hypnotics requires to be considered. Obviously, it is better they should be done without if possible, but their disadvantages are more than counterbalanced by the restoration of energy provided by some hours of sleep. The assistance of suitable drugs, wisely selected, and not pushed to the extent of establishing a "habit," is so helpful that preconceived notions should not be allowed to prohibit their administration. Whatever hypnotic be chosen, the best results are obtained by giving it for three or four nights in succession rather than by leaving it to the patient's judgement to take as he pleases. By anticipating the risk of a bad night, the evil habit of broken sleep may be frequently escaped. The bromides are the simplest and least objectionable of all sedative drugs. They ought to be administered in full doses of 30 grains, and their efficacy will be much enhanced by combination with small doses of chloral hydrate. The latter drug has been handicapped by an unfortunate reputation for a dangerous influence upon the cardiac centres. This danger, if it exists at all except when the drug is exhibited in large doses, is grossly exaggerated, and may be disregarded altogether when the heart is sound. Ten grains given in combination with 30 grains of the bromide of sodium or potassium will be found efficacious in a large number of cases. The combination ought to be given half an hour before bedtime, and it may be repeated safely after two hours if the initial dose fails to produce the required effect.

When this fails, a trial may be made of bromidia in drachm doses, of chloralamide in 30 grain doses, or of chloralose in 6 grain doses; all of which are variants of chloral in combination. There are other alternatives to choose from; one of the following may be selected and administered in the form of a cachet:

Medinal	...	...	... in 7 gr. doses;	or
Trional	...	...	... in 15 gr. ,,	or
Sulphonal	...	...	... in 20 gr. ,,	or
Adalin...	...	...	... in 10 gr. ,,	or
Chloretone	...	...	... in 15 gr. ,,	or
Bromural	...	...	... in 10 gr. ,,	

Paraldehyde is valuable and should not be lost sight of, but it is a nauseous drug, and leaves such an unpleasant and tell-tale odour in the breath that it is not desirable except in cases where there is mental excitement and extreme restlessness. In these circumstances arises also the question of morphine and atropine, and there can be no doubt that one-quarter of a grain of the former with one-hundredth of a grain of the latter, given hypodermically for a limited number of doses, often saves the situation where milder remedies fail in their effect. This combination is specially indicated in cases where pain, from whatever source, contributes to the sleepless nights. Just as in the case of chloral, so in that of morphine, the spectre of evil after-effects or the possible creation of a drug habit cause it to be withheld in many instances in which its beneficent effect far outweighs any theoretic fear of evil consequences. Its abuse is no argument against its legitimate use, and of all the remedies we possess against the hopeless misery of insomnia to which nothing else has brought relief, it is a stand-by whose reliability and potency may always be depended upon. Combination with atropine increases its efficacy, and minimizes some of its penalties. It often happens with hypnotics, as with so many other drugs, that a combination of two or more is productive of happier results than the administration of any one by itself. There is space only to mention a few such combinations that answer well:

(*a*) Fifteen grains of trional with half a grain of codeia.
(*b*) Twenty grains of chloralmide with thirty grains of potassium bromide.
(*c*) Ten grains of aspirin with seven grains of Dover's powder.
(*d*) Ten grains of bromural with one-sixth of a grain of morphine.
(*e*) Five grains of zinc valerianate with one eighth of a grain of heroin.

In cases in which there is a persistent high-tension pulse dependent upon sclerotic changes in the arteries, and the patient gets to sleep on first going to bed, but wakes within two hours, nitro-glycerine is of inestimable value. A tabloid containing 1 minim of the 1 per cent. solution of the drug put into the cheek the last thing at night and left to melt there gradually, often prevents increase of tension after getting to sleep, and may be safely repeated should the patient awake during the morning hours.

Electricity is said to be sometimes useful as a sedative agent, but its effects are uncertain and may prove to be exciting rather than soothing. Hypnotism also has its advocates, but, though possibly useful in carefully selected cases, it cannot be regarded as other than a doubtful and experimental remedy.

Finally, it is well to recognize the value of philosophy as a hypnotic. Submission to the inevitable and a cheerful acceptance of the duties and bothers of every day will go far to promote the likelihood of good sleep at night. The prayer of R. L. Stevenson is worth remembering:

> The day returns and brings us the petty round of irritating concerns and duties. Help us to play the man; help us to perform them with laughter and kind faces, let cheerfulness abound with industry. Give us to go blythely on our business all this day, bring us to our resting beds weary and content and undishonoured, and grant us in the end the gift of sleep. Amen.

THE "BUFFER-SALTS" OF THE BLOOD.

BY

W. M. BAYLISS, D.Sc.Oxon., F.R.S.,

PROFESSOR OF GENERAL PHYSIOLOGY, UNIVERSITY COLLEGE, LONDON.

WHILE I quite agree with Dr. Benjamin Moore (June 29th, p. 720) that the expression "buffer-salts," as applied to the constituents of the blood plasma, is undesirable and misleading, I am unable to share his views as to the reason why it is so. In the first place, the name "buffer" does not suggest the correct interpretation of the way in which these substances do their work. Their action is rather to soak up, as it were, an excess of hydrogen—or hydroxyl—ions by the formation of compounds which are much less dissociated electrolytically than the acids or alkalis added. The word arises from a mistranslation of the original word, "*tampon*." I owe some apology to the readers of this JOURNAL for calling attention to some points which I have already discussed elsewhere, especially in my *General Physiology*, but I hope that some purpose may be served by bringing them together in this place.

Dr. Moore's account of the history of the name "buffer-salts" is not quite complete. Its origin is to be found in a paper by Fernbach and Hubert, published in the *Comptes rendus* of the French Academy in 1900 (vol. cxxxi, p. 293), where *tampon* is used to express the soaking up of hydrogen ions by such salts as sodium bicarbonate. The fact itself is most clearly seen with this salt, and the whole mechanism of its action, together with the similar action of the phosphates, has been explained in detail by Lawrence Henderson in a series of articles in the *American Journal of Physiology*, commencing in vol. xv in 1906. The complete discussion is given in vol. xxi, p. 427. To put the matter briefly, although somewhat incompletely: when an acid which is stronger than carbonic acid, such as lactic acid, which is dissociated with the production of a large percentage of hydrogen ions, passes into the blood, it combines with a part of the bicarbonate contained in the plasma, forming sodium lactate, and is therefore neutralized. At the same time, carbon dioxide is driven off and escapes by the lungs. But, even if it did not escape, there could be only an unimportant rise in the hydrogen ion concentration, because carbonic acid is an extremely weak acid and is scarcely dissociated at all.

To return to the word *tampon*. The original meaning of the name, which is probably that which the French writers had in mind, is that of a plug of cotton-wool pressed into a wound or elsewhere in order to stop bleeding. It has come later to be used for a railway buffer. It is, in either case, not quite the right word for the case we are dealing with. What we want is something to suggest the use of a mop or swab to absorb blood or exudation, not to stop haemorrhage by pressure. The name *tampon*, however, was used by Sörensen in a long series of researches (*Études enzymatiques*), published in French in the reports of the Carlsberg Laboratory at Copenhagen. It will be found on p. 19 of the eighth volume (1909). This work was also translated into German, and will be found in the *Biochem. Zeitsch.*, vol. xxi; on page 149 of this paper the word *tampon* is translated "Puffer," and hence got into English as "buffer," a quite inappropriate word. The buffer absorbs the energy of the moving train, not the train itself.

In its application to blood the use of the name is unnecessary, since the only "buffer-salt" of any importance is the sodium bicarbonate of the plasma; phosphate is present here only in insignificant amount. In its behaviