:—The candidates for vaccination were the negative reactors to intradermal test of P.P.D. in doses of .00002 and .005 mg. These persons were vaccinated within a period 2-3 weeks of showing negative response to P.P.D. This period exceeded 4-5 weeks in a few cases.

The site of injection was right deltoid muscle. This site was painted with Tr. Iodine and was washed after 3-5 minutes with 95 per cent ethyl alcohol. When the skin became dry either .1 or .15 mg. of B.C.G. was slowly injected intradermally with tuberculin syringe and a .26 gauge platinum needle. scrupulous care was taken to make the injection uniformly superficial by the same vaccinator in all the cases.

The following reactions were observed after the vaccination as done above. The reactions were not modified by sex, degree of Indian blood or constitutional type. Reactions were less among younger children of pre-school age and ulcers healed quickly among those living in Arizona than among those in Alaska. The varied reactions seen were due probably to individual resistance, texture of skin (with consequent difference in administration of vaccine) and difference in the lots of vaccine to some extent.

Forty-eight hours after the injection, of either .1 or .15 mgm. of B.C.G. a sharply defined nodule about 4 mm. in diameter and 1 mm. in height was observed. During the first 2 weeks of local inflammation decreased and the nodule increased to the average size of 6 mm. From the 3rd to the 4th weeks the nodule still increased in size and softened in the centre in many cases. From 4th to 8th weeks, there was ulceration in 75 per cent of the cases. A dull aching pain at the site of injection and a sense of fullness in the axilla was reported in a large number of cases. Axillary lymph glands enlarged in 5 per cent of cases. The above subjective symptoms disappeared when ulcer formed and discharged exudate. Healing occurred in three months and a soft scar 5-10 mm. in diameter resulted. The resulting ulcer was also noted to belong to two kinds (1) like the punched out syphilitic chancre in 40 per cent cases and (2) in the rest, like typical tuberculous ulcer with undermined edges and crater-like opening. It is interesting to note that acid fast bacilli are found in the initial stage in the discharge.

From the percentage of the conversion to positive reactor from negative stage it was found that the age of culture which varied from 7-30 days and such rotation of culture medium as 2-7 generations of B.C.G. in bile free media after 2 to 3 generation in bile potato medium did not affect the antigenicity or avirulence of the B.C.G.

Regarding the dosage of the vaccine Kereszturi, Rosenberg and Park found that highest percentage of positive tuberculin reactions was obtained with intradermal injection of .15 mgm. B.C.G. vaccine while larger doses produced cold abscesses without materially increasing the number of positive reactions.

Since a total of 98.3 per cent of those injected intradermally with .1 to .15 mg. of B.C.G. reacted to tuberculin one year later and since none developed suppuration of axillary lymph glands it is evident that the above doses are doses of choice.

Kereszturi, Rosenberg and Park observed that one year after intracutaneous injection of B.C.G., 75 per cent of their cases were tuberculin positive, that after 2 years 45 per cent were positive and up to 3 years only 42 per cent were positive.

Arouson, Pan and Saylor found that of 1,482 persons ranging in age from 1-19 years vaccinated intradermally with B.C.G., 1,883 or 98.3 per cent reacted to .00002 or .005 P.P.D.

Regarding the risk of the B.C.G. vaccine as seen in the present American study, among 1,565 vaccinated, Koch's phenomenon was observed in 5 cases. 3 of these were tuberculin positive and were vaccinated through mistake. In 2 cases probably super-infection occurred due to a long interval of 5 weeks which elapsed between tuberculin test and vaccination; one of the cases died from miliary tuberculosis. In conclusion as stated before, most of the present American workers feel that the protective value of B.C.G. vaccine is difficult to establish because of (1) the degree of subsequent infection with tubercle bacilli with varying virulence and (2) the standard of natural resistance of the individual and results claimed up to now is due to different technique in maintaining culture, difference in aging of the culture and the dose and route of administrations. So, according to the American thinkers, they would like to observe the B.C.G. vaccination and assess all facts concerned before they would pronounce their final opinion about its protective value.

Now let us consider the work on this subject done in Scandinavia. This vaccination has been practised there from 1926. It is being systematically done in Norway from 1928, in Denmark from 1930 and Sweden from 1927. In Sweden, 27,000, 57,000, 87,000 and 1,12,000 people presented themselves for vaccination during the years 1942, 1943, 1944 and 1945 respectively. It is obvious from the above figures of voluntary vaccination how the public share in the confidence of the doctors there. At present, there is a bill pending in the Norwegian parliament for introduction of compulsory B.C.G. vaccination. Indeed their statistics of morbidity and mortality lend a support to their confidence in the efficacy of B.C.G. vaccine. According to Hertzberg, if the mortality due to tuberculosis for all ages up to 50 years in Oslo be taken to be 100, the corresponding figure among the B.C.G. vaccinated group for the same ages would be 18. Similarly, if the number of infectious tuberculous cases among the unvaccinated group be 100, then among the group vaccinated with B.C.G. it would be 10. In Scandinavia, the laboratories at Berghe, Gotenberg and Copenhagen issue freshly prepared vaccine every week to be used in course of 10 days. The vaccine is issued in 2 strengths, e. g., .5 mgrm per 1 c.c. for intradermal injections and 20 mgrm. per 1 c.c. for scarification. At Bergen, the multiple puncture instrument of Birkhaug is used. The sites of injection in these countries are over deltoid muscle in the adult male and over the groin or below thigh in cases of children and women. The dose used is .05 mgm. or 1 c.c. intradermally. A papule 1 to 10 mm. appears which heals without any scarring in 60-70 per cent of cases. In fact five intradermal injections do not lead to any complication but if given subcutaneously or too deep, local ulceration or abscess formation may occur. Occasionally there is severe reaction

which clears up in 12-18 months. In infants, intradermal administration is very difficult. Therefore the puncture method is used. The dose used is also heavy, and is as much as 20-40 mgm. and is sometimes given in two divided doses over two arm. The reason is that the defence mechanism of the infants are not fully developed and therefore requires greater stimulation with bigger dose and takes longer time to develop allergy. The infants are inoculated within 6-24 hours after birth. Before and after inoculation the adults are segregated in any suitable place for 8 weeks and the children for 12 weeks after inoculation. The object of segregation is to protect the negative tuberculin reactors from superinfection with tubercle bacilli during this period of development of allergy. This superinfection actually happened in Stockholm in 1944. 200-300 persons who were vaccinated with B.C.G. were exposed to infection shortly before vaccination and developed Pulmonary Tuberculosis.

Full scheme of vaccination is stated as follows:—

- (1) Tuberculin test is done (i) Negative reactors are segregated for 6-8 weeks in a non-tuberculous convalescent home or boarded in a non-infectious environment.
- (2) A second tuberculin test is done, if found negative.
- (3) B.C.G. is injected intradermally in a dose of .1 c.c. (.05 mgm.).
- (4) The inoculated persons are segregated for 6-8 weeks as in (1) (i).
- (5) A third tuberculin test is done; if found positive and a skiagraph taken shows nothing abnormal, the person can return to his environment; otherwise a 2nd B.C.G. injection and a 4th tuberculin test after 6-8 weeks of segregation is undertaken. Usually, at this stage a large number of conversion is seen. The children and adults are x-rayed every year for 10 years; in the children the skin test is done, in addition, up to 10th year.

From the above details, it is crystal clear that Scandinavian countries have gained a lot of experience in the line more than any other country. Their enthusiasm over this mode of prevention of tuberculosis is justified from the following statistics:—Among the vaccinated the annual incidence and mortality of tuberculosis is 2.6 per cent and .2 per cent respectively. The corresponding figures among the unvaccinated and tuberculin negative group is 17.6 per cent and 1.8 per cent respectively. It would not be out of place to cite here some figures from Russia in this connection. In 1927 10 new born infants were vaccinated and 2,981 infants in 1935. From 1940 every infant was vaccinated. From the literature available it appears that Scandinavia and Russia have been using B.C.G. vaccine for a much longer time than the American workers in the field. That probably explains the American scepticism. Still, at least, one of the workers in America Dr. Joseph D. Aronson of the University of Pennsylvania recently said at the Tropical Medicine Congress, Washington, that studies conducted over the past eleven years among American Indians, who have a high tuberculosis death rate, showed 3 times as much of the disease and 9 times as many deaths among the unvaccinated persons as against those vaccinated.

Also it may be mentioned here that Turkey has been preparing B.C.G. vaccine in her Central Institute of Hygiene, but it is not known whether the vaccine has been used to any great extent.

So it is high time that India should introduce the B.C.G. vaccine when the World Health Organisation is coming to demonstrate the

technique of B.C.G. vaccine. This is more so because India due to poverty, disease and ignorance, is virtually in a morass whence she has got to be delivered by all possible means. This is a safe, cheap and fruitful measure and so very suitable for the Government of India at the present state of things, to adopt as a general public health measure. Here is one other point to consider. In India, where 90 per cent people live in villages it is very likely that 50 per cent of the population up to 20 years of age is uninfected with tubercle bacillus as Col. R. Vishwanathan puts it. This is a vast virgin field where tuberculosis is expected to cause havoc and B.C.G. to fight the menace. According to the Swedish authorities the following are the special groups which come under the jurisdiction of B.C.G. vaccine:—(1) Nurses, (2) Medical students, (3) School leavers between 13-14 years, (4) Conscripts, (5) School teachers, (6) Expectant mothers, (7) Seamen, (8) Dental Surgeon, (9) any other non-reactor. This classification can be adopted with alterations required for our country. As for example, the labour recruited from villages for the mines and factories should claim the earnest attention of the B.C.G. vaccinators. The children and the newborn babies with tuberculous parents or relatives are other good examples. The maternity homes, if afforded facilities, will play an important role.

In conclusion I would emphasize the importance of establishment of separate laboratories for B.C.G. vaccine and separate band of energetic workers. Any attempt to minimise expenditure by any short-cut or stop-gap arrangement will land us in disaster as is evident from the Lubeck catastrophe, the unfortunate events in Stockholm in 1944 and studies of Gildemeister. Such an untoward event will make the measure so much unpopular among Indian mass who is usually chary of vaccination that all hope of success will be dashed to ground. So it will be wise to tread on the sure ground even if it would mean a "goes slow" process and would cost something for that would be sound economy. As soon as the people could see some benefit and little or no reaction from the vaccine, it will automatically gain popularity and extend its own field.

(Calcutta Medical Journal, June 1948.)

Extracts.

ORAL PENICILLIN IN TREATMENT OF PNEUMONIA IN THE ADULT.

ANDERSON, T., and LANDSMAN, J. B.: B. M. J. 2 : 950-953, 1947, 8 refs. 3 figs.

Authors in a previously published paper had shown that there is very little to choose between the two ways - (penicillin and sulphonamides) of treating pneumonia except for an advantage in favour of penicillin because of its lack of toxicity but disadvantage of multiple injections. They used penicillin by the intramuscular and oral routes in a series of 90 cases of pneumonia. Alternate cases were treated in each group. In the intramuscular penicillin group; 50,000 units were given as an initial dose followed by 20,000 units at four hourly intervals for 5 days. The mean total dosage of penicillin was 800,000 units. In the oral penicillin group, tablets of calcium penicillin with 0.5 g. of sodium citrate were used. The tablets were administered with 1-2 ozs. of milk and the daily fluid intake was restricted to 2 pints. 60,000 units were administered every 3 hours for the first 2 days. The mean total dosage given orally was 16,50,000 units. The bacteriological and clinical control was

similar in both series. The average duration of fever in uncomplicated cases were "intramuscular" group 1-9 days; "oral" group 1-4 days. Complications developed in 12 of the patients given intramuscular penicillin and in 16 of those given oral treatment. Authors consider that oral administration of penicillin is a satisfactory method of treatment for pneumonia, but, they add that sulphonamides constitute an adequate method of treatment for the majority of cases of pneumonia more especially in younger age groups; but for those who require penicillin the "oral" method offers advantage of easy administration.

J. C. PATEL.

METAL IN OUR FOOD

BY N. C. DUTTA

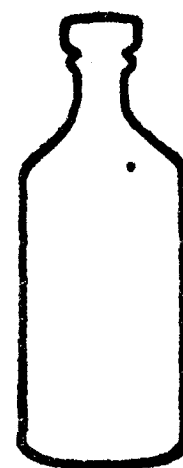
Aluminium Vessels: Dr. Monier Williams (1935) has collected and examined all the informations available upon the subject of toxicity of aluminium and concluded that there is no convincing evidence that aluminium cooking vessels are harmful. Aluminium vessels can be used for frying, boiling or for cooking, or for storing milk, curds and acid liquids without fear of absorption of harmful amount of the metal. Weakly alkaline water brings about quickest destruction of aluminium. The interior darkening of aluminium vessels during use is due to the small percentage of iron left behind on the surface. This dark film is strongly adherent and has a distinctly protective action and hence need not be removed.

Salt is known to favour corrosion of aluminium. The corrosion by salt is increased in the presence of acids, Acid foods containing salt should not be stored long in the vessel, since pin pricks may appear in many aluminium vessels. These present an undesirable appearance and may set up bacterial contamination. This is, however, entirely preventable if proper care is taken.

Aluminium is readily attacked by alkali resulting in the formation of aluminates. Aluminium vessels and cooking utensils are liable to the damage if cleaned too often with soda. Aluminium container used in milk industry tend to become slightly coated with organic materials which are somewhat difficult to remove and readily set up bacterial contamination. This difficulty has been overcome by cleaning with sodium carbonate containing a small proportion of sodium silicate.

Aluminium is quite harmless as food container and cooking utensils. But some persons may be susceptible and show an idiosyncrasy even to small quantities. They should avoid the use of aluminium utensils.

Tinned Vessels: Corrosion of tinned vessels is favoured by exposure to air, by the acidity of food and heating. The problem of contamination of food stuffs from tinned brass vessels is further complicated by the fact that lead is often mixed with tin for tinning vessels. A further complication may result by irregular tinning of the vessels or the mechanical wearing away of tin during use. The brass or the copper, as the case may be, being then exposed to the acid food and may gain access to the food material. Acid foods should not be stored in tinned vessels for fairly long periods. Small quantities of tin consumed over a long period may produce minor disturbances in health which are quite distinct from ill health.



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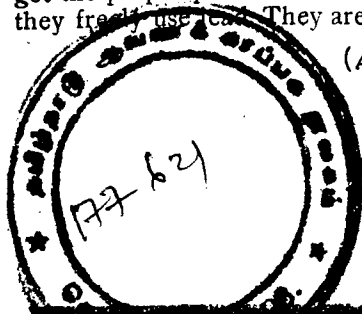
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Copper in food from Vessels: Brass, bronze, tinned brass and tinned copper vessels are the common source of contamination of food with copper. Brass and bronze vessels are quite unsuitable for cooking and storing articles of food. Larger quantities of copper than the amount necessary for physiological function in the body can exert harmful effect on the system.

Lead in Food: Traces of lead, however small, in water or food indicate a potential danger. According to some 0.5—1 part per million lead constitutes gross contamination, while others consider that 0.1 part per million should not be exceeded. Besides drinking water other substances like sardine oil, canned sardine, soda water, baking powder, tinned meat and fruits, cider etc., have been found to be contaminated with lead. Sardine cooked in oil in a tinned vessel may contain from 7-50 parts per million of lead. Canned fish may contain from 8.48 parts per million.

Lt. C. Candy (1933) found that lead poisoning was fairly common in India which he attributed to the habit of "tinning vessels". The tin used is often adulterated with lead. Kalai-wallahs use tin only when they get the proper price for tinning. For those who want cheaper tinning they frequently use lead. They are quite ignorant as to the toxic effect of lead.

(Abstracted from the Indian Journal of Medical Sciences, March, 48 p. 137-149.)



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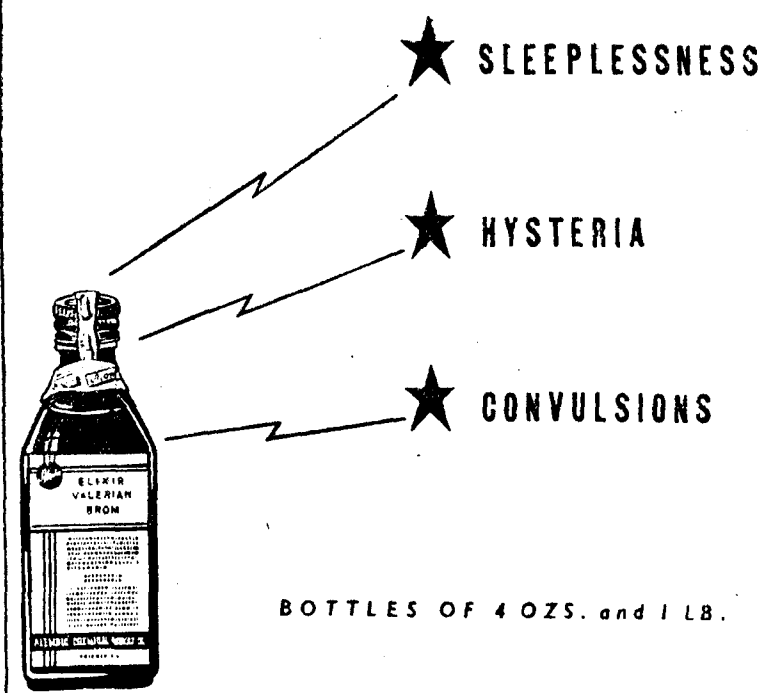
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MEDICO-SURGICAL SUGGESTIONS

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Editor: Dr. P. R. Venkappaya

Established 1932

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVII

NOVEMBER 1948

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HEART-DISEASE IN THE UNITED PROVINCES*

By. S. S. MISRA†

Heart disease in these provinces is one of the commonest causes of morbidity and mortality affecting people of all ages and both sexes and from all strata of society. There is, however, a great deal of mis-conception amongst the laity and even amongst many medical men, as regards the diagnosis of organic heart-disease and its management.

AETIOLOGY

The following figures are obtained from an analysis of cases admitted in the K. G. Hospital, Lucknow, during 1945. Out of a total of 2106,122 (under 6 per cent.) were of heart-disease, mostly in a state of advanced failure because patients seldom enter hospitals, unless very ill. Of these, 26 (21 per cent.) died in hospital. No autopsies were performed. The ages varied from 8 to 70 years. There were 83 males and 34 females; of these 87 were Hindus and the rest 35, predominantly Moslems.

Of these 122 cases:—

Rheumatic carditis .. 45 cases (37 per cent)	Syphilis ... cases (2.5 per cent)
Arteriosclerosis without hypertension .. 28 „ (23 „)	Subacute B. Endocarditis ... 2 „
Hypertensive failures .. 21 „ (17 „)	Cardiac Neurosis ... 2 „
Secondary to Chronic Bronchitis and Emphysema ... 20 „ (16 „)	Patent Ductus Arterialis ... 1 „

The above table reveals certain surprising points. Rheumatic carditis was responsible for 37 per cent. of cases, i. e., over 1 in 3. This would appear strange to English writers who authoritatively claim that acute rheumatism as a factor in cardiac morbidity plays a very minor role in this country. The majority of the cases showed a concomitant mitral lesion of the obstructive type. Aortic lesions were comparatively much fewer and a few cases showed both aortic and mitral lesions. Another surprising point is the comparative rarity of auricular fibrillation in this group, only 6 cases out of 45 (13.3 per cent).

The youngest patient showing rheumatic carditis with failure was aged 8 years only and the oldest was 40 years of age and had had

*Paper read before the 3rd Conference of the Association of Physicians in India, held in Bombay, in December, 1947.

†Physician, K. G. Medical College, Hospital, Lucknow.

compensated rheumatic carditis for over 20 years. Two developed pericardial effusion which had to be tapped.

Arteriosclerosis with hypertension was responsible for 28 cases (23 per cent). The youngest was aged 40 years and there were as usual many more males than females. (One reason is that women-patients seldom come to hospital). Coronary thrombosis often preceded by anginal pains is a frequent history.

Hypertensive failures were frequent, 21 cases (17 per cent). Age varied from 35 to 65 years and the predominating sex was the male. The duration of the hypertension before failure supervened was unknown in all hospital cases, but in one private case, it lasted for over 15 years and ranged about 200 m.m. mercury systolic and 120 m.m. diastolic during which the patient lead an active life. In this case, failure set in twice and was controlled with rest, digitalis and mercurial diuretics. Two cases were probably of malignant hypertension in view of the short history of symptoms and the rapid downward progress.

The next most frequent cause of failure was chronic bronchitis with emphysema, 20 cases (16 per cent). The majority were over 45 years of age and chronic bronchitis had lasted for years before the supervention of emphysema, and secondary failure. In several cases the emphysema with its concomitant masking of the cardiac and the hepatic dullness was not noticed because of bronchiectasis (proved with lipiodol bronchography) producing fibrotic contracture of the lung.

Cardiovascular syphilis was responsible for only 8 cases (2.5 per cent.); this diagnosis was based on a past history of syphilitic infection, some other signs of syphilis and a positive Wassermann reaction. This very low incidence of syphilis as an etiological agent appears intriguing. The patients were all men over 40 years of age.

Two cases of subacute bacterial endocarditis were encountered—one in a girl who had had rheumatic carditis for several years, and the other in a male aged 48.

Only one case of congenital heart-disease was admitted—probably a patent ductus arteriosus. Finally, two cases of cardiac neurosis were admitted as in-patients, though cardiac anxiety is much more frequently encountered in consulting work. In some cases, persons were being treated for years as cardiac invalids because of a functional extra systole, or palpitation, or hypertensophobia or precordial pain.

PATHOLOGY

It is regretted that no post-mortem data can be given because of the rooted objection to permit post-mortems in this part of the country. It would greatly advance our knowledge in all departments of medicine if even partial post-mortems could be made available.

It is necessary to stress here that most medical men and medical students are unduly obsessed with the various audible murmurs in the mitral and the aortic areas and their timings, forgetting the basic fact

that it is the status of the myocardium which determines the onset of the symptoms of heart failure.

In rheumatic failure the onset is not determined by the intensity of the various murmurs but by the degree of myocardial damage. In arteriosclerosis, the increasing cardiac ischaemia produced the symptoms of angina pectoris and coronary thrombosis. The arteriosclerosis was usually universal.

In hypertensive cases, failure usually supervened when the limit of cardiac hypertrophy had been passed.

SYMPTOMS AND SIGNS

They were very varied. The majority of the cases came in a state of total biventricular (left and right sided) failure, with symptoms of back pressure, *viz.*, dyspnoea and cough with congested lungs, raised intravenous pressure, distended jugulars, enlarged liver, anasarca, tachycardia, hypotension and increased cardiac size.

Most of the failures came on with normal rhythm, even in rheumatic cases. The various murmurs are not described here. In two cases pericardial effusion was sufficiently embarrassing to need tapping.

A purely left ventricular failure was not uncommon in the earlier phases of hypertensive decompensation producing cardiac asthma or effort dyspnoea or effort angina, going on to coronary thrombosis.

Frequently these symptoms, *viz.*, cardiac asthma, effort dyspnoea, effort angina and coronary thrombosis were observed in non-hypertensive arteriosclerotics.

Later on, in all cases, right ventricular failure supervened.

The above group of symptoms was also frequently observed in severe cases of anaemia (of whatever origin), and completely disappeared when the anaemia improved.

A great deal of judgment is necessary in the diagnosis of early cases of angina pectoris, particularly when the presenting symptom is effort dyspnoea and not effort pain.

The retrosternal situation of the pain produced as a result of a decreasing amount of exertion, its frequent association with a loaded stomach and exposure to cold, and its relief on rest, are important factors. There may or may not be generalised arteriosclerosis with or without hypertension. A screen examination may or may not reveal alteration in the size of the heart and the electrocardiograph is seldom abnormal. In these cases, a carefully performed exercise-tolerance-test is of greater value than the above aids.

Many mild cases of coronary thrombosis are missed and will continue to be missed, so long as the electro-cardiograph is regarded as infallible. Experience shows that even leads IV and V are often deceptive. Particular difficulty is experienced when persistent dyspnoea and not persistent retrosternal pain is the presenting symptom.

In consulting practice, cases of cardiac anxiety are encountered frequently. The presenting symptoms are usually functional extrasystoles

or precordial pain or palpitation or breathlessness unrelated to effort. Careful history-taking usually reveals an abnormal psychological situation, while physical examination including exercise-tolerance-test, screening and electrocardiography are always negative.

One should also remember the not infrequent cases of functional systolic apical murmurs who have been forced to lead the lives of "cardiac" invalids.

Similarly, hypertensophobia has become a fashionable disease due to old ideas of what constitutes high blood pressure (age plus 100).

Cases of heart-failure secondary to chronic bronchitis and emphysema will show a most important sign, the masking of the cardiac and hepatic dullness except in those cases of bronchiectasis where fibrosis produces increasing contraction of the lung. There will be history of chronic cough for many years.

Syphilitic cases usually present symptoms of cardiac asthma or angina pectoris or coronary thrombosis or aortic incompetence. Other stigmata of syphilis are usually present.

Subacute bacterial endocarditis presents a picture of fluctuating pyrexia, multiple embolic phenomena (pericardial hæmorrhages, hæmaturia, etc) slight splenomegaly and clubbed fingers, while a blood culture reveals the streptococcus viridans.

DIAGNOSIS

A great deal of responsibility rests on the profession; early and correct diagnosis may be made in many cases so that preventive steps may be taken to check, as far as and if possible, the further advance of the disease process.

In rheumatic cases, it is the exception rather than the rule, to find a history of acute rheumatic fleeting synovitis. In young children, the most frequent history is that of recurrent coryza and sore throat. If this sequence is kept in mind and the condition treated suitably, the heart may be saved even if a slight lesion has appeared. As mentioned before, the various murmurs are of little significance; what matters is the degree of myocardial damage.

Cases of arteriosclerosis without hypertension are particularly difficult to diagnose and receive the vague label of chronic myocarditis. Usually the arteriosclerosis is generalised, so that the radials, brachials and temporals can be felt to be thickened. In some cases, it is well known that only the coronaries may show arteriosclerosis whereas the rest are healthy.

A puzzling group of persons one occasionally comes across, is where peripheral arteries like the radials and brachials are thickened in persons who are young (15-35 years), have no hypertension, no renal disease and no cardiac abnormality as shown by screening, electrocardiography and the exercise-tolerance-test.

Angina pectoris and coronary thrombosis should be kept in mind in all cases of apparently causeless effort-dyspnoea and effort-pain.

Hypertensive failure is relatively easy to diagnose provided the blood-pressure is taken in every case as a routine matter.

Most cases of chronic bronchitis gradually go on to emphysema with masking of the cardiac and hepatic dullness and secondary heart failure. Syphilis as a cause of cardiac failure appears to be a much less commoner factor than one would gather from the books.

Cardiac neurotics occupy a prominent part in consulting and out-patients' practice and need careful handling. By careful history-taking physical examination and radiological aids, one should be able to convince a person of the soundness of his cardiovascular apparatus. The Da Costa syndrome (neurocirculatory asthenia or D. A. H.) must be very rare in civilian work.

Particular difficulty may be experienced in making it certain and to convince the patients that an apical systolic murmur is functional, because he has been told for years that his heart is damaged.

Similarly, hypertensophobes remain a difficult problem because of the wide-spread belief in the exploded formula of hundred plus age or hundred plus $\frac{\text{age}}{2}$. Experience shows that systolic and even diastolic pressures vary a great deal in different persons and in the same person at varying times. Very little importance should be attached to systolic pressures below 160 M. M. and diastolic pressures below 100 M. M. of mercury.

All patients known to have rheumatic heart-disease or a patent ductus arteriosus should be regarded with suspicion if they have prolonged pyrexia of unknown origin. If embolic phenomena are present and especially if the spleen is palpable, blood culture should be done to exclude subacute bacterial endocarditis. Congenital heart disease appears to be rare in this country, though one occasionally comes across dextrocardia, co-arcuation of the aorta, Fallot's tetralogy, pulmonary stenosis, and a patent ductus arteriosus.

PROGNOSIS

When heart failure has once supervened, the outlook is usually grave. This series shows 26 deaths in hospital out of a total of 122 cases (21 per cent). The actual figure would be very much higher because many such cases leave hospital as they want to die at home.

A case of failure in which signs of failure persists when the pulse has been brought down to 80-90 p. m. with digitalis has a bad outlook. Falling blood pressure in a hypertensive is also bad.

At the same time, it must also be realised that in many cases a lot can be done to check the downward progress, specially in the early stages.

Till recently, subacute bacterial endocarditis was regarded as almost uniformly fatal, but in the last 3 years many cases of recovery have been reported with the prolonged use of penicillin combined with heparin. In this series, both the cases were treated with 50,000 units penicillin every 3 hours for 24 days and good doses of heparin were simultaneously

given. Both became afebrile and symptomless but both died within six months—one with a relapse and the other due to hæmorrhage in the brain, probably due to the bursting of a mycotic aneurysm.

TREATMENT

Prevention is always better than cure and is practicable in many cases, provided the patient is intelligent and co-operative.

In many early rheumatic cases, it is possible to prevent recrudescence by removal of septic foci and the use of a small daily dose of sulphanlamides for prolonged periods, as has been reported by a number of American workers.

Arteriosclerosis is an irreversible process; but, provided the patient takes care to live well within the limits of his inefficient heart, he can have many years of useful life. Even cases of severe coronary thrombosis provided they survive the first six weeks or so, can live for years, if they are careful.

A great deal can be done for hypertensives by gradual weight-reduction, suitable diet and rest, and a judicious use of recent drugs like extract of serpentina. The recent operative treatment of lumbodorsal sympathicectomy appears promising.

Speaking in general terms, reduction of weight, proper diet, regulated bowels, good sleep, and proper apportioning of rest and exercise, and massage can prolong a useful life for many years, provided the patient agrees to live well within the limits of his damaged heart.

As regards actual treatment of failure, it is the same in most cases.

In addition to rest, suitable food, regular bowels, good sleep, regulated active and passive exercises, and massage, our sheet anchors are digitalis and the mercurial diuretics.

Venesection is a very valuable therapeutic measure in all cases of advanced back pressure.

In auricular fibrillation, I have tried crude cinchona (owing to non-availability of quinidine) in two suitable cases in which normal rhythm was restored.

In one case of persistent congestive failure following coronary thrombosis, methyl thiouracyl was tried for one month in an attempt to produce artificial myxœdema and thus give some relief to the heart. It failed to give any relief.

In two cases of subacute bacterial endocarditis as said above, 50,000 units penicillin every 3 hours for 28 days with heparin produced an apparent temporary cure. Fever disappeared, blood cultures became sterile, and the embolic phenomena stopped.

One relapsed after 3 months and died despite penicillin, and the other died of cerebral hæmorrhage.

In my experience, extract of serpentina has proved very beneficial in controlling hypertension, in addition to the general measures described above. I seldom give more than one five-grain tablet a day. In

hypertensive crisis, I have found intravenous combined with oral nicotinic acid of value.

In one case of proved syphilitic myocardial failure (history of syphilis, repeated abortions, positive W. R. and Kahn, and aortic regurgitation), the patient was saved from apparently certain death by the prolonged use of penicillin—30,000 units 3 hourly for 2 weeks—preceded by a course of pot. iodide in grains 10 c. d. s. for two weeks. His W. R. has now become negative and he has gone back to his sedentary job and has been symptomless for 15 months now, though the aortic diastolic murmur persists.

A case of patent ductus arteriosus was diagnosed and advised to undergo the operation of obliteration of the duct, as most of these cases develop subacute bacterial endocarditis later. He refused, but even if he had agreed, there is none available to undertake the operation in this country—so far as I know.

Most cases of heart-failure secondary to chronic bronchitis and emphysema present an almost hopeless proposition. They can be temporarily relieved by repeated venesection and the general cardiac treatment outlined above, but most of them relapse soon.

SUMMARY

An analysis of 122 consecutive cases of heart disease admitted in this hospital during 1945 has been done.

The various ætiological factors, the symptoms and signs, and their diagnosis, and treatment have been described. Some misconceptions have been clarified.

Recent advances in treatment have been mentioned.

(*Indian Journal of Medical Sciences September 1948.*)

"SPRUE" DIAGNOSIS AND TREATMENT.

By DR. K. NARAYANA MURTHY M. D.

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The Diagnosis of Sprue from its clinical standpoint should be based upon the following cardinal symptoms: (1) Morning diarrhoea with pale clay coloured foul smelling stool, the colour of the stool in the South Indian being often brown or greenish yellow due to less quantity of fat and the presence of leucobases, (2) Boggy and distended abdomen (3) glazed and ulcerated tongue (4) progressive emaciation with severe anaemia without temperature and (5) the disease being marked with remissions and exacerbations and (6) there is often the history that the patient was suffering from some form of chronic dysentery.

From the laboratory standpoint the following investigations are to be made to clinch the diagnosis. (1) X-ray examination after a barium meal. The test revealed positive evidences of the disease and greatly facilitated the diagnosis when other evidences were lacking. These observations were made first by Pillai and Murthi. (2) Agglutination test with the serum of the patient against Flexner group of organisms.

(3) Fractional test meal (4) Estimation of the total fat, neutral fat and fatty acids in stool. It is found that the fat content of the stool of patients suffering from other diseases and on milk diet was almost same as that of the stool in cases of sprue. Yet it is possible that this test may be of some prognostic value if we know the total intake of fat since the fat in the stool is found to decrease in proportion to the improvement of the case. (5) Bacteriological examination of stool. (6) A complete Cytological examination of the blood (7) The van den Bergh test (8) the inorganic and organic calcium content of the serum and (9) the blood cholesterol.

The above tests really will not be of much value from the standpoint of differential diagnosis from the following diseases: (1) H&H diarrhoea which is commonly met with in Ootacamund and Coonoor (2) Low morning country diarrhoea which we come across in the deltaic areas of Kistna and Godavari rivers (3) Chronic dysentery either amebic or bacillary dysentery (4) Chronic Pancreatitis or Gee's disease (5) Flagellate diarrhoeas (6) Famine diarrhoea (7) Nutritional diarrhoea in infants or adults (8) Coeliac disease (9) A diarrhoea common in Indian women during puerperium called "Sutika" and (10) a Diarrhoea in young adult Indian often associated with pernicious anæmic blood picture called "Asthenic" diarrhoea and (11) Tubercular enteritis (12) Stomatitis due to other causes (13) Mucus diarrhoea in infants (14) Setatoreaidiopathic (5) Pellagra.

The sign and symptoms of the above diseases and to differentiate them from sprue is not very difficult. But it is here that I would like to stress the importance of diagnosing conditions of sprue as a post dysenteric syndrome as I have discovered during my investigations that majority of cases of chronic dysentery pass on to the condition of sprue if improperly treated or inadequately treated. However it is very difficult to say in which of the chronic dysenteric cases symptoms of sprue are likely to develop. Possibly intestinal allergy may be the determining factor. A high eosinophilic count and a high urinary proteose are found in some of my cases of chronic dysentery which ultimately turned out to be real cases of sprue. Anyhow a high eosinophilia is a good prognostic sign in cases of sprue.

Treatment. From the knowledge of the course and general characteristics of the disease it is reasonable to expect that the treatment is often prolonged difficult and sometimes unsatisfactory. But I am sure a timely institution of appropriate measures is almost invariably followed by surprisingly good results. Therefore the success of the treatment depends upon (1) tackling the disease at an early stage (2) regulating the diet in accordance with the condition of each individual and (3) persistent treatment for some months after the last relapse and keeping the patient under observation. However skillful and intelligent the doctor may be, it is not often possible to get success unless we have the close co-operation of the patient. The treatment can be roughly classified

under the following 4 heads:—(1) general, (2) dietetic (3) medicinal which may be sub-divided into (a) drugs specific (b) local measures and (4) Symptomatic.

General:—In no other disease co-operation of the patient is so essential as in sprue. A slight indiscretion in food or drink may undo the good results achieved after months of treatment or it might flare up a quiescent or an unsuspected condition. Therefore it is always essential to explain to the patient the dreadfulness of the disease and the hope of getting over it if he simply carries the Doctor's instructions. Every patient with a certain amount of severity of the disease ought to be confined to bed and the diet is so arranged as to give rest to his digestive apparatus and to leave small residual products which as far as possible are not favourable to the growth of bacteria. Intelligent patients will often tell us which food suits them and which food disagrees with them and it is these patients that contribute a great lot towards our successful treatments. The doctor must prescribe diet in each individual according to the needs and requirements of the individual. Endless number of diets have been recommended for sprue. These diet-cures have come into existence because the disease has different manifestations in different countries though the original infection might have been caught in the Eastern Tropics. The disease is peculiar that it is found only in Eastern Tropics and nowhere else in the world. There are different stages in the course of the disease wherein a corresponding change in diet regime has always to be made and different people are accustomed to take different diets and the nutritive values of the same food are not constant. Thus the dietetic treatment has to be varied at times in the most essentials and its management ought to be made to cover the different conditions under which we come to tackle the case. Let me first mention about the milk diet. This is often most unsuitable to our Indian patients. There is so much of intolerance particularly in those individuals who are unaccustomed to take milk. In its place home made butter milk is found to be more congenial and well tolerated by the patients. However Manson Bhar and Low attach great importance to the milk diet. In all severe cases Sippy's diet ought to be the diet of choice. Milk can be given in the following forms:— (1) Diluted milk (2) alkalized milk and (3) citrated milk (4) barley water or rice boiled with water and milk added to it (5) peptonised milk (6) condensed milk (7) butter milk (8) humanized milk (9) whey (10) albumin water (11) Horlicks and other malted milk.

Fruit Diet. Vanden Berg claimed excellent results with fruit diet. Indigenous fruits such as sapotas, Pappayya, Bananas, Pomegranates, baelfruit form an excellent diet to the patient. Pine apples, Grapes and other acid containing fruits are not suitable to the patient. The fruit diet combined with milk diet may at times yield very satisfactory results. The good effect of the fruit diet is probably due to its vitamin content plus the caloric value of its fruit sugar.

Meat Diet. This is advocated by Cantlie. This suits majority of the non-Brahmin individuals. In severe cases it is my practice to put the patient first on milk diet and subsequently switch him on the meat diet. The carbohydrates are completely cut off and the diet ought to consist of proteins alone. Recently Sir Hamilton Fairly brought out a preparation of milk containing a greatest proportion of proteins with little amount of carbohydrate and fats which preparation he named it as "Sprulac". Another preparation is Eledon by Nestles Company who have marketted buttermilk in the powder form. These two preparations are found to be useful in the management of even very severe cases of sprue.

Medicinal: Calcium, parathyroid, Hydrochloric acid whenever it is found defective, charcoal powders. Tr. gentianco-adrenaline, bismuth and emetine in mixed types of dysentery all have to be thought of in treating the cases. The intestinal antiseptic, such as thymol, menthol, betanaphthol etc., are very harmful to the patients. The specific treatment consists in the administration of Crude Liver Extract, Nicotinic acid and riboflavin. Any reliable brand of liver extract such as Lilly's. Evans, T.C.F. Sionia is of value. Autolized vaccines prepared from monilia are of no value. In cases of severe anæmia we are to institute liver therapy.

Local measures to clear out focal sepsis must be adopted. Listerine, Glyco-thymoline can be used as mouth washes. A solution of optochin can be painted over the ulcer of the tongue, for pain due to deglutition 5 to 10 min. of adrenaline if swallowed before a meal is found to give relief. If the anus is ulcerated hazeline cream can be applied with benefit or any of those preparations of Recto-Serol, Anusol or adrenaline-chlorotone ointment.

The most distressing symptoms are acute diarrhoea, intestinal colic, meteorism, pancreatitis, hiccough, myalgia, insomnia, mental worry, helmenthiasis, severe anæmia, hæmorrhages and tetany though rarely dementia and dermatitis as in pellagra. Acute diarrhoea must be checked with starch and opium enema. For tympanitis cut down all carbohydrates give charcoal and turpentine stupes to the abdomen. Myalgia is relieved by massage to the wasted muscles and pilocarpine $\frac{1}{4}$ to $\frac{1}{8}$ th gr., can be injected if the symptoms are severe. Insomnia is best treated by morphia or pulvis doveris. Hiccough is controlled with liq. trinitrini and spt. chloroformi. Yellow santolin is used if there is ascariasis. Constipation is treated with Isaphfgul seeds which give a good mucoid material when they are soaked in water over night. These seeds are available in plenty in our Indian Bazars and they have to be used in preference to that of the paraffins. Mental worry is relieved by hospitalising the patients and allowing any sympathetic friends to attend on him. Anæmia is treated with liver extract. Vitamin B₂, Nicotinic acid and Rivoiflavin, Folic acid, Insulin and Glucose can be given to make the patient put on weight when all other measures fail.

