of these stones the calcium-phosphate imbalance is even more important than the vitamin A deficiency (Ranganathan, 1931). We find that the incidence of such stones can be very greatly reduced in rats by adding to the vitamin-A-poor and lime-rich diet an amount of sodium phosphate sufficient to form, with the excess of lime, insoluble calcium phosphate in the bowel. The further addition of vitamin A completely prevents the disease. I may therefore claim with some reason that the problem of "cattle stone" in India has been solved so far as the laboratory can solve it.

FUNCTION OF VITAMIN A IN THE PREVENTION OF STONE

In my last lecture I referred at some length to the effects of vitamin A deficient diets on epithelial structures throughout the body. No tissue suffers more severely from want of this vitamin than that of the urinary tract. It seems to me very probable that desquamated, keratinized epithelium from this tract may form the nidus round which calculus deposition occurs. It is true that in rats infection, as a rule, rapidly supervenes; and this, no doubt, may be in part responsible for the chemical composition of one variety of rat stone—the ammonium-magnesium-phosphate variety. But although naked-eye evidence of infection is the rule, exceptions occur in which this variety of stone is found without any obvious cystitis. Further, cystitis is no less common in rats suffering from calcium carbonate stones, and in these ammonium-magnesium-phosphate is conspicuous by its absence.

In my experiments I have found that the volume of urine excreted depends to a great extent on the presence or absence of vitamin A bearing ingredients in the diet; when absent or small in amount the volume of urine is low; when present in sufficient quantity it is normal or high. Sodium phosphate has also a very marked effect in this regard, greatly increasing the urinary excretion. It is significant that associated with the addition of vitamin A bearing substances (whole milk, cod-liver oil, or radiostoleum) to stone-producing diets, and of these substances and sodium phosphates to such diets containing an excess of lime, the urinary excretion from being scanty becomes copious, and at the same time stone is prevented.

There is, of course, another direction in which vitamin A acts in the prevention, and its deficiency in the causation, of stone. I refer to its power to prevent infection of the urinary tract, and to the influence of its deficiency in favouring such infection. This brings me to the last of the influences which may determine the occurrence and distribution of stone in India—infection.

INFECTIOUS INFLUENCES

The work of Rosenow and his colleagues of the Mayo Foundation is no doubt familiar: his experimental production of gall-stones in animals by infection with streptococci from cases of cholecystitis in man; and, more recently, his production of urinary calculi by the devitalization and infection of teeth in dogs with streptococci from cases of nephrolithiasis. Rosenow's procedure is, first, to produce "septic foci," using, for the disease he wants to produce, streptococci obtained from a case of the particular disease in man. He finds the coccus to be specific: that from cholecystitis will produce gall-stones; that from nephrolithiasis, urinary calculus. This sequence of events is probably the same in essentials as that occurring in rats: in these, foci of devitalization are produced in the urinary tract by the defective diet, and, in some forms of stone at least, chance infection may do the rest. But the point of special interest to India in Rosenow's work is that a specific kind of infection may, as he and Meisser suggest, be associated with stone, and

thus account for the prevalence of the disease in certain localities. Personally, I am quite prepared to believe that this may, to a limited extent, be so; for although I have shown that the distribution of stone in India may, in some part, be accounted for by the kind of cereal used by people whose diets contain an insufficiency of vitamin A bearing ingredients, this is not the whole story, nor does it explain the occurrence of stone in all localities in India or in all individuals. Bilharzia, though a frequent cause of stone in Egypt, does not appear to be so in India; and in infection by bilharzia malnutrition is a potent favouring influence.

MECHANISM OF STONE PRODUCTION

This lecture has dealt with the causation of stone, not with the mechanism of calculus deposition. My researches have been mainly of the practical kind: my business being to tell the people of India how they can themselves avoid stone and prevent it in their cattle. It matters little to them, though it is of great interest to the medical scientist, whether the deposition of stone can be most satisfactorily accounted for by faulty metabolism due to dietetic causes, by infection, or by physico-chemical disturbances in the urinary tract. I have little doubt that both faulty food and infection may induce the physico-chemical disturbances responsible for stone deposition; but I know that a properly constituted diet will go a long way to prevent both infection and physico-chemical disturbances. It seems to me that all three agents—dietetic, infectious, and physico-chemical—play their part in the genesis of stone, and in designing its architecture; on occasion, and in certain individuals or in certain places, the star part may be taken by one or by the other. In India the star part is taken by diet.

The President and Council of the College have signally honoured me by their invitation to tell something of my research activities in India, and I have been deeply conscious of the responsibility this honour has imposed upon me. I have purposely chosen to refer only to those of my activities which I have thought might be of special interest to surgeons. Even with this limitation much has had to be omitted or passed by with but a few words. But if what I have said may serve to indicate directions in which the newer knowledge of nutrition touches upon the Art of Surgery—to indicate lines of investigation which hold out the prospect of the solution of certain surgical problems—then I shall have fulfilled, in some small measure, the duty imposed upon me by the invitation to address this great College.

A CASE OF TABOPARESIS TREATED BY HYPERPYREXIA INDUCED BY HOT BATHS

BY

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AND

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The treatment of general paralysis by hyperpyrexia has now become recognized as the most beneficial form of therapy for this disease which is known to us. Of the methods of inducing hyperpyrexia, the introduction of malaria parasites into the patient's blood has so far been found the most reliable and the most effective. This is no new observation, for Sir J. Purves-Stewart quotes a dissertation by Foster, written so long ago as 1848, on the beneficial effects of malaria on insanity.¹ The first systematic use of this treatment in general

paralysis was introduced by Wagner-Jauregg in Vienna in the year 1917.² Since then the method has been used with considerable success all over the world. In spite of this success the effects of malaria are less reliable than might be desired. Some patients do not contract the malaria at all, in spite of transmission of plasmodia to their blood, while in other cases the malarial infection fails to persist sufficiently to give the twelve attacks of fever which are regarded as the desirable course of treatment. On the other hand, troublesome relapses of the malaria are found to occur, and a certain number of fatal results from cardiac failure have been recorded. Other chemical (for example, sodium nucleinate) or toxic (for example, tuberculin) methods of producing hyperpyrexia have not proved any more reliable, and have hardly stood the test of time.

GENERAL PRINCIPLES

While on a visit to San Francisco one of us had the good fortune to see the work of Drs. H. G. Mehrtens and P. S. Pouppirt on the treatment of various nervous affections by hot baths. This work has since been published,³ but hardly does justice to what seemed remarkably striking results in the cases of general paralysis treated. A certain amount of doubt still seems to persist as to whether the results of malarial treatment are due to some specific effect of the plasmodium or its toxins on the progress of general paralysis, or simply to the hyperpyrexia induced. If it can be shown that treatment by hot baths is successful, then this would seem to afford definite proof that the hyperpyrexia is the beneficial agency. Further, there can be no doubt that this purely physical measure, if successful, has undoubted advantages over any other pyretic form of treatment. It does not involve the introduction of foreign toxins; the pyrexia can be accurately and exactly controlled, both as to extent and as to duration; and, provided that certain technical details are observed, the treatment is simple, easily applied, and safe.

The chief danger of this treatment is not so much hyperpyrexia as dehydration; for, as will be seen from the details of this case (confirmed by experiments on normal subjects under the same conditions), there is a very considerable loss of weight during the bath, due to secretion of sweat, which is quickly made up after the bath. This was born out by certain observations of Mehrtens. He found that this hyperpyrexial treatment relieved the gastric crises of tabes, though it did nothing to cure the tabes—a fact which we have confirmed in one case treated by this method. When the vomiting from the crises has been prolonged and severe, the patient is already severely dehydrated, and unless he is given plenty of fluid (preferably by rectum) before he is put into the bath he is apt to undergo the most alarming collapse. In all cases treated by this method, therefore, it is wise to provide means whereby fluid can be at once introduced into the system either by the rectum or subcutaneously. Care should be taken at the commencement of the treatment to determine the reaction of the individual patient to the hot bath, as it sometimes happens that his temperature may continue to rise one to one and a half degrees after he has left the bath; and if his temperature is already 106° F., as frequently happens, this may be undesirable.

We made use of a large reclining bath as described below, and the patient's temperature was recorded by a special self-recording electric thermometer prepared for us by the Cambridge Scientific Instrument Company. This instrument is of great delicacy and accuracy, and enabled us to know exactly what was happening in an initial experiment, and to give a graphic record of the pyrexia induced. We do not consider that such an instru-

ment is essential for carrying out the treatment, so long as care is taken to establish the patient's reactions, since it is expensive and has the disadvantage that short-circuiting is very apt to occur in the lead between the rectal thermometer and the recording apparatus.

CASE HISTORY

History of Present Illness.—Male, aged 35. In September, 1927, there was "apparent blood poisoning, believed to be due to eating pork. After attending various doctors, who said that he was suffering from digestive trouble and nervous dyspepsia, he showed no sign of improvement. Gradually fits of shaking commenced, which he could not control, and he had a feeling of numbness in his left leg." In 1928 the patient became irritable and depressed, and felt "as if his nerves were in great torment." He became impulsive and seemed to be losing his self-control. Then his memory began to fail. He forgot almost everything he was told and could not remember where he had put things. His work "seemed to be sapping every bit of his mind and strength." Sometimes he would be holding a cup or a glass and would seem to forget that he was doing so until he dropped it, and then the smashing of the glass would pull him together. This happened frequently. Since 1928 he has occasionally had "slight rheumatic pains and numbness in his knees and legs"; but he will not admit to any shooting or stabbing pains. About this time co-ordination became noticeably affected. He began to have difficulty in walking steadily. The numbness of the left leg increased, and his wife noticed that "he was throwing his legs out in a peculiar way when walking." On several occasions "his legs seemed to give out and throw him down on the ground." These tumbling-down episodes became more frequent, being especially marked in the dark or when he tried to turn quickly. In June, 1929, he had an attack of influenza. After this his general shakiness was greatly increased. His speech now showed a marked defect, and was hesitating. He would begin talking at his ordinary speed, then suddenly stop as if he could not get the use of his tongue, and then start off again very rapidly. When reading aloud to his wife he would mix up his sentences and run his words into one another so badly that she could not understand what he said. He began to be morose and unsocial, and shunned the company of other people.

In November, 1929, the patient removed to a house with a back entrance, as he had found that the neighbours in his old district were remarking on his speech and gait. His condition gradually became worse. He had to give up playing cards, one of his favourite recreations, as he could not remember which cards had been played. He became more and more irritable, and this mood alternated with fits of profound depression. He found increasing difficulty with his work in the designing department of a tweed factory; and when he came home at night he would spend the whole evening sitting by the fire without speaking to anyone. He became suspicious of his wife and easily upset by his only child (a girl aged 4 years). Formerly, he was passionately attached to this child, but now he began to be annoyed with everything she said or did. On one occasion he knocked her down a flight of three steps. One day towards the end of December, 1929, the patient's wife was calling on a neighbour and left the child in her husband's care. He became annoyed with something, left the child alone in a room with a fire, and went away, after locking all the doors in the house. When his wife returned she found the child screaming with fear, as she had never been left alone before. Two hours later the patient returned, having suddenly realized that the child was in danger from the fire. When he got into the house he collapsed completely, and for two days was continually shaking and weeping. In January and February, 1930, there was a continued deterioration in the patient's condition. When he spent money he could not remember what he had spent it on. He was becoming markedly emotional. If walking at night he had to be supported by his wife, and fell down frequently. He complained continually about his food, and his wife found that "he could digest

only invalid's diet." He was sleeping very badly. Inco-ordination was affecting him generally, and in kissing his child he would kiss her chest or her shoulder in an attempt to reach her face. Much against his inclination, the patient's wife persuaded him to see another doctor, and he was brought to see us on March 10th, 1930.

History of Past Illnesses.—Apart from the common maladies of childhood, and from several attacks of influenza, the patient did not admit to any previous illness. He would make no admission to syphilitic infection. He said that he was gassed in France in 1916, and at that time had a skin rash, which was treated by inunction with a blue ointment. Pressed further for an admission of the date of a primary syphilitic infection, he still strongly denied it. But when we offered him a loop-hole he accepted it readily, and said, "Of course I might easily have got it through using other men's towels."

Examination.—On March 10th, 1930, the main feature was a marked general coarse tremor of arms, hands, head, etc. He seemed to be alert, but in answer to questions betrayed marked lack of confidence in himself. He tended to be voluble, and it was difficult to keep his attention fixed on any one subject. His memory for dates and events, even of recent occurrence, was definitely poor. He had a greatly exaggerated opinion of his own importance and of the value he was to his employers; but he had none of the exaltation and delusions of the fully developed general paralytic. Speech was grossly hesitant, and he had a marked stammer. The slurring and clipping of syllables and fusing of words made it difficult to follow much of his conversation. Writing was jerky and of poor quality. The letters were pointed, unevenly spaced, and irregularly formed. There was a coarse tremor of the hands and arms; but, by concentrating his attention on this, the patient was able to control it to a great extent. It was most marked on movement. Tremor of the lips was pronounced, particularly when he was speaking, and there was constant tremor of the tongue. His gait was very unsteady. The feet were thrown out and brought down hard, and he walked on a broad base. Romberg's sign was present, and when turning sharply the patient had to be firmly supported to prevent a fall. The arm movements were unsteady, and the finger-nose test was poorly performed. Sense of position was also impaired. With the legs crossed the patient could not tell which leg, or which part of the leg, was touched, though he could feel the actual touch perfectly well. There did not appear to be any actual loss of power either in arms or in legs. There were no areas of hyperaesthesia. Sensibility to touch, pain, and temperature was unimpaired. Sensibility to vibration was below normal limits, though not entirely absent. The patient has had a slight strabismus for many years. There was neither diplopia nor nystagmus. The pupils were of medium size. The left was slightly larger than the right, and was not quite regular in outline. Reaction to accommodation and light was normal, and there were no pathological changes in the optic fundi. The knee-jerks and ankle-jerks were absent, and other tendon reflexes were normal. Skin reflexes were unchanged, and the plantar responses were flexor.

A blood Wassermann reaction taken on March 25th, 1930, was strongly positive. On April 6th a lumbar puncture was performed. The cerebro-spinal fluid was under considerably increased pressure, but it was quite clear. The following report was received:

Foam test ...	...	...	Positive.
Globulin test ...	...	...	Positive.
Protein ...	...	...	0.10 per cent.
Cells ...	...	...	15 per c.mm.
Colloidal gold test...	...	...	0000114433.
Complement-fixation test...	...	...	Strongly positive.

It was then decided to adopt the experimental hot bath treatment in this case as the symptoms of general paralysis were not yet in an advanced stage. On April 25th, 1930, an injection of sodium nucleinate was given, and a leucocyte response was shown as follows: before injection, 6,600 per c.mm.; after injection, 9,100 per c.mm. This is a wise precaution before beginning hyperpyrexial treatment, since it demonstrates the patient's capacity for reaction.

TREATMENT

On April 29th, 1930, the following procedure was adopted. The patient was weighed (stripped), and after five minutes' rest on a couch the mouth temperature, pulse rate, and respiration rate were recorded. A sensitive recording galvanometer of the moving-coil type (thread recorder; Cambridge Scientific Instrument Company) was used to make a continuous graphic record of the rectal temperature. This apparatus was placed in the dressing-room leading off the patient's bathroom. We could thus watch for any sudden rise or fall in the patient's body temperature, and at the same time observe his general condition as he lay in the bath.

