Second movement: Relax, so that the lumbar curve is restored by elastic recoil.

Faults.—At first patients usually lift the lumbar spine instead of the coccyx. When they have stretched it correctly they are apt to revert to spasm of the erector spinae, instead of mere recoil by relaxation.

6. Back Flattening against a Wall.

Position: Standing with feet four inches from the wall (nearer makes the exercise too difficult); thighs sloping backward till buttocks rest against the wall; trunk relaxed.

First movement: Slowly uncoil back from below upwards so that the spinous processes rest evenly against the wall.

Second movement: Increase the pressure of the lumbar spine against the wall by contracting the abdominal muscles.

Third movement: When the lumbar and thoracic spines are flat against the wall try to flatten out the cervical spine against it while pushing the occiput upwards on the wall. It is, of course, impossible for a normal individual to touch the wall with the whole spine at once; indeed, the cervical stretching should not be attempted until the lumbar region is mobile. This is an excellent exercise for mobilizing a rigid spine without violence.

When the patient is an adept at the above exercise he should first be taught to *stand correctly* by getting the back stretched against the wall as in Exercise 6, and then gently raising him forward to the upright position, while he keeps the back flat and the abdomen retracted. These weakly individuals cannot maintain the position long at first, and should not be asked to do so.

The next stage is to *walk* with the body balanced correctly, and at first it is difficult to teach them not to try to hold up the ribs by hunching up the shoulders, but to push the chest up from below by contraction of the abdominal muscles. The arms must be made to swing freely and loosely from the shoulders.

Finally, some *rapid exercise* should be given to induce deep respiration, such as skipping, but it is harmful to give this until the fundamentals of balance are acquired correctly, and even then it should be stopped short of fatigue. Indeed, with children, once correct control of the body has been acquired, their spontaneous play will provide enough forms of rapid exercise.

Supports.

For elderly people whose muscles are too atrophied to allow of more than a moderate recovery of tone it may be desirable to order some form of external support. These patients are very likely to show signs of strain in the sacro-iliac and lumbo-sacral joints, often associated with arthritis, but their symptoms are readily relieved by a support which corrects the lordosis and supports the pendulous abdomen.

To achieve this any support must bridge completely across the lumbar hollow—a requirement that is more often forgotten than remembered by belt-makers. In women, if they are not too heavy, a well fitting corset may suffice. Dr. Goldthwait has a useful method of reinforcing the corset in its pull round the pelvic bones by attaching 6-inch webbing to the side seams to form an outer belt, which fastens in front by small straps and buckles. Another useful device of his is to apply inside the back of the corset a leather shield carrying two upright steels of only moderate spring, so that the corset continually pulls the patient back against these, thus reducing the lumbar curve. For men a leather support with similar steels is useful; it should support the lower ribs at the back, but not reach above the umbilicus in front, so that respiration is free. Supports of this type do not interfere with development of the trunk muscles, while they prevent overstrain of the weak muscles when fatigue sets in, for in adults the amount of rest that should be practicable for children is rarely obtainable.

NOTE BY DR. GOLDTHWAIT,

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A paper such as Dr. Forrester-Brown has presented is worthy of much greater consideration than is commonly given to scientific communications, since the principles underlying it are fundamental, dealing with structure or the anatomy, and function or the physiology, the two great basic subjects of medical education. That all persons are not made alike is obvious to all who really observe the human species, and that these variations, because of their varying activities, must be associated with variations in

physiology should hardly require argument. A racehorse must have a different physiology from the Shire or Clydesdale, and the same should be expected of the different types in the human family. The more our patients are studied from this point of view the more easily are the conditions understood.

The way the body is used is naturally important if the world's standards of high efficiency are to be obtained. The drooped relaxed figure is less good from every point of view than the erect alert figure, and with recent studies the practical appreciation of this fact (this was shown most strikingly by the war experience) has found scientific confirmation.

Suggestions such as Dr. Forrester-Brown has made are not only of value from the point of view of general health, but of the greatest value in understanding and controlling the chronic patients as they present themselves for treatment. It is with these that the results of the two features mentioned by Dr. Forrester-Brown—that is, structure and peculiarity of use—are most easily seen, and once such appreciation is had, relief is hopefully to be expected.

After thirty-five years of practice dealing almost wholly with the chronic patient, the belief has become increasingly more certain that, until these features are recognized, the chronic patients will continue to represent the great reproach to our profession that they are to-day.

THE SYMMETRICAL UREA COMPOUNDS AS CHEMOTHERAPEUTIC AGENTS.

BY

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It has been my aim for some years past to find a drug or drugs suitable for use in the acute stage of disease. The first preparations introduced were colloid manganese hydroxide (1917) and manganese butyrate (1920), the latter being still the best preparation in use for furunculosis. But, to combat widespread infections caused by the staphylococcus and other Gram-positive and Gram-negative micro-organisms, it has been necessary to search for compounds capable of conducting more electricity to the host's protective substance (protein particles in the plasma) than can manganese butyrate. I should, perhaps, mention here that, according to my view of morbid processes, disease occurs when the protein particles in the plasma generally, and those constituting the protoplasm of the leucocytes locally, have to part with some of their electrons at the bidding of an invader, be it a micro-organism or a chemical intoxicant.¹ In the search for more efficient conductors two paths lay open: (1) the preparation of an organic compound of manganese possessing a vehicle with a larger nucleus than butyric acid; (2) the preparation of an organic compound made up of an enormous vehicle and depending for the conductor action upon the liberation therefrom of one or more positively charged sodium or hydrogen atoms. Search along the first path proved fruitless, but along the second path fruitful. With the assistance of Dr. F. H. Fairbrother of the British Dyestuffs Corporation, and Dr. J. Thomas of the Scottish Dyes, Ltd., the chemotherapeutic armamentarium has been enriched by four compounds, whose uses form the substance of this article.²

SUP. 36.

"Sup. 36" is the symmetrical urea of para-benzoyl-para-amino-benzoyl-1-amino-8-naphthol-3-6-sodium sulphonate.

The action of this compound depends, I believe, upon the liberation of positively charged and conductor functioning

sodium atoms from the 6-positions. The drug can be injected intravenously or intramuscularly in 0.005 to 0.02 gram doses. In the former method the solution must be freshly prepared, but stock solutions will do for the latter, provided the powder has been dissolved in doubly distilled water. Never more than three injections are

In cases of pneumonia, pulmonary thrombosis, and oedema following influenza or prolonged anaesthesia, and occurring in pregnancy, should the patient be in great pain or badly asphyxiated, the action of Sup. 36 should be enhanced by daily subcutaneous injections of oxygen (300 c.cm.). Inhalations of oxygen are of little value, and

CHART 1.—B=Sup. 36 0.01 gram.

CHART 2.—B=Sup. 36 0.01 gram.

required in any one course, and often two or even one suffice. In particularly acute conditions the first two injections should be prescribed on successive days, and the third injection four, five, or six days later.

Sup. 36 is indicated in acute staphylococcal infections, in non-metallic intoxications, and in such conditions as pulmonary thrombosis and oedema, venous thrombosis, and the pernicious vomiting of pregnancy.³ Almost any

the drug is best injected by means of a Bayeux apparatus—a method brought to my notice by Dr. H. L. C. Noel.

Owing to the high mortality of pneumonia and to the fact that no previous chemotherapeutic preparation has proved of value in this infection, I will describe in brief three severe cases which (it seems fair to suppose) owe their life to Sup. 36. In the first case, represented by Chart 3, the patient was delirious at the time the Sup. 36

CHART 3.—B=Sup. 36 0.01 gram.

CHART 4.—B=Sup. 36 0.01 gram. D=Sup. 36 0.01 gram and subcutaneous oxygen 400 c.cm.

sapraemic condition may be combated by Sup. 36. In purulent conditions I have found it abort the lesions if pus has not formed already, and to cause pointing if pus was present beforehand. The moment pus has formed it should be liberated through a tiny incision, and the local application of strong antiseptics and fomentations should be avoided. Oedema, due to the collecting of lymph, may form around the lesion, and this is apt to cause severe pain and to call for the use of leeches if the lesion is connected with bone—for example, in an acute mastoid, where the timely use of Sup. 36 may render an operation unnecessary. Septic throats, acute and chronic rhinitis, influenza, bronchopneumonia and pneumonia, provided the lesion is not caused by the streptococcus, tend to vanish at once under Sup. 36. In bronchopneumonia the temperature falls to normal one or two days after a single injection, and the objective signs vanish a few days later. Should the temperature rise about one degree at nighttime after the initial fall, the inference may be drawn that there is some hidden focal infection in another part of the body and not necessarily in the lungs. Charts 1 and 2 depict the course of events which have occurred in thirty-nine cases.

CHART 5.—A=Sup. 36 0.01 gram and oxygen 300 c.cm. B=Sup. 36 0.01 gram. C=Oxygen 300 c.cm.

was injected. The patient was under the care of Dr. S. L. McBean.