The criteria of cure are the improvement in the weight of the patient with a general sense of well being, (2) well formed stools, (3) Ulceration of the tongue disappearing, (4) distention and discomfort not being present, and (5) anæmia rapidly improving to a certain stage. Vitamins in general do not seem to modify or cure the disease but really are of some value, as there is tendency for us to label sprue as one of the deficiency diseases—essentially anutritional disorder.

Prognosis is good in recent cases and in those that take early treatment. It is bad for patients over fifty, for long standing cases, for careless and injudicious patients and for those who cannot or will not take a special diet.

(Indian Medical Record, Sept. 1948).



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Extracts.

THE ANTI-AMEBIC DRUGS.

CLASSIFICATION.

Amebocidal drugs have been classified as follows.—

- (A). *The emetine group* :
 (1) Ipecacuanha (ipecac) ; (2) emetine hydrochloride ; (3) emetine-bismuthiodine.
- (B). *The oxyquinoline derivatives* :
 (1) Chiniofon ; (2) vioform ; (3) iodoquin ; (4) Diodoquin.
- (C). *The organic pentavalent arsenicals* :
 (1) Carbarsone ; (2) Treparsol ; (3) Acetarzone.
- (D). *Miscellaneous drugs* :
 (1) Succinylsulfathiazole ; (2) penicillin ; (3) trilactic ; (4) kurchi bark ; (5) bismuth subnitrate ; (6) Shadocol (sodium tetraiodo-phenolphthalien).

THE DRUGS.

1. *Ipecacuanha* : The efficacy is due to its two chief alkaloids, emetine and cephaline. This drug is not used now a days.

2. *Emetine* : It is used in the form of the hydrochloride. The dosage for adults consists of one grain subcutaneously, not to exceed twelve grains within a period of forty days. It should never be given to children under eight years of age and to those over this age the dose must never exceed one-third of a grain daily. The patient should be hospitalized and one grain of the drug is given subcutaneously daily for adults on successive days for a period of not exceeding eight to ten days, and the course should not be repeated within a shorter interval than one month.

Emetine relieves the acute symptoms in about 85 per cent of cases. Alone the drug does not result in the cure of amebic infections in more than 10 to 15 per cent of patients. It is effective in the treatment of liver abscess and amebic hepatitis and at present the only drug available. It should be reserved only for use in the control of acute symptoms of severe diarrhoea and dysentery. Emetine is more effective against motile forms than against the cysts. As a result of myotoxic action, emetine produces cardiac arrhythmias and can cause severe acute degenerative myocarditis which may result in sudden cardiac failure or death. The use of emetine is contraindicated in myocardial, kidney and liver damage. It is also definitely contraindicated in children under eight years of age and is best not used during pregnancy.

3. *Emetine Bismuth-Iodine* : This is the drug of choice in the treatment of amebic infections. It contains 20 per cent iodine, 12 per cent bismuth, and 58 per cent emetine. The adult dose is 0.2 gm. (3 gr.)

daily for twenty-one consecutive days. Rest in bed to prevent or lessen nausea and liability to cardiac failure is recommended.

4. *Chiniofon* (anayodin and yatren) : This compound contains 26 to 28 per cent iodine. It is prepared in keratin-coated or uncoated pills each containing 4 grains (0.25 gm.) Three to four pills (12 to 14 gr.) are given to an adult by mouth thrice daily for eight to ten days. For children one grain per ten pounds of bodyweight is given thrice daily for the same period of time. Following meals 12 to 16 gr. (three or four tablets) are given by mouth for seven days, if no endameba histolytica are found in the stools over a period up to six months, no further treatment is necessary. If the stools remain positive, the treatment is repeated following a rest period of at least seven days. No precautions are necessary regarding diet or exercise except in cases manifesting symptoms.

The drug is effective in about 90 per cent or more. It should not be used in the presence of iodine intolerance or liver damage and must be given with caution to patients with thyroid disease.

5. *Vioform* : It contains between 37.5 and 41.5 per cent iodine. It is prepared in the form of gelatin capsules each containing 4 gr. (0.25 gm.). The dose for adults is 4 gr. (one capsule) thrice daily for ten days. Twice this dose is recommended for severe infections. For children the dose is one-third grain per fifteen pounds of bodyweight thrice daily for ten days. The course may be repeated following a rest period of seven days. There is no interference with the patient's daily routine. The drug has an efficacy of about 80 per cent. It is more toxic than chiniofon but less toxic than carbarsone. Contraindications for its use are essentially the same as for chiniofon.

6. *Diodoquin* :—Its iodine content is 63.9 per cent. It is prepared in tablets containing 3-2 gr. (0.21 gm.). For adults the dose for the treatment of amebiasis is from 22.5 to 30 gr. (seven to ten tablets) daily for two to three weeks. The dose for children consists of one tablet daily per fifteen pounds of bodyweight. The tablets are given in divided doses following meals, and the course may be repeated after a rest period of seven to ten days. It is the least toxic of the amebocidal drugs. The drug destroys the cysts, and sterilizes the cyst-carriers.

7. *Carbarsone* : It contains 28.85 per cent arsenic. It is directly amebocidal. It is more effective than acetarzone and has a therapeutic index eight times higher. The action is on the cystic form. The drug does not act on ameba in abscesses of the liver and other organs. The adult dose is 0.25 gm. (4 gr.) taken orally twice daily for ten days. The course of treatment may be repeated in resistant cases after an interval of ten days. Carbarsone can also be given rectally as a retention enema, and is used in this manner for acute dysentery with motile ameba in the stool or dysentery cases that have proven refractory to the oral administration of the drug. It is employed daily for five days at least in

the form of retention enema containing 200 c. c. of a 2 per cent sodium bicarbonate solution containing 1 per cent carbarsone. A rapidly acting sedative as sodium amytal is given orally in a dosage of 0.2 gm. (8 gr.) in order to produce sleep, thus allowing the patient to retain the drug and if the enema is expelled it should be repeated until at least five enemata have been retained.

Carbarsone is absorbed readily after oral administration and is excreted rather slowly in the urine. Rest periods between courses are imperative to prevent cumulative toxic effects. Its use is contraindicated in the presence of liver and kidney disease. It is the best of all amebicidal drugs. It eliminates the infection in from 85 to 95 per cent of cases. Carbarsone treatment should be reserved for those infections which have proven incurable with iodine compounds.

8. *Treparsol*: It is an arsenobenzolic derivative of the salvarsan type and is supplied in the form of tablets containing 0.25 gm. (4 gr.) The recommended dose is 0.25 gm. (4 gr.) thrice daily with meals for four days; cessation of the treatment for ten days; and finally 0.25 gm. thrice daily for four days. The tablets should be chewed with the food as this causes greater dispersion of the arsenic.

9. *Acetarsons*: It contains from 27.1 to 27.4 per cent of arsenic. It is supplied in tablet form. Each tablet contains 0.25 gm. (4 gr.) This drug is very little used now a days.

OTHER DRUGS.

The bacterial flora of the intestines has some bearing on the virulence of amebic infection. A purely amebic infection is rare, for every infection is complicated by the presence of pathogenic bacteria which have penetrated into the tissues via lesions produced by the amebæ. Many of such cases complicated by secondary bacterial invasion do not respond favourably to specific anti-amebic therapy and tend to become chronic. By combating the bacterial infection present in the colon and following this with amebicidal therapy that many of the so-called 'resistant' or chronic forms of the infection can be treated successfully. Three or four such therapeutic agents are discussed below:

1. *Succinylsulfathiazole* (sulfasuxidine): The total dosage recommended is 80 gm. given in divided doses of 1 gm. every three to four hours. A standard course of antiamebic treatment is given after completion of the antibacterial therapy.

2. *Penicillin*: An initial injection of 100,000 units intramuscularly is followed by 88,000 units at three-hourly intervals with a total dosage of two million units.

3. *Trilactic* is anhydrous form of lactic acid which dissolves slowly in water, decreases the pH of the large intestine, and promotes the growth of acidophilic bacteria. For acute dysentery 40 to 50 gm. of trilactic are given daily in divided doses of four and given in pulverized rice or semi-fluid oatmeal for seven days and then gradually decreased after the acute stage has been arrested. For chronic amebiasis without

dysentery three to four tablespoonfuls daily divided into two doses, morning and at night are given. This is an entirely new form of anti-amebic therapy.

4. *Kurchi* bark: This drug has direct action on the amebæ. The standard fluid extract of kurchi bark contains about 0.032 gm. ($\frac{1}{2}$ gr.) of the alkaloids in 4 c.c. The dose of the extract is 8 c.c. thrice daily for as long as four to six weeks in chronic infections. The dose of kurchi-bismuth-iodide varies from 0.25 gm. (4 gr.) orally twice daily for ten days in chronic amebic infections to as much as 0.65 gm. (10 gr.) twice daily for ten days in severe amebic infections.

5. *Bismuth subnitrate*: A heaping teaspoonful, equivalent to about 180 gr. in weight, mechanically suspended in almost a tumbler full of plain, or better effervescent water, or in milk, is given every three hours day and night, lessening the amount only when improvement occurs.

Shadool (also called opacol and T.I.P.): is sodium tetraiodophenolphthalein. One half bottle of the dye is given to children under six years of age and all over this are given one full bottle of the dye. A saline cathartic is given the next morning. No special dietetic measures and no other medication is employed with the dye.

K. G. Nix; *New Orleans M. & Surg. J.*: 100: 108; 1947.

AMOEBC OR TROPICAL LIVER ABSCESS AND AMOEBC HEPATITIS

By T. J. AGARWAL M. S. (BOMBAY)

Amoebic abscess of the liver is a fairly common condition in this country. It is caused by infection with *Entamoeba histolytica*. The protozoan reaches the liver through the large bowels via the blood stream. The pathology is well known, but to recapitulate a few points will be quite in order. The infecting organism is a protozoal parasite of Rhizopoda type. It has two forms. The vegetative and the cystic. The vegetative is not the infective form for human beings, as it is destroyed by the acid gastric contents. The cystic form is the infective form and it is most resistant even under unfavourable environments. It is carried to the bowel either with food or drink contaminated with flies or through fingers of carriers. The cyst breaks its chitinous wall and vegetative forms are developed. It attacks the wall of the bowel and its preferential sites are right side of colon, but terminal ileum, sigmoid and rectum are quite often affected.

It multiplies in the wall of the intestine, and the toxins which it liberates, cause a coagulative necrosis of bowel wall in the submucous layer. This resembles toxic necrotic caseation of tubercular infection to a certain extent. This causes pressure necrosis of the mucosa and ulcers form in the wall of the large bowel. These ulcers may remain asymptomatic for a long time or even for all time. If the necrosis is quite massive, even perforation can occur in amoebic colitis, though it is not common.

The blood vessels in the area surrounding the ulcer get clotted due to the toxins. This clot in the vessels is infected with E.H. The proteolytic enzymes dissolve and break up this clot which is carried as an infected embolus through the portal circulation, and it gets lodged in the liver.

Here it will cause amoebic hepatitis. Amoebic hepatitis is almost as common as acute amoebic dysentery. In a doubtful case of dysentery tenderness of the liver and slight enlargement of liver is the surest way of diagnosing as the dysentery to be amoebic rather than otherwise. Other factors are now suitable in the form of massive infection, absence of any emetine treatment, lowered vitality of the patient, hypo-proteinemia etc, the amoebic hepatitis goes on to abscess formation. The process is much the same as in the bowel wall but on a much larger scale. There is massive coagulative necrosis of the liver tissue which liquifies due to the proteolytic enzymes, and it can reach very large proportions as can be seen clinically by the huge size of the liver, the relatively mild toxic and febrile reaction of the nonbacterially infected pus and the large quantity of pus found in these cases.

Clinical features. It is mainly for this that note is written. It was expected that practitioners in this country would be on look out for this trouble and not many cases would be allowed to reach the extensive stage, but the facts are otherwise.

Fever. This is the most important clinical feature. The pyrexia is very irregular. It can simulate any of the known pyrexial diseases like malaria, enteric, tuberculosis etc. By far the commonest type is intermittent fever, but remittent and continuous are also seen. The fever is accompanied with a rigor, not quite as severe as in malaria, or in urinary tract infection. It is most often mistaken for the all prevailing malaria, and it would be impossible to imagine a case without having some anti-malarial treatment before getting to be correctly diagnosed. Here I may digress a little in trying to justify Indian Physicians, for exhibiting anti-malarial treatment without demonstrating the parasites in blood film. We know that it is not scientific but it is practical and it works. The causes of this attitude are to be found in the small number of physicians for a vast country; lack of well equipped and trained pathologists, poverty of the masses, and extreme prevalence of malaria and that too of the malignant tertian type, which does not give a positive smear unless taken early in the course of infection.

Fever, when continuous in type is diagnosed 'Typhoid'. Here every fever which lasts more than three or four days is typhoid, be it malaria, dengue, amoebic hepatitis, poliomyelitis, syphilis and what not. In one of the cases the physician recognised the liver enlargement, but he was so 'obsessed with the diagnosis of typhoid. that he said that it was a liver complication of typhoid. On the other hand some cases may be absolutely afebrile.

Enlargement of liver. Next to fever this is the most common finding, and has to be looked for. It may be lobular, smooth, elastic, or even definitely cystic feel in neglected cases. The liver is always tender and may even be painful. Now there are numerous causes of large livers such as sub-acute hepatitis, malignancy, secondary, or primary heart failures (congestive type) hydatid cysts, nodular cirrhosis and other rare causes and they should always be considered and excluded. But a really large tender liver with temperature and leucocytosis is amoebic hepatitis in India till aspiration and a full course of emetine have proved otherwise.