The metal thermometer, containing a delicate thermopile, was inserted into the patient's rectum while he was resting on the couch. As soon as the temperature was recording steadily he entered the bath. This was an ordinary reclining bath, and it was filled to the brim with water at a temperature varying in different experiments from 106° to 110°. A waterproof canvas cover was stretched across the bath and tightly bound down, there being a slot for the patient's neck, so that only his head was out of the water. Heat loss from evaporation was thus cut down to a minimum; and an attendant, watching a thermometer in the bath, kept the temperature even by the addition of a little hot water as required. Five minutes after the patient had entered the bath the mouth temperature, pulse rate, and respiration rate were recorded. These readings were repeated five minutes before the patient left the water. The duration of each treatment varied from forty to fifty-three minutes, the majority being about fifty-two or fifty-three minutes. The patient was then wrapped in blankets and made to rest on a couch for one and a half to two hours. The mouth temperature, pulse rate, and respiration rate were recorded twenty minutes after he left the bath; and the rectal temperature was recorded until the patient was ready to dress. He was then weighed again and the loss of weight noted. A specimen record shows a typical reaction.

During the several series of treatments, various forms of trouble were experienced with the delicate recording galvanometer, and a number of the baths were given without the use of this apparatus. On these occasions the mouth temperature, pulse rate, and respiration rate were recorded every ten minutes. In the earlier experiments we started with a high temperature (110° to 108°) and gradually lowered it when the patient showed signs of distress. But later we found that it was more satisfactory to start with a temperature of 106° to 107°, and to retain that level throughout the experiment. By this method we were able to reach and maintain a body temperature equivalent to that of the bath, thus producing a more sustained hyperpyrexia. Pulse rate usually reached a level of 120 to 140, respirations 50 to 65, and body temperature 105° to 107° (frequently 106°).

The patient invariably manifested some degree of distress during the last fifteen to twenty minutes of each session. Breathing became very rapid and shallow, and occasionally there was marked cyanosis. He sometimes complained of singing noises in his ears, of fullness in his head, and frequently of headache. On three occasions he became light-headed, but only twice was it considered necessary to finish the treatment before the expiry of fifty minutes. We found that fifty-three minutes was as

long a period as the patient could reasonably be asked to remain in the water. On almost every occasion distress was marked not later than forty-five minutes after the commencement. The average loss of weight during each bath amounted to $4\frac{1}{2}$ to $5\frac{1}{2}$ lb., the minimum being 3 lb. and the maximum 6 lb. 10 oz. By the next morning this loss had sometimes been more than made up. During the nine months of treatment the patient showed a net gain of 47 oz. (9 st. 11 lb. 13 oz. to 10 st. 12 oz.), and at one time he actually reached 10 st. 7 lb. 1 oz. The treatment did not hinder him from going to his work. He left work at 4 p.m. and started his bath at 4.45 p.m. Then he left for home at 7.30 p.m. (by which time he had cooled down to 100° to 101°), had his supper, and went to bed; by next morning he was fit to resume work.

The results of this experimental treatment have been most striking. Until July there was no definite change in the patient's condition, though there did not seem to be any progression of the disease. The course of eight baths in July, however, produced a very marked improvement. This was noticed particularly by the patient's wife, who said that he was no longer depressed, and only occasionally irritable. His speech was clearer, and his gait was slightly more steady. He was eating much better, and his insomnia had gone. The blood Wassermann reaction at the end of July remained strongly positive. Baths were started again in October, and twelve were given by the middle of November. Steady progress, both mental and physical, was shown. The patient's employers remarked on the improvement in his work, and he felt that he was much less easily tired. We noticed a distinct betterment in co-ordinated movements, and he could get into and out of his bath unaided. Up till that time he had to be assisted on both sides, especially when getting out of the bath.

On November 21st a complete examination of the cerebro-spinal fluid (which was still under fairly high pressure, but not so great as in April) was again made, with the following results:

Clear, colourless, no clot	
Foam test	Positive.
Globulin test	Positive.
Protein	0.09 per cent.
Sugar	0.07 per cent.
Cells	12 per c.mm.
Colloidal gold test...	0000421100.
Complement-fixation test...	Strongly positive.