In the second case, represented by Chart 4, the patient developed a patch in the second lung when the lung first involved was beginning to regress under treatment with Sup. 36. The patch referred to was more of the nature of a reactionary inflammation and subsided at once with a third injection.

The patient was under the care of Dr. E. Hogan.

In the third case, represented by Chart 5, the patient did not receive the first injection until the tenth day. The two injections failed to have a dramatic effect, but the patient was old and the heart was beginning to fail. For the next few days the heart was stimulated with digitalis, strychnine, and camphor, and the third injection was made when the heart

was considered to be sufficiently recovered. The day following the third injection the patient registered a distinct improvement, and this was followed by an uneventful recovery. The patient was under the care of Dr. W. H. Harwood-Yarred.

Although this drug appears to be invaluable in the pulmonary complications following prolonged general anaesthesia in elderly people it will not prevent these

if given beforehand. Indeed, if it is injected before the patient leaves the operating table there is a grave risk of pulmonary shock ensuing, owing to the large size of the molecule precipitating the protein particles in the pulmonary capillaries. I have found glycosuria, albuminuria, and acetonuria occurring after an operation vanish under Sup. 36, also similar conditions in pregnancy, provided the protein particles have not been precipitated in the renal or cerebral capillaries. Vomiting in pregnancy is quickly relieved, and acute venous thrombosis and puerperal fever (provided the trouble is not caused by the streptococcus) respond to treatment at once. Acute attacks of asthma may rapidly subside after a single injection, and I have found the drug invaluable in urticaria, angio-neurotic oedema, and in certain mild cases of hay fever. It is indicated in such septic conditions as whitlow, lymphangitis, adenitis, periostitis, and osteomyelitis, and a timely injection may render an operation unnecessary. It has proved of value in clearing up the dermatitis occasioned by organic preparations of sulphur and by such compounds as para-phenylene-diamine (furdermatitis), and tri-nitro-methyl-nitramine (tetryl), and in intoxications caused by certain amino compounds—guanidine, for example. It may be used also as an antidote in cases of insulin intoxication.

Sup. 36 has been used with great success in canine distemper, foot-and-mouth disease, and equine influenza (the coughing of horses). I have injected courting dogs unable to travel by train because of train-sickness with success.

SUP. 468.

"Sup. 468" is the symmetrical urea of para-benzoyl-para-amino-benzoyl-1-amino-4-6-8-sodium sulphonate.

The action of this compound appears to depend upon the liberation of positively charged and conductor functioning sodium atoms from the 4-6-8-positions. According to my observations, a positively charged conductor metallic atom is liberated from a sulphonic group only when the group is positively charged. The conductor action of Sup. 468 is much greater than that of Sup. 36, and this renders it useful in streptococcal infections. The drug is best injected intramuscularly in 0.001 to 0.003 gram doses. In acute streptococcal infections, such as erysipelas, rheumatic fever, puerperal septicaemia, etc., I inject 0.001 gram on the first day, 0.002 gram on the second day, and then 0.003 gram every other day until the lesion vanishes. In septicaemic cases I inject in addition 0.1 gram doses of auramine intravenously on the first two days, and 30 c.cm. of antistreptococcal serum subcutaneously on the first three days. Auramine is a di-phenyl-methane dyestuff, introduced by Fairbrother and Renshaw.⁴ Although Sup. 468 gives excellent results in streptococcal infections, provided it is prescribed before the patient's resistance has got beyond stimulation, the effect is not so dramatic as follows the use of Sup. 36 in staphylococcal, influenzal, and pneumococcal infections. Often, when the temperature has come down to normal, it rises again for a few hours, but seldom more than once.

Sup. 468 is useful in chronic streptococcal rhinitis, so-called "vasomotor rhinorrhoea," and asthma, and certain forms of chronic asthma and streptococcal arthritis after the enlarged and clumped protein particles have been broken up by subcutaneous injections of oxygen. In cases seemingly not being benefited by Sup. 468, owing to the large size of the nucleus of the compound in-

creasing the hydration of the protein particles, its action may be turned to good account by injections of the patient's own blood, a manoeuvre which causes dispersion of hydrated protein particles, or the injections may be followed by two injections of Sup. 36.

SUM. 36.

"Sum. 36" is the symmetrical urea of meta-benzoyl-meta-amino-benzoyl-1-amino-8-naphthol-3-6-sodium sulphonate.