History of Dysentery: This is a most tricky thing. Our physicians are terribly misled by this. From this point of view, it is hardly possible to find a man in India who has escaped some bowel disturbance (of infective origin) at some time of his life, and so an attempt to labour this point is futile. But this is emphasized in text books and when one thinks of amoebic, one thinks of dysentery first and liver long afterwards. But amoeba may invade the body without causing dysentery, not even diarrhoea or the slightest tenesmus. If we understand the pathology of this invasion, it is not surprising either most cases will admit having had dysentery at some time or the other, but almost none will come out with it. So also will, we suppose most cases suffering from any other ailment admit of having had dysentery.

No attempt was made to eliminate this point, and in no case were *Entamoeba histolytica* demonstrated in stools. But most cases had effective treatment with enterovioform and acetarsol to cure any quiescent amoebic infection, if still persisting in the bowels.

General condition of most of these cases is very unsatisfactory by the time they come under observation, due to the disease affecting the vital organs like liver, due to long illness, fever and due to the specific proteolytic action of the organism and last but not the least due to the starvation which was inflicted on these patients for the 'Typhoid cures'. One may almost say that they are living in spite of the doctors, who ignore all the modern literature about the value of high protein and high caloric diet in disease like typhoid.

There is anaemia, pallor almost a trace of jaundice which may be quite marked in some cases and toxic changes in kidney, heart muscles and spleen. Right lung needs particular emphasis. If the enlargement is upward particularly, to a certain extent generally the right base shows changes varying from a few crepitations to complete solidification. Screening will show the right diaphragm to be partially or completely fixed. Right pleural sac may have more fluid, serous if reactionary or purulent if the abscess has burst in the pleural cavity. One specimen in J. J. Hospital Museum shows it to have even burst in the pericardial sac. In two of my cases there was a bronchobiliary fistula without the pleural sac being infected or attacked, as shown by the large amount of anchovy sauce pus coughed up.

Laboratory data. Leucocytosis is the most important. The point is well emphasised in his book by Sir Leonard Rogers. It will diagnose the doubtful case. There is always a mild leucocytosis 10,000 to 12,000 and a slight rise in polymorphs. 70-per cent to 80 per cent. Thus there is both an absolute and relative rise in polymorphonuclear leucocytes.

This will differentiate subacute hepatitis, in which there is leucopenia and jaundice is more marked, and where there is diminution in

leucocytes, malaria and other conditions for which this disease is often mistaken in its early and quickly curable form.

Urine. Has only a negative value, but must always be examined to find out the state of kidneys.

Stool examination. We discussed this point under dysentery. It is always worth while. In most cases one could always demonstrate the vegetative form or cysts.

Examination of pus is regularly useful to exclude coccal infection. E. H. are almost never found in it, as they stay behind in the abscess wall to do more mischief.

Treatment. Emetine, 1 gr. daily if the patient will stand it or $\frac{1}{2}$ if his myocardium is very badly hit is started as soon as diagnosis is reasonably certain. (10-12. gr. in all).

Aspiration is delayed for 2 or 3 days if patient will and can wait. In doubtful cases aspiration may initiate the treatment. Care is to be taken in proper sterilisation, a wide bore needle of 3 size and a good apparatus. All the pockets should be properly emptied as far as possible as it is always a multi localised abscess scattered throughout the liver substance.

The site of the aspiration is to be judged in each case. It should allow of total evacuation of pus. After one or two aspiration, serous fluid will be aspirated.

Sulphadiazine has been given to almost all patients with various justifications: (a) long condition. (b). secondary infection (B. coli are present quite often they are revealed by smell) (c.) Bowel infection to clear the secondary germs.

Diet. A generous diet is at once ordered. Only the vegetarians have to be cautioned against too much ghee and oil as to them the generous diet always means more fats. Almost all things are allowed milk, fruit juices, bread, boiled fish, eggs, mutton, vegetables. No butter and as little ghee as will allow the man to eat his food.

Iron. Ferr. Syp. has been used as the drug of choice and most patients have needed it in full doses.

Amm. chloride, and urotropine as the time honoured drugs have now been discarded.

Enterovioform or acetarsol in 10 days course of either is given to eradicate any residual infection in bowels.

(The Medical Review of Reviews, Sept. 1948).

QUINIDINE

By L. N. KATZ

Quinidine prolongs the refractory period of the heart and the electrical systole of the ventricle. It prolongs conduction in the ventricles in the auriculoventricular junction and, to a certain extent in the auricles. It decreases the excitability of the myocardium and acts as a 'soothing agent' on ectopic pacemakers. It depresses the sinus node and tends thereby to slow the heart rate. It paralyzes the vagus nerve which tends to neutralize to a certain extent its direct effects. By slowing the heart it causes an increased amplitude of contraction. In large doses it

depresses the myocardium. In large doses by its direct action on musculature of blood vessels it causes a fall in blood pressure.

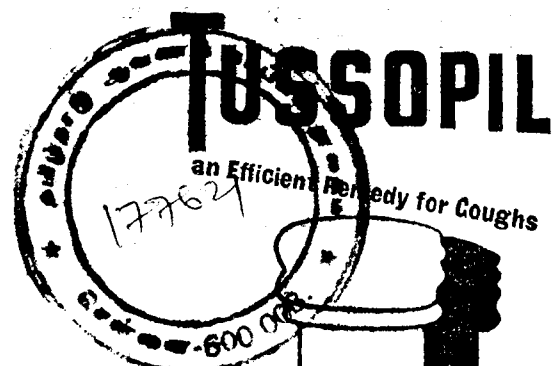
Quinidine is rapidly absorbed and excreted. With oral route, its maximum effect is obtained in 2-4 hours with intravenous or intramuscular administration, the effect is produced in $\frac{1}{2}$ —1 $\frac{1}{2}$ hours. With the oral route, minimal residual effects persist for 6-8 hours and the effect is completely gone and no further urinary excretion occurs in 12-24 hours.

Toxic Effects:—To test idiosyncrasy a dose of 0.2 gm. by mouth is given and the effects are noted after 2-3 hours. The toxic effects are tinnitus, vertigo, visual disturbances, nausea, vomiting, diarrhoea, headache, confusion, syncope, fever; skin rashes, petechiae and angio-neurotic edema. Serious effects are asthma, depression of breathing and even respiratory arrest. Ventricular fibrillation and embolism may occur during quinidine therapy.

Indications:—These are seven:—

1. In paroxysmal tachycardia of supraventricular origin.
2. In paroxysmal ventricular tachycardia, chaotic heart and in some cases of paroxysmal ventricular fibrillation.
3. As a prophylactic in the prevention of recurrent paroxysmal arrhythmias.
4. To suppress frequent premature systoles. In normal patients this should be employed when the premature systoles cause distressing symptoms. Quinidine may be used when digitalis causes premature systoles. It may be used prophylactically in cases of mitral stenosis with frequent auricular premature systoles in order to prevent or delay the onset of auricular fibrillation. The most important use of the drug is the suppression of ventricular premature systole in patients with coronary disease in acute infarction cases or in chronic cases. The drug will avoid the development of paroxysmal tachycardia and ventricular fibrillation. In the presence of ventricular premature systoles in coronary disease quinidine is one of the important and potent forms of therapy.
5. Recently it has been shown that quinidine in large dose will abolish in most cases, the mechanism of the Wolff-Parkinson-White syndrome. This is used only diagnostically.
6. Quinidine is useful in converting auricular fibrillation to a sinus rhythm. The drug is effective in about 50 per cent of all cases and of these about one half recur. Best cases are of paroxysmal auricular fibrillation and persistent auricular fibrillation cases with minimal of heart disease and of less than six months duration. Quinidine is also recommended in cases of longer standing auricular fibrillation with advanced heart disease accompanied by frequent emboli. Quinidine is to be used cautiously in these cases. It may be used after thyroidectomy to convert a persisting auricular fibrillation to sinus rhythm. It may be used cautiously in patients with recent myocardial infarction to convert recent auricular fibrillation to sinus rhythm.
7. Quinidine has been used to convert auricular flutter to sinus rhythm. It is less effective than in fibrillation.

Contra Indications:—Absolute contraindications is idiosyncrasy or sensitivity to the drug as shown by chinchonism or by respiratory or circulatory collapse. It is also contraindicated in acute infections and subacute bacterial endocarditis as it depresses the heart muscle. It is also



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contraindicated in cases of pronounced cardiac enlargement and heart disease of long standing. Heart block is also a relative contraindication unless frequent premature systole are also present.

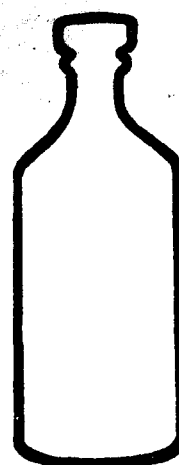
Methods of Administration:—Oral route is the best. In every instance a test dose of 0.2 gm. should be given and the reactions are watched. For therapeutic effect 0.4 gm. should be given every two hours until the arrhythmia is broken or until five doses have been given. This may be repeated for 2-3 days, the dose being increased each day by 0.2 gm. If toxicity symptoms appear the drug is stopped.

When the arrhythmia is broken 0.2 gm. of quinidine should be given three times a day for one week.

The drug is discontinued (i) when the rhythm has been returned to normal (ii) When a significant increase in heart rate occurs. (iii) When intraventricular block occurs.

Intramuscular therapy is indicated when more rapid action is needed, or when oral administration is not feasible. This is given under close observations in the hospital. Intravenous route is rarely necessary and is dangerous. 0.2-0.4 gm. of quinidine are dissolved in 10 c. c. of water and given very slowly. It is used only when ventricular tachycardia has precipitated pulmonary edema or severe congestive failure.

(Abstracted from the J.A.M.A.)
(April, 17-48, p. 1028-1031)



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HYPERTENSION AND ITS TREATMENT BY SURGERY*

DR. R. N. COOPER, M.S. (ENG.), F.R.C.S. (LOND.)

I accepted your invitation to deliver this Sir Nil Ratan Sircar Memorial lecture with the greatest pleasure because it gave me the opportunity, as an Indian, to pay homage to a great man and a great physician whose fame had spread into countries other than his own.

Besides there was a personal reason which prompted me to accept your invitation. Years ago this great and good doctor had given his services to my late father freely and liberally when he consulted him during his short sojourn in Calcutta. This lecture gives me the opportunity to express my sense of gratitude and my appreciation of his services to my father.

I have chosen "Hypertension and its Treatment by Surgery" for the purposes of this lecture for the simple reason that I feel that the benefits of surgery are withheld from patients because of insufficient knowledge of this subject in the profession.

My two visits to America with an interval of nine years between them, have given me the opportunity to study the problem in an unbiased manner, and to realise that surgical treatment of hypertension has now emerged from its early phase of trial and error and has now been placed on a rational basis ensuring freedom in every case with a surprisingly small mortality rate.

Cases of hypertension may be classified under any one or more of the following heads :—

(1) Renal—(Chronic nephritis, chronic pyelo-nephritis, chronic pyonephrosis).

(2) Cerebral—(Intracranial tumours).

(3) Cardio-Vascular—(Coarctation of the Aorta).

(4) Endocrine—Tumours of the Pituitary and adrenal glands).

(5) Essential Hypertension.

Many of these conditions are amenable to Surgery. Numerically the last group is the largest. It is not possible to go into the details of differential diagnosis within the space of this paper. Before arriving

*Sir Nil Ratan Sircar Memorial Oration delivered at the Calcutta Medical Club on 18th August, 1948.

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at the diagnosis of Essential Hypertension it is necessary to exclude the four other causes.

As regards the aetiology of Essential Hypertension only a conjecture can be made in the light of our present knowledge. However, a good deal is known about the natural history of the disease and patients are divided into four groups according to the heights of their blood pressure and the severity of the accompanying retinal changes. To appreciate and to understand the rationale of treatment it is but right to consider at some length our present concept about the Aetiology of the disease.

Goldblatt and his co-workers (1934-40) showed that persistent hypertension could be produced, in experimental animals, without impairment of renal function by employment of a silver constricting clamp on the main artery of both the kidneys or by constriction of the main artery of one kidney and excision of the other. Relief of constriction of the arteries results in a return of the blood-pressure to normal. After five years of hypertension, no significant disturbance of renal function was found. Autopsy did not show changes in any of the arteries except the retinal. The alteration in the blood supply of the kidney as the result of application of the constricting clamp produces some humoral substance which has a constricting effect on the peripheral arterioles. Obstruction to the peripheral circulation so produced results in hypertension. Under these experimental conditions a substance called Renin was isolated from extracts of the kidneys. Renin produces a prolonged rise in arterial tension without vaso-constriction. However when Renin circulates in blood it combines with an "activator" to form another substance called Angiotonin. This reaction is supposed to be of the nature of an enzyme. Angiotonin which has now been obtained in a crystalline form causes both a vaso constriction and a rise of blood pressure. Unlike adrenaline it does not cause a fall of cutaneous temperature. It is argued that renal ischaemia produces a Renin-like substance which by some enzyme action is converted into angiotonin. Page demonstrated the presence of a substance identical with angiotonin in the peripheral blood of hypertensives.

By ingenious methods Smith and his co-workers have established means of estimating the functions of glomeruli and tubules separately as also the rate of blood flow in cubic centimeters per minute. From these studies they have shown that in the horizontal position the normal human kidney functions at about fifty per cent of maximal capacity. Assumption of the erect posture brings down the blood flow to a significantly low level. This is due to a reflex constriction of the afferent renal arterioles. Smith and his associates, further found that in the hypertensives even in the horizontal position the blood flow is relatively less than in the normal human being. With the assumption of the erect posture the blood flow is further reduced. In this connection Ravich makes an interesting observation. He examined 200 pyelograms of patients with

hypertension. He was amazed at the regularity with which the pyelograms showed the existence of intra-renal pelvis. Almost all quadrupeds have an intra-renal pelvis. In man with the assumption of the erect posture the usual type of pelvis is the extra-renal pelvis. An intra-renal pelvis in man is ill adapted to the upright posture and leads to an overcrowding at the renal hilum. This interferes with renal circulation.