Towards the end of January, 1931, we decided to give the patient another series of baths. This series was more prolonged than any of the previous ones, and sixteen baths were given by February 23rd—a total of forty-one. The result of this final series was exceedingly satisfactory. The patient is now a different man, both mentally and physically. In a letter which we recently received from his wife (an intelligent woman) she says:

"At the present time he has double the energy. He rarely gets depressed, never irritable, and he is mentally much sharper. Previously he was irritable beyond all words, and if things did not go just as he wanted he was beyond endurance. He walks faster and stronger, his speech is much clearer, and his writing is greatly improved. He can now digest almost anything, and he sleeps generally from 10 p.m. till 6 or 7 a.m. without waking."

In conversation with us, she said that all their friends were remarking on the recovery of her husband's memory. He enjoyed playing cards again, and could do so in an intelligent way. He was a different man to live with, and was like the husband of three or four years ago. In walking in the dark she gave him no assistance, but he never fell.

Our examination at the end of February showed that he was alert and much more confident in himself. He still tended to be rather voluble, though much less so than a year ago; and he could now concentrate on the point under discussion. There was a very marked

improvement in his memory. Speech was definitely better. It was sometimes slightly hesitant, but the slurring had gone. Writing was more even. The tremor of hands, arms, and lips was completely absent. There was still some tremor of the tongue, though it had greatly decreased. Gait was much steadier. He continued to walk on a broad base, though he did not throw his feet out so far. Romberg's sign was indefinite. When turning sharply there was some unsteadiness, but he could turn quickly without support and did not fall. Condition of arm movements was now good, and his sense of position was more accurate. There were no definite changes in the reflexes.

On April 6th, 1931, lumbar puncture was again performed. The cerebro-spinal fluid was still under pressure. A complete examination showed:

Foam test	Positive.
Globulin test	Positive.
Protein	0.06 per cent.
Sugar	0.08 per cent.
Cells	50 per c.mm.
Gold curve... ..	4444332000.
Complement-fixation test...	Strongly positive.

We have asked the patient's wife to send us a monthly report of her husband's condition. Meanwhile all treatment has been suspended.

COMMENTARY

It is to be noted that only the last gold curve is a true paretic curve. All other symptoms are suggestive of taboparesis. It will be admitted that the symptoms of this patient have improved very materially. His reflexes and Wassermann reaction are so far unaltered. The cerebro-spinal fluid shows signs of approaching a more typical paretic type, though the protein is definitely less and there is a slight diminution in the intensity of the Wassermann reaction. It should be clearly understood that we do not wish to draw any conclusions from this one case, but he has had no antisiphilic or other sort of treatment than the hot baths. We hope that others who have more clinical material with which to work than ourselves may be induced to try this treatment and prove or disprove its utility. If it should prove successful, we believe it has much to commend it when compared with other methods of inducing hyperpyrexia.

We are indebted to the Bath Spa Committee and to Mr. John Hatton for the facilities allowed us in the bathing establishment, and to the attendants for the assistance given us in carrying out this experiment.

REFERENCES

- ¹ Purves-Stewart, Sir J.: *Medical Annual*, 1928.
- ² Wagner-Jauregg: *Wien. med. Woch.*, 1921, lxxi, 1105.
- ³ Mehrtens and Pouppirt: *Arch. of Neur. and Psych.*, 1929, xxii, 700.

INDICATIONS FOR THE INDUCTION OF PREMATURE LABOUR*

BY

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Under this title I want to include the indications for the induction of therapeutic abortion as well as the induction of premature labour; for in a large number of cases we may be faced with the problem of whether to evacuate the uterus in the early stages of pregnancy or to allow it to proceed, and, later, to induce premature labour.

NEPHRITIS

The commonest case brought to us for this reason is the chronic nephritic. In these cases one has to consider three things: first, the number of pregnancies; secondly, the term of pregnancy at which signs or symptoms of

* Read before the Bath and Bristol Branch on March 25th, 1931.