Its action appears to depend upon the liberation of conductor sodium atoms in the 6-positions from a compound having the amino-benzene groups positively charged, instead of negatively charged as they are in the para-compounds. Such an arrangement enables the vehicle of the compound to cause a marked lowering of the surface tension of the protein particles, with the result that the conductor groups when liberated are freed in closer contact with the medium upon which they are going to act than is possible when the amino-benzene groups are negatively charged. In virtue of this ability to lower surface tension Sum. 36 has a more powerful conductor action than Sup. 468; this may explain why the drug is useful in infections occasioned by Gram-negative micro-organisms, which happen to be on a higher plane of evolution, so to speak, than the Gram-positive. Sum. 36 is best injected intramuscularly in 0.002 to 0.01 gram doses every fifth day on two or three occasions. It is indicated in pure gonococcal infections, such as urethritis, vulvitis, and ophthalmia. In urethritis and vulvitis I have found two or three injections every fifth day to cause the discharge to stop and the subjective symptoms to disappear, but the treatment should be augmented by a course of vaccines. If a urethritis is on the point of involving the posterior part of the urethra, and a vulvitis the cervix, an injection of Sum. 36 may precipitate an epididymitis in the former case and a salpingitis in the latter, owing to the initial effect the drug has in increasing the size of the protein particles (hydration). If this complication occurs two injections of Sup. 36 should be prescribed. In ophthalmia two injections of 0.005 to 0.01 gram, according to the age of the patient, should be made at three days' interval. Only very acute cases of gonococcal arthritis associated with a copious urethral discharge should be treated with Sum. 36, because in all other cases the carbon disulphide product of diethylamine (contramine) is more useful.

SUM. 468.

"Sum. 468" is the symmetrical urea of meta-benzoyl-meta-amino-benzoyl-1-naphthylamine-4-6-8-sodium sulphonate.

This drug has been used with success in malaria, in the piroplasmiasis of horses, and in trypanosomiasis in dogs.

I have not used the drug in human beings on a scale large enough to form an opinion as to the conditions and the doses in which it should be employed.

FOURNEAU "309."

Fourneau "309" is the symmetrical urea of meta-benzoyl-meta-amino-methyl-benzoyl-1-naphthylamine-4-6-8-sodium sulphonate.

Fourneau "309" possesses a greater conductor action than Sum. 468 because it contains in addition two negatively charged methyl groups, from which are liberated two positively charged conductor functioning hydrogen atoms. In trypanosomiasis Fourneau "309" has a greater lethal effect than Sum. 468. Sum. 36 temporarily paralyses a few trypanosomes, and Sup. 468 and Sup. 36 have no action at all upon them. For help in elucidating these points I am indebted to Dr. J. G. Thomson and to Dr. A. Robertson. It is still a moot point as to whether Fourneau "309" is the same product as Bayer "205." All these symmetrical urea compounds are soluble in water, and, broadly speaking, are non-toxic in therapeutic doses. Occasionally an injection may produce a mild form of shock, but this is met with only in individuals who show an idiosyncrasy towards compounds of benzene. A severe form of shock can be readily overcome by injecting 500 c.cm. of a 10 per cent. solution of glucose intravenously and 500 c.cm. of oxygen subcutaneously. In rabbits particularly the administration of Sum. 36 makes the serum give a positive van den Bergh reaction without damage to the liver.

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ACUTE SUFFOCATIVE PULMONARY OEDEMA.

THE note on acute suffocative pulmonary oedema by Dr. M. Cohen, published in the *JOURNAL* of March 20th (p. 528), has induced others who have had cases of this condition under their care to place them on record, with the treatment adopted. From the number of cases here reported the condition is apparently not extremely rare.

I.—MORPHINE; PITUITARY EXTRACT.

I HAVE treated three cases of acute suffocative pulmonary oedema in the last three years.

The first (in 1923) was a lady over 80 years of age who had a mitral systolic murmur and was subject to attacks of bronchitis. I found her sitting propped up in bed, cyanosed, and bringing up large quantities of frothy pink-stained fluid without effort. I gave her morphine sulphate 1/4 grain with atropine sulphate 1/120 grain, and the next morning she was sitting up in bed, fairly well, and able to eat a good breakfast. She died last year from bronchitis and failing heart.

The second case (in 1924) occurred in a lady aged about 60 years. She had walked home rather quickly after supper, and when she got to the gate of her house about 10.30 complained of feeling weak and faint. She was assisted to bed and I was sent for at 2 a.m. I found her in a practically unconscious condition, cyanosed, and bringing up the same slightly coloured fluid as the previous case, but not in such large quantities. Against my better judgement I gave the same hypodermic, but she did not respond and died an hour later. Possibly if she had received treatment earlier she might have lived.