Smith and his associates also found that, in the hypertensives, the glomerular function is unimpaired in the early stages but the tubular function is adversely affected.

Experimentally, hypertension can be shown to have a neurogenic origin. Hypertension can be produced by injecting fluids under pressure in the cisterna magna or by perfusing brain stem with blood containing increased amounts of lactic acid or by injecting Kaolin intracerebrally. Stimulation of the paraventricular nuclei in the walls of the third ventricle results in a widespread discharge of activity along the sympathetic nervous system.

Immersion of the hand in ice-cold water for about thirty seconds causes a definite rise of blood pressure in the hypertensives. Employing this test in school children it was shown that some react strongly to this test. When the family history of these hyperreactors is traced it is found that either one or both the parents of these children have been hypertensives. Thus a hereditary factor is introduced.

It must be conceded that hypertension produced under experimental conditions differs from essential hypertension as observed in human beings. However the experimental evidence suggests certain possibilities in the probable aetiology of the disease. Piecing these disjointed facts it is possible to formulate a theory which can explain the genesis of hypertension.

Possibly due to congenital sensitivity of the autonomic nervous system, stimuli arising in the brain induce extensive vaso constrictor changes in the whole body. Such changes in the renal arterioles produce an ischaemia of the tissue giving rise to the formation of a pressor substance of the nature of renin. This substance circulating in blood is converted into Angiotonin by enzyme action. Of necessity such discharges of increased activity of the autonomic nervous system will be transient. Later probably some damage to the tubular function of the kidney keeps on producing a pressor substance continuously. This is converted into Angiotonin-like substance which maintains not only a heightened blood-pressure but also vasoconstriction and the heightened blood pressure becomes continuous. Persistent vasoconstriction leads to organic changes in the blood vessels and the obstruction to peripheral circulation becomes irreversible.

The physiological basis of surgical treatment of hypertension is very simple and consists in preventing the brain stimuli from reaching the vaso constrictor fibre of a fairly extensive part of the body. This can be achieved by doing an extensive sympathectomy which will block the

flow of constrictor impulses to the splanchnic area, the adrenals and the extremities.

To appreciate the rationale of surgical treatment a few points in the anatomy and physiology of the autonomic nervous system may be recapitulated.

The upper extremity gets its autonomic nerve supply from the 4th to the 8th thoracic spinal cord segments through preganglionic fibres which runs upwards in the sympathetic trunks. The lower extremity is supplied by preganglionic fibres which are derived from the Spinal cord segments from the 9th thoracic to the 2nd lumbar. These fibres run downwards in the sympathetic trunk. As regards the autonomic supply to the viscera it may be observed that the fifth to the ninth thoracic segments contribute fibres to the greater splanchnic nerve, the tenth and eleventh segments contribute fibres to the lesser splanchnic nerve and the twelfth segment contributes fibres to the last splanchnic nerve. It therefore follows that if both the upper and lower extremities and the abdominal viscera are to be denervated the preganglionic fibres from the fourth thoracic to the second lumbar should be sectioned.

One of the most important functions of the autonomic system is to supply vaso constrictor fibres to the limbs and the viscera. The total capacity of the vascular bed in the body is greater than the volume of the blood. Should the whole bed be dilated to its utmost capacity by cutting off all vasoconstrictor fibres, the total volume will be so trapped in the dilated mesh-work of arterioles and capillaries that efficient circulation would be impossible. Ordinarily to ensure proper circulation and adequate oxygenation, active vaso constriction must be in force over large areas all the time. The most common vaso constrictor stimulus is cold. Hence has arisen the Hines-Brown cold test to ascertain the degree of active constriction still available in the individual. The vasoconstrictor reactions are the most intense in the extremities. The arms and legs comprise 65 per cent of the body surface and by their efficient vaso constrictor response regulate in major part the elimination and storage of body heat. In hypertensive there is an increased vasoconstriction and the relief of this spasm by the section of the sympathetic fibres over a fairly large area of the body is the physiological basis of surgical treatment of hypertension. It naturally follows that such relief will be really effective in the early stages of this disease when hypertension is the result of active vasoconstriction in the peripheral arterioles and when organic changes have not yet occurred in the walls of these blood vessels.

It is therefore essential before embarking on the treatment of hypertension to know before hand the relative extent of muscle spasm and organic changes in the peripheral blood vessels. This can be ascertained by estimation of systolic and diastolic blood pressure under various conditions. If the vessel walls are still capable of responding to

vasoconstrictor impulses, the blood pressure will show definite fluctuations under various test conditions. Thus blood pressure in the lying posture will be lower than that in the erect posture. Application of the Hines-Brown test will show a slight rise of blood pressure. The blood pressure during sleep will be lower than in the waking state. The administration of Sodium Amytal and Sodium Nitrate will produce an appreciable drop in the blood pressure. Under these circumstances it will be found that the pulse pressure is never more than half the diastolic pressure so long as the blood vessels are actively influenced by vasoconstrictor impulses. Once organic changes in the walls of the arterioles set in, the blood pressure readings during the application of the above tests remain more or less steady and do not show these fluctuations. Besides the pulse pressure is more than half the diastolic pressure. The wider the pulse pressure the greater is the fibrosis of the arterial walls. Naturally sympathectomy therefore is likely to be successful from a therapeutic stand point when pulse pressure is less than half the diastolic pressure. From this point of view Smithwick has graded hypertensives into three Types. The width of pulse pressure in the resting horizontal posture is compared with half the diastolic pressure after two days of complete rest in bed.

Type 1 patient has a pulse pressure less than half the resting diastolic pressure.

Type 2 patient has a pulse pressure more than half the diastolic pressure but less than half the resting diastolic pressure plus nineteen m.m.

Type 3 patient has a pulse pressure which is more than half the diastolic pressure plus twenty m.m.

The results of sympathectomy are encouraging in Types 1 and 2 and discouraging in Type 3.

Sympathectomy can be either post ganglionic or preganglionic.

In post-ganglionic sympathectomy, the post-ganglionic fibres degenerate as the influence of the excitator cells is removed. Because of this degeneration of the post ganglionic fibres it is found that after a time the denervated limb becomes hypersensitive to adrenalin. Thus when the Stellate ganglion and the first thoracic ganglion are removed in the case of Raynaud's disease the sympathectomy performed is of the post ganglionic type. The vasodilatation resulting from this type of sympathectomy is very satisfactory for a short time. Very soon however the limb begins to be sensitive to adrenalin, and the good result obtained by sympathectomy is not sustained under certain conditions. Thus it is well known that under emotion of fright an extra amount of adrenaline is poured out into the system. This adrenaline produces an intense vasoconstriction in the denervated arteries of the limb, with the return of symptoms of Raynaud's disease. If the sympathectomy done is of the preganglionic type, the vaso constrictor impulses are effectively cut off

and yet the post ganglionic fibres do not degenerate. As the post ganglionic fibres remain intact the denervated vessels do not show any increased irritability to Adrenaline. Thus to obtain a permanent block to the transmission of vaso constrictor impulses, it is necessary to do a preganglionic sympathectomy. However when a preganglionic sympathectomy is done there is a definite risk of regeneration of the preganglionic fibres; and special precautions are necessary to prevent this occurrence by the employment of suitable technical modifications.

It is hardly worthwhile to discuss the symptoms of high blood pressure. The rate of progress of the disease may be rapid or fairly slow. However, there is a definite sequence of events as is to be expected from ætiological considerations already discussed. In the early stages there are transient rises in the diastolic and systolic blood pressures of the patient. These are the result of peripheral arterio spasms brought on by emotional or other environmental stimuli. Other than during these times the blood pressure remains normal. As the disease progresses, the diastolic pressure of a patient at rest begins to rise. It may be brought to normal levels by sedatives. The next phase of the disease is that in which the diastolic elevation remains fixed. The extent of the elevation of diastolic element of the blood pressure is caused by an increase in the total effective peripheral resistance. Realising that hypertension is two or three times as deadly as Cancer and that it attacks a comparatively young age-group it is essential that due attention be paid to its treatment. As the disease advances damage to renal function or heart musculature or the retina becomes manifest.

The eye-ground changes from a convenient basis for classification of Hypertension into four Groups:

In Group (i) there is arteriolar constriction only.

In Group (ii) there is tortuosity and nicking of veins at crossings.

In Group (iii) arteriolar changes are more marked with associated retinitis marked by the presence of hæmorrhage, or exudate or both.

In Group (iv) there is papilloedema with hæmorrhage and exudate. This group has been known as the Malignant Hypertension group.

In group (i) there are younger patients as a rule, with a predominance of females and a milder degree of hypertension as judged by blood pressure ranges.

This disease is generally progressive and a patient belonging to a given group at the time that he first comes under observation, does not necessarily stay in that group. Hence every patient suffering from hypertension should be overhauled from time to time. So long as he remains under Group (i) he does not need the help of Surgery. In fact he may remain all his life in group (i). The case history of such patient deludes many a patient and his medical adviser into believing in the efficacy of a particular dietetic regime or a therapeutic measure. Let not the case

histories of Group (i) cases cheat the patients in the other groups out of their chances of being benefitted from surgical measures. Excluding the hypertensives that belong to Group (i), medical treatment has little to offer except Faith, Hope and Charity!

As will be shown later surgical treatment can give relief of symptoms in almost every case, and a definite lowering of blood pressure and a prolongation of expectancy of life in appreciable number of cases. Even the retinal changes show a regression. According to Peet one in every five cases of even malignant hypertension can have life prolonged after operation. Naturally the prospects are brighter in the other groups.

However, surgery can be abused. A proper selection cases is a prerequisite for surgical success. Peet who submitted his first report of 850 cases in 1940 puts down the following conditions for a successful result:

- (1) The patient should be below fifty years of age.
- (2) The systolic pressure should be over 170 and the diastolic pressure should be below 105. This raised pressure should be continuous over a given period of time and not intermittent with periods of blood pressure coming within normal. In literature 150/100 has been considered the maximum normal.
- (3) The various tests already referred to should indicate that fibrosis of arterial wall has not occurred.
- (4) Renal function should be adequate as indicated by—
 - (a) an urea clearance of over 40 per cent;
 - (b) an ability to concentrate urine to a specific gravity of 1.020 at least;
 - (c) an excreting capacity exceeding 20 per cent of phenol-sulphonaphthalein, and
 - (d) a non-protein nitrogen estimate not exceeding 44 mgms per cent.
- (5) The heart should be relatively well compensated.
- (6) There should be relatively normal cerebral function.

Cases in Group (iv) often fall short of these conditions. But in such cases, with increasing experience a Surgeon can afford to take risks.

It is not possible to give an account of any operative technique in detail. Brief mention may be made of the types of sympathectomies now being done in America.

(1) Peet in 1938 did a one stage bilateral supradiaphragmatic resection of the greater and the lesser splanchnics and the 9th to the 12th dorsal ganglia.

(2) In 1935 Adson carried out a two stage bilateral subdiaphragmatic resection of the splanchnics and the 1st and 2nd lumbar ganglia.

(3) In 1938 Smithwick combined the Adson-Peet technique and removed all the splanchnics with the sympathetic chain from the 9th dorsal to the 2nd lumbar ganglia in two stages.

(4) Poppen modified this still further. From 1942 onwards he resects by a combined supra and infradiaphragmatic approach all the splanchnics with the ganglia from 4th thoracic to first or second lumbar ganglia. This is a bilateral operation and one side is done at a time. Now every one is agreed that the more extensive the resection the better is the ultimate result. The Poppen technique not only denervates the abdominal viscera but also both the extremities. Perhaps there is also a denervation of the adrenal glands. This probably inhibits the secretion of adrenaline and helps to bring about a good result.

The operation of extensive sympathectomy is done in two stages with the patient in the lateral posture. It is preferable to do the right side first; because when the second stage operation is done there is considerable circulatory collapse and any pressure on the heart would further embarrass the circulation. Blood transfusion at the time of the operation is a great help.

It is not possible to describe the operative technique in any detail. Only the salient points will be emphasised.

As regards anaesthesia some surgeons prefer a positive pressure anaesthesia to counteract any damage to the pleura. However Poppen prefers a high spinal anaesthesia with a sensory level at the third thoracic segment. This anaesthesia may be supplemented by Pentothal Sodium and curare to induce shallow respirations. The patient is placed in a lateral slightly prone position with pillows or inflatable rubber bags to support the spinal column in a more or less straight line and prevent any sagging of vertebral column.

The incision extends from the level of the sixth rib over the eminence of the paraspinal muscles to the eleventh rib and is then carried in a curved direction anteriorly to a point just below the border of the twelfth rib.

The iliocostal and longissimus dorsi muscles are separated over the 8th and the 11th ribs and about 4 cm. of these ribs are removed close to the vertebrae. The pleura is separated from the endothoracic fascia. The line of cleavage is indicated by a yellow line due to the presence of fat. Through these two windows it is possible to reach the ganglionic chain as high as the fourth thoracic and as low as the twelfth thoracic ganglia respectively. A third window is created below the twelfth rib to obtain access to the lumbar ganglia. The lumbar fascia is incised and the psoas identified. After cutting the fascia on the psoas the sympathetic chain comes into view.

Through these three windows the sympathetic chain is mobilized and the thoracic chain divided just above the fourth thoracic ganglion after severing the rami communicantes. Below the diaphragm the greater and the lesser splanchnics are severed at the point where they enter the coeliac ganglion and the last splanchnic nerve where it enters the aortico-renal ganglion. The sympathetic chain is sectioned below second lumbar ganglion. The lumbar ganglia have a definite influence on the

ejaculatory power in the male. However, there is a difference of opinion as to the relative importance of these ganglia in this respect. Some maintain that the first lumbar ganglion is all important and therefore many surgeons dissect the sympathetic chain down to the second ganglion on one side but not below the first ganglion on the second side. However Poppen removes the chain down to the second ganglion on either side. An analysis of his cases, shows that the power of ejaculation is not controlled predominantly by the first or the second lumbar ganglion. It is possible that in an erratic system like the sympathetic the power of ejaculation is in all the four lumbar ganglia. In one of Poppen's cases, after sympathectomy, erection, libido and potency improved and the patient became a father after ten years of married life. In an attempt to prevent regeneration of the preganglionic fibres tentalum clips may be placed on the chain above the third thoracic ganglion, below the second lumbar ganglion and at the site at which the splanchnics have been divided at the coeliac and aorto-renal ganglia. The chain so severed from its connections is now pulled out through the aperture at the eleventh rib.

To obtain a bloodless field of dissection coagulation of bleeding points with a diathermy machine is essential.

After a unilateral sympathectomy there is a dramatic fall in the blood pressure for three or four days. The patient is encouraged to get up on the fourth day after putting on a firm bandage on both the lower extremities and a corset on the abdomen. Assumption of the erect posture without these precautions would induce syncope in the patient as the blood pressure would drop to a dangerously low level. In about a week's time the blood pressure reaches the preoperative level. Now the sympathectomy may be repeated on the opposite side. After the second stage there is a dramatic fall of blood pressure for several days. The patient is encouraged to get out of bed with bandage and corset. After about the seventh day there is a rise in the blood pressure which may go up to the preoperative level except in the sitting and lying posture. However, in favourable cases blood pressure continues to fall over a period of several months.

Patient is discharged from hospital on the fifteenth day. He returns after a month for a check-up. The blood pressure is taken in the erect posture with the bandage on one leg taken off. If there is no appreciable drop in the blood pressure the bandage on that leg is left off. At the end of another month, the same test is repeated and the bandage on the second leg is left if the blood pressure does not drop. A month later the abdominal support is dropped if the test for blood pressure is satisfactory.

For a correct estimate of the benefits derived from this operation, a sufficient number of years must be allowed to elapse to prove that the operative survival curve is materially prolonged as compared with that of medically treated cases of Keith, Wagner and Barker. These authorities

showed that the mortality ratio in medically treated cases in four years, for the first group was 80 per cent; for the second group 42 per cent; for the third group 78 per cent and for the fourth group 98 per cent.

In literature a blood pressure of 150 systolic and 100 diastolic has been considered to be the maximal normal. But it is not enough to be able to reduce the blood pressure to this level by the operation. The patient should also be able to resume his work. At present therefore results are determined by (a) the lowering of blood pressure level, (b) the reversal of electrocardiographic changes, (c) diminution of the size of the heart as seen by X-rays, (d) improvement in retinal vessels, (e) the capacity to return to work.

Judged by these standards 100 consecutive selected cases showed an improvement in 71 per cent of operated cases in Poppen's series.

An extension of the operation already described for hypertension has been named a total or near total sympathectomy. The particular indication for this operation is the presence of severe cardiac pain along with hypertension. The heart is supplied with sensory nerve fibres through the upper four thoracic ganglia. In this operation the whole thoracic chain is removed in the first instance. The lumbar chain is removed on another occasion.

(Calcutta Medical Journal, September 1948.)

CIRCULATORY DYNAMIC IN CHOLERA THEIR MECHANISM AND PROGNOSTIC SIGNIFICANCE.

By A. ZAKI, M.D., AND M. M. RAGAB, M.D.

Tutors in the Medical Unit—Farouk 1st University.

INTRODUCTION.

Cholera as a Dehydrating Disease:—In cholera, the evacuation of profuse watery stools, and the vomiting of large quantities of fluid lead to a state of dehydration and collapse, which naturally vary with the severity and duration of the disease. Owing to this, several tissues shrink. This can be seen clinically and post mortem. Clinically, the dehydration manifests itself in the following:—

- 1—Skin is shrivelled with loss of elasticity.
- 2—Eyes become sunken, with low tension of the eyeball.
- 3—Tongue becomes dry—thirst is complained of.
- 4—General temperature is lowered and body becomes cold, livid, and moistened with clammy sweat, yet rectal temperature may be high.
- 5—Urine secretion is depressed.
- 6—Circulatory system suffers severely:
 - (a) Veins Collapse.
 - (b) Pulse becomes rapid, feeble, thready, and may become impalpable.
 - (c) Blood pressure is reduced; systolic pressure may register 50 mm. Hg. and may be unregistrable; diastolic pressure is variable.

Mechanism of Fatal Issue:—Death when it occurs, is usually accompanied by circulatory failure and collapse. Rogers (1) considers that the great problem in cholera is to restore and maintain the circulation, and that if this could be done, the "toxin" will be rapidly excreted through the kidneys, and recovery will take place. Although the element of toxæmia is debatable, yet the failure of circulation may be partly toxæmic. In a certain investigation published elsewhere (2), it is shown that choleric toxæmia as well as metabolic toxæmia, secondary to dehydration (azotæmia, acidosis etc.) play a part in the course of the disease.

PRESENT INVESTIGATION

The role of dehydration in the production of the circulatory manifestations in cholera as well as the mechanism of the various circulatory disturbances are the subject of the present study. This investigation also comprises the following items:—

1—The relation between the degree of circulatory failure and the degree of dehydration.

2—The role of the circulatory dynamics in relation to clinical manifestations, severity, progress, and final issue.

SCHEME OF WORK

1—**Clinical examination of the cases:**—General condition, skin, eyes, tongue, thirst, abdomen, and veins. These are noted on admission, after the administration of 6 litres of saline solution given in approximately 12 hours, and later after giving 16 litres of saline and 5 per cent glucose at a rate of 1 litre every 2 to 4 hours, depending upon the severity of the case. The dose is repeated after the patient becomes normal.

2—**Circulatory studies:**—(a) pulse rate and character. (b) Blood pressure and pulse pressure. (c) Venous pressure: The zeropoint is taken as 5 cm. below the level of the sternum at the costochondral junction. (d) Circulation time: 10 cc. of calcium gluconate are given.

The results of the circulation time were not recorded for some of the bad cases because these patients were unable to appreciate the heat sensation produced by the calcium injection.

INTERPRETATION OF RESULTS

Venous pressure:—It can be seen from Tables II and III that the grading of cases of cholera, according to the general condition and dehydration, corresponds to the circulatory studies. Thus, the venous pressure is not extremely lowered in moderate cases (grade I). In grade II, it is usually above 5 cm. of water and is within the range of 8 cm. of water, while in grade III it is either not measurable or, at most 2 cm. of water. Those cases in which it could not be measured were usually fatal.

Blood Pressure:—The blood pressure readings correspond to the same grading. Systolic pressure is above 110 mm. Hg. in grade I, between 70 and 100 mm. Hg. in grade II cases and below 70 mm. Hg. in grade III cases. If it is 50 mm. Hg. or below, the case is usually fatal. There were, however, 5 cases in which although neither the

systolic nor the diastolic pressures could be measured on admission, yet the response to treatment was good. Similarly the diastolic pressure indicates the severity and fatal issue of the case. Thus a diastolic pressure above 65 mm. Hg. is usually met with in grade I; above 80 mm. Hg. in grade II cases, while in grade III case, it is lower than 80 mm. Hg. and is frequently unregistrable. Some cases whose diastolic pressure was raised recovered. The mechanism of this rise is discussed later.

Pulse:—Pulse determinations yielded results which gave the same indications as stated under blood pressure. Thus a pulse rate below 100 per minute was found in grade I, about 100 to 110, in grade II, while a pulse rate of 120 or more was met with in grade III cases. The pulse was even imperceptible in some cases.

Circulation time:—Figures ranging between 12" and 22" were recorded for cases of grades I and II, while in normal subjects the circulation time was found to be between 15 and 18 seconds. This circulation time became shorter after treatment by 2" — 5". This absence of prolongation of circulation time in the presence of the above findings circulatory failure shows that this procedure cannot be used in gauging the severity or progress of the condition.

The above findings show that there is definite relation between the circulatory changes and the degree of dehydration. The quick restoration of the former by correcting the latter, even when this done quickly shows that dehydration rather than toxæmia is the most important factor underlying these circulatory dynamics.

DISCUSSION.

The role of dehydration in the production of circulatory failure:—Severe and sufficiently protracted loss of the gastric and intestinal contents leads to shock. The picture is identical with that of traumatic shock, but the evidence of dehydration in the skin, mucous membranes, and eyeballs are usually more markedly pronounced in the cholera patient. Dehydration in cholera does not only lead to loss of water, but also to loss of salts—the former was shown to be more pronounced than the latter. In severe cases, the blood volume is markedly diminished. Moreover it is so highly concentrated, as shown in another publication that the resistance to the flow resulting from its increased viscosity is a probable accessory factor in diminishing the venous return to the heart, i.e., oligæmia plus highly concentrated blood will act together in diminishing the venous return to the heart. This produces diminished cardiac output and peripheral circulatory failure. This fact is supported by the quick and splendid results met with after intravenous infusion of large volumes of saline solutions. The best examples of this are seen in grade III cases, in which at the start, the venous pressure and blood pressure were so low that they were unregistrable. Yet after the introduction of 6 liters of saline solution intravenously, normal levels were nearly reached in some cases.

Mechanism of low Venous Pressure in Cholera:—It is an old clinical observation that the veins are collapsed in cholera cases, but no measurements of the venous pressure and circulation time were recorded in such cases. The measurements obtained in this work are correlated firstly with the degree of dehydration, and, secondly, with the other circulatory findings, e.g., blood pressure and pulse rate. Diminution in venous pressure is met with in peripheral circulatory failure, and is, perhaps, the most characteristic feature of this condition; readings may be as low as 1—2 cm. of water. This decrease of venous pressure demonstrates that circulatory failure is peripheral and not central, and that its level runs parallel to the degree of failure. The work dealing with the mechanism leading to low venous pressure in cholera, shows that dehydration and subsequent oligæmia together with increased viscosity are the main factors. In health, however, when the circulating blood volume, and, consequently, the venous pressure are changed, a number of compensatory mechanisms will oppose this tendency. To produce a raise in venous pressure, however, the infusion should be rapid, and, even then, this is temporary. The removal of a comparatively large volume of blood affects the venous pressure when the circulatory mechanisms are healthy. The main mechanism which acts in health is transudation of fluid from the blood stream into the tissues or *vice versa*; this cannot occur in cholera, owing to tissue dessication which should be corrected first before any restoration of venous pressure is expected. Moreover, in health, the tone of the veins will vary in order to allow the veins to adapt themselves to blood volume to maintain the venous pressure. The veins constrict during pressor reflexes. This mechanism may occur in mild cases in which the peripheral failure is compensated for by vasospasm as shown by occasional occurrence of high diastolic pressure. On the other hand, the peripheral vasoconstriction may lead to diminished entry of blood into the veins and tend to lower the venous pressure. In all forms of peripheral circulatory failure there deficient venous return to the heart. Since the heart functions only as a force pump, it cannot compensate for the defects in the peripheral mechanism which results from a deficient venous return. This produces a diminished cardiac output. However, an attempt at compensation is made by peripheral vasoconstriction and acceleration of the pulse rate. This can only occur in mild or moderate cases where the integrity of these mechanisms is not severely depressed. Peripheral compensation can also be achieved through acceleration of the velocity of blood flow. Estimations of circulation time in our cases do not suggest this mechanism in cholera, possibly because it is counterbalanced by the marked hæmoconcentration in this disease tending to prolong it. Moreover, the decreased muscle tone of these patients diminishes the effect of this factor in helping the venous return.

Effect of Saline Solution on Venous Pressure:—It has been stated that transfusion in a healthy circulatory system is soon counteracted by a

number of compensatory mechanisms which allow the circulating blood volume and the venous pressure to become normal shortly after the transfusion. Contrary to their findings in health, Caughey and Richards found that, in patients with heart failure, the slow administration of salt solution produces a pronounced elevation of venous pressure. In addition, venesection produces a marked drop both in the circulating blood volume and venous pressure. On the other hand, in peripheral circulatory failure, a large transfusion may be followed by a marked rise in venous pressure which is not usually the case in the absence of circulatory failure. In such patients, a transfusion of 600 cc. of saline resulted in a rise of venous pressure from so low a pressure that it could not be measured by the direct method to 6.5 cm.

Findings in Cholera cases:—In all grades of cases, the transfusion of 6 litres of saline within 12 hours caused a marked rise in the venous pressure to about normal. After another administration of 10 litres, the additional rise was slight, showing that the first transfusion had raised the venous pressure to a level very near to the normal for this particular patient.

Prognostic Significance of Venous Pressure in Cholera Cases:

In all cases, the venous pressure is lowered because of the above described mechanism, which leads to oligæmia, hæmoconcentration, vasoconstriction and absence of muscle tone, and immobility. The degree of lowering of the venous pressure runs exactly parallel to the clinical condition of grade III cases. The venous pressure could not be measured in the first 8 cases, and these died shortly afterwards. In the remaining 6 cases, venous pressure ranged between 1—2 cm. of water. One of these 6 cases (case No. 4) died on the 6th day from anuria, although the venous pressure rose after treatment from 1.5 to 4 cm. There were 12 cases of grade II; in 10, the venous pressure ranged between 3 and 4 cm. One of these (case No. 20) died on the second day from anuria, but it should be noticed that his case was the only one in which the venous pressure readings were not raised after treatment. The remaining 2 cases of this grade (cases No. 2 and 14) had a venous pressure of 1.5 and 2 cm. respectively; they improved, however, and the venous pressure rose after treatment. Eight cases of grade I had a venous pressure ranging between 4 and 9 cm. Anuria did not develop in any of the cases and the venous pressure rose after the administration of 6 litres of saline solution.

Significance of Blood Pressure Determination:—The primary cause of the symptoms in peripheral failure is the diminished blood flow through the various organs which result from the diminished cardiac output and the failure of the compensatory mechanism. Due to this decreased cardiac output, the blood pressure is lowered.

Both systolic and diastolic values are affected more or less proportionately; with very low systolic blood pressure, it is often impossible to obtain even a rough estimate of the diastolic pressure. In

general, the height of the blood pressure is proportional to the general condition of the patient. However, there are cases with pallid, cold skin pale, cold extremities, low venous pressure etc., in whom the arterial tension is maintained for hours or days at the normal level or even a higher one. This is apparently due to the constriction of the arterioles in the extremities and elsewhere. There is hypersecretion of adrenaline which also plays a part in producing this vasoconstriction. Thus, in such cases, when the diminished cardiac output tends to lower the blood pressure this tendency is, to a certain extent, counteracted by the peripheral vasoconstriction. Sooner or later, however, this diminution in cardiac output gains the upper hand and the arterial blood pressure drops, though not to such a low level as would result, had no constriction of the peripheral vessels occurred. Finally, deficient blood flow, through the vasomotor centre causes relaxation of the arterioles and blood pressure falls to mortal levels.

Findings of blood pressure in cholera cases:

Grade III cases:—In 4 cases of this group neither the systolic nor the diastolic pressure could be measured, (cases 4, 7, 8, and 9). They all improved, but case 4 died on the 6th day from anuria. Cases 1, 2, and 3 had a systolic pressure of 50, 50 and 40 and a diastolic pressure of 20, 30 and 20 respectively. They all died shortly after admission. Cases 5 and 6 had a systolic pressure of 75 and 65 and a diastolic pressure of 50 and 30 respectively; they all recovered.

Grade II case:—Case 21 who had an initial blood pressure zero recovered after treatment. The fall of systolic blood pressure was moderate in cases 10, 14, 16, 18, and 19. In the remaining 6 cases of this group, the systolic blood pressure was markedly lowered, ranging between 60 and 70 mm. Hg. In cases 10 and 14, the diastolic pressure was slightly higher before treatment than after improvement; venous pressure in these cases was 3 and 5 cm. respectively. In cases 16, 18, and 19 the fall was slight. In the remaining cases the fall in the diastolic pressure was marked. All of these cases recovered.

Grade I cases:—In all the cases the fall in the systolic pressure was slight. In cases 24 and 28 the diastolic pressure was not changed. In cases 23 and 25, 27 and 29, the fall in the diastolic pressure was 5 and 13 mm. of Hg. In cases 22 and 26 the diastolic pressure was higher before than after treatment; the corresponding venous pressures of these 2 cases were 7.5 and 4 respectively.

Thus it can be stated that although the fall in the blood pressure corresponds more or less to the severity of the case, yet, in some cases, this does not prove useful as a prognostic gauge; the venous pressure is a more accurate criterion.

Significance of the Pulse Rate:—In peripheral failure, the pulse is usually rapid. The heart rate may reach 140 beats per minute. The factors influencing the heart rate in peripheral failure are;

1—The reflex initiated by the low blood pressure, causing acceleration.

2—The reflex from the low venous pressure, causing bradycardia (Bainbridge reflex).

3—Finally, there is bradycardia, probably, due to anoxæmia of the pacemaker.

Case findings in Cholera:

Grade III cases:—Pulse was imperceptible in 5 out of 9 cases. In 3 cases it was above 120. In 1 case it was 100 and very weak (case 5). It was imperceptible when the blood pressure was not measurable. The lower the blood pressure the faster was the rate and *vice versa*; (e. g. case 5, with a rate of 100 per minute, had the highest blood pressure of 75 over 50 mm.).

Grade II cases:—Pulse imperceptible in 1 case. 3 cases had a pulse of 90, 1 case, 95, 3 cases 100, 2 cases 110, 1 case 115, and 1 case, 140. The only patient who died in this group was case 20 (from anuria on the second day). His pulse rate was 110.

The pulse rate does not seem to bear a definite relation to the level of blood pressure or venous pressure. This is due to overlapping of the above mentioned factors.

Grade I cases:—The pulse rate was usually below 100 Judging from the rate after the treatment, the pulse was not extremely changed. No cases died.

Peripheral failure and Anuria:—In peripheral circulatory failure the urine volume is diminished may be to 300 cc. per 24 hours; or complete anuria may occur at the beginning. Urine is free from albumin and is of a high specific gravity (1030). This is due to the impaired blood flow to the kidneys, which results from:

1. Diminished blood volume.
2. Arteriolar vasoconstriction in the peripheral organs. This affects the kidneys.

Both these factors cause decrease in the venous pressure as well as in the urinary volume.

Findings in Cholera Cases:

Grade III cases:—Six patients were completely anuric on admission; of these, 3 died shortly afterwards and 3 improved. 3 other patients had a urine volume of 100 cc. per 24 hours; of these, 2 survived and 1 died on the 6th day from anuria (after initial improvement).

Grade II cases:—2 cases were completely anuric on admission and both recovered. 3 cases passed 100 cc of urine in the first 24 hours; of these 1 died from anuria on the second day. The rest of the cases passed from 200-300 cc. of urine per 24 hours and recovered.

Grade I cases:—One case passed 100 cc of urine per 24 hours; the rest passed more than 100 cc.

Thus the occurrence of anuria is related to the severity of dehydration and the level of the venous pressure.

CIRCULATION TIME IN CHOLERA

Grade III cases:—The circulation time could not be measured in grade III cases because the patients were not in a condition to perceive the heat sensation produced by the calcium injection.

Grade II cases:—The circulation time ranged between 12 and 22 seconds. After treatment it dropped by 3 to 4 seconds.

Grade I cases:—It ranged between 15 and 22 seconds; the diminution after treatment was 2 to 5 seconds.

Although these figures show that the circulation time may be prolonged in cholera, yet this prolongation is slight and bears no relation to the severity of the condition nor to the degree of reduction in the venous pressure and the blood volume. Therefore, it neither measures the degree of circulatory failure nor the progress of the case.

CONCLUSIONS.

(1) The disturbed circulatory dynamics in cholera are mainly the manifestation of peripheral failure. The latter is due mostly to dehydration with its consequence of hæmoconcentration and oligæmia.

(2) The venous pressure was lowered in all cases; the degree of lowering was proportionate to the severity of the case. It has a definite prognostic value, and can be utilised as an objective measure for the severity of the clinical manifestations of dehydration. Accordingly its quick correction should be the aim in the treatment of cholera. The mechanisms of this decreased venous pressure in cholera were considered to be:—

- 1—The oligæmia.
- 2—The hæmoconcentration and increased viscosity.
- 3—The compensatory vasoconstriction.
- 4—The diminished muscle tone.

(3) The B.P. is lowered, both systolic and diastolic, and bears some relation to the clinical severity, although to a lesser degree than the venous pressure. It is mainly due to the oligæmia, diminished venous return to the heart, and subsequent diminished cardiac output. The higher the diastolic pressure the better the prognosis; it indicates some degree of compensatory vasoconstriction.

(4) The circulation time was only slightly prolonged and proved of no value in this direction.

(5) The pulse rate, although accelerated in all cases, bears no relation to the B.P. and venous pressure changes; accordingly it is not a dependable prognostic sign.

Extracts.

SNORING

ROBIN (*Proc. Roy Soc. Med.*, 41:151, 1941, Ref. *Practitioner*, 160:496, 1948) writes that snoring "is a symptom of unbalanced breathing, caused by a combination of several physical conditions". Organic causes of snoring are (1) nasal obstruction, and (2) pathological changes in the pharynx. Snoring may also be due to functional dysfunctions of the central reflex governing the tone of the glosso pharyngeal musculature. The basic cause of snoring is, of course, mouth-breathing. There are three main groups of snorers—the child, the adult and the elderly person. In the majority of children cure can be obtained by removal of adenoids and tonsils; the failures include persistent mouth-breathers and children with infective or allergic rhinosinusitis. When snoring starts in an adult it is usually due to some organic cause. The third group, elderly men and women, is the largest and the fundamental casual factor seems to be lack of tone. Treatment is classified under three headings:—(1) Irrational methods, chief among which is amputation of the uvula. This rarely gives relief, but may modify the degree

and pitch of the snore. (2) Rational methods: (a) The removal of prevention of nasal obstruction so as to obviate mouth-breathing. In some cases the application of decongestive nasal drops before retiring produces a peaceful night; in others nasal operation may be necessary; in some benadryl therapy is beneficial. (b) Change of position of the head to prevent the tongue from falling back. In many persons snoring occurs only when they lie on their backs, and this can be prevented by sewing a cotton reel into the back of the pyjamas or nightdress. (c) Alteration of the position tongue, soft palate and jaws, by breathing, swallowing, and phonetic exercises, by the wearing of orthodontic splints. (d) Keeping the mouth closed during sleep, by wearing an "Andresen" splint, or by placing a strip of adhesive plaster across the corner of the mouth. (e) Altering the texture of the soft palate and faucial pillars, by injection of a sclerosing solution into the pillars. This method, advocated by Jerome Strauss, has so far failed to produce a high percentage of cures. In conclusion, the author states that many a potential snorer may have been prevented by the removal of tonsils and adenoids.

A METHOD FOR PROLONGING THE ACTION OF PENICILLIN

CARLINFANTI AND MORRA (*Schwetz. med. Wechnschr.* 77:1286, 1947, Ref. *Practitioner* 160:75, 1948) describe a simple method for prolonging the action of penicillin and maintaining a satisfactory concentration in the blood, which is stated to produce results equal to those obtained by injections of oily solutions. The penicillin is injected by subcutaneous route into the thigh or arm after the circulation of the injection area has been retarded by the application of a rubber tourniquet, using a pressure slightly less than the minimal arterial pressure. The tourniquet must not be left in place for more than one to five hours, according to the amount of penicillin injected, i.e., 10,000 to 100,000 units. Using this method the number of injections can be reduced to three of 75,000 units in twenty-four hours, or five of 100,000 units in forty-eight hours, or the quantity of penicillin injected may be reduced to 80,000 units, giving eight injections of 10,000 units in twenty-four hours. It is probable that with doses of 800,000 to 800,000 units that a single injection might suffice to maintain a satisfactory penicillin concentration in the blood for twenty-four hours. In illustrative graphs it has been shown that after injection of 16,000 units the blood concentration level was maintained for four hours, the tourniquet being removed $1\frac{1}{2}$ hours after injection; after injection of 75,000 units it was maintained for $8\frac{1}{2}$ hours, the tourniquet being removed after $5\frac{1}{2}$ hours, and after injection of 100,000, the level was maintained for $8\frac{1}{2}$ hours, these levels being in comparison with $2\frac{1}{2}$, $4\frac{1}{2}$ and 6 hours blood level concentration when no tourniquet was used. The pressure exerted by the tourniquet must be regulated by the absence of

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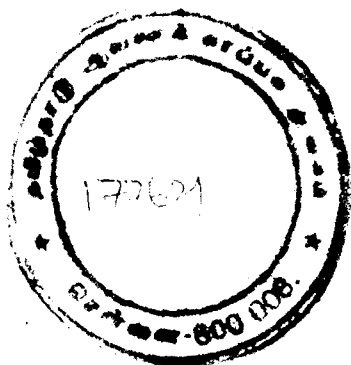
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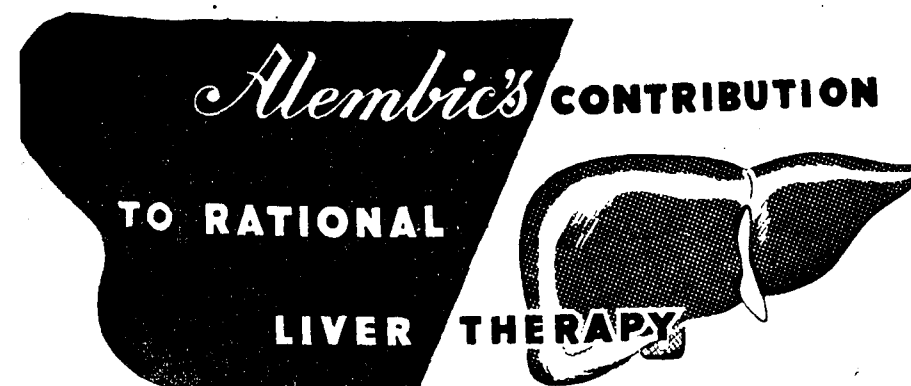
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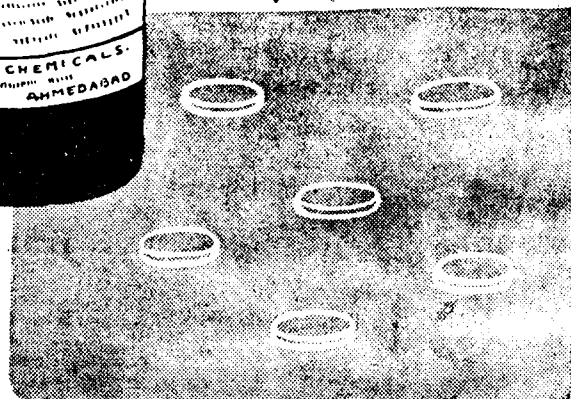
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