My last case was a little girl aged 9 years. Her history is rather interesting. In 1923 she had an attack of rheumatic fever which was complicated by (1) left pleural effusion which

was aspirated, (2) pericardial effusion which I also had to aspirate, (3) endocarditis, which left her with a double mitral murmur. Last year she was sufficiently recovered to allow her to take a certain amount of gentle exercise and an occasional motor drive.

In July I got a telephone message to say she was dying. I found her deeply cyanosed, panting, very exhausted, and bringing up quantities of the same pink-stained, frothy fluid as the previous cases. I had an idea that morphine would make things worse, so I gave 1/4 c.cm. of B. W. and Co's. original strength pituitary extract, and as within fifteen minutes her pulse and general condition had improved I gave her another 1/4 c.cm. At the end of another half-hour she was so much better that I felt it safe to leave her. Next morning she was as well as before the attack and has had no attack since.

All three of these cases had no history of a previous attack, and all had valvular disease of the heart. If dissociation of the action of the two ventricles is the cause, why should morphine give relief? Would not pituitary extract appear to be the more rational line of treatment in these cases? It would stimulate the feebly contracting left ventricle and could hardly induce the forcibly contracting right ventricle to further efforts. I recognize, of course, the danger of "flogging a tired horse," but does not the converse—"doping a sleeping horse"—hold good in the case of morphine? I have seen three or four other cases in which the patient was apparently drowning in his own sputum in which pituitary extract gave relief. They could not, however, be called cases of acute suffocative pulmonary oedema.

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ALFRED MERRIN, F.R.C.S.I.

II.—ATROPINE; DIGITALIN; STRYCHNINE; AMYL NITRITE.

THE following five cases show that acute suffocative pulmonary oedema occurs in a variety of chronic diseases. The attacks may be single or recurrent; they are of sudden onset, and occur particularly at night. The treatment varies with the underlying conditions.

Case 1.—A man, aged 65, was treated by my late partner, Dr. A. Greenwood, for five years; it was a typical case of chronic parenchymatous nephritis, complicated by mitral and aortic regurgitation. Early in May, 1925, fine crepitations were heard in the lungs, creeping up from the bases, and on May 24th the patient had an acute attack of pulmonary oedema. I injected subcutaneously atropine sulphate 1/50 grain and digitalin 1/100 grain; the attack lasted about an hour. The next day the patient had another attack, and, in spite of the same treatment and an injection of strychnine 1/60 grain, died a few hours later.

Case 2.—A man, aged 47, had had asthma for more than twenty years. On April 4th, 1925, at 9 a.m., he had an attack of acute pulmonary oedema, and was treated with subcutaneous injections of atropine and strychnine and inhalation of amyl nitrite; the expectoration subsided, but the lungs filled up again rapidly, and he died two days later.

Case 3.—I was called to see a man, aged about 60 years, at 2 a.m. on July 14th, 1925, because "he was gurgling in the throat and thought to be dying." He was a tall, well built man of ruddy complexion, and had come to Bournemouth on a holiday. He felt perfectly fit all day, but awoke suddenly with intense dyspnoea and a feeling of impending death. During the attack he was deeply cyanosed, orthopnoic, speechless, with an occasional shallow cough which brought up much froth. A very hasty examination of the chest showed the presence of varying dullness and coarse moist sounds. As he was almost pulseless I injected digitalin 1/100 grain subcutaneously. There was immediate improvement in the pulse, but he complained of pressure in the head and giddiness. I therefore gave him an inhalation of amyl nitrite. The effect was wonderful; his colour became ruddy, his breathing improved, and the gurgling and expectoration almost disappeared. I re-examined the chest, and found that most of the moist sounds had gone. At 3 a.m. he felt choking again, and leaving him another amyl nitrite capsule I hurried back to my surgery for some instruments, and on my return venesected him, drawing off only 8 oz. The improvement was instantaneous, and when I left at 4 a.m. the patient was asleep. The next day I found his systolic blood pressure was 240 mm. of mercury. Within the next four weeks I reduced his blood pressure to 180 mm.; he had no more attacks and returned home to London.

The next two cases are interesting as the underlying disease is mediastinal neoplasm, which is not a common condition.

Case 4.—A man, aged 65, was under my care on and after February 18th, 1925, complaining of stridor and increasing dyspnoea with acute exacerbations typical of acute pulmonary oedema. He had mitral and aortic incompetence, and x rays showed retro-sternal neoplasm behind the manubrium. The attacks were treated with atropine sulphate, and in the interval large doses of potassium iodide and stimulating expectorants. He died suddenly on May 20th, 1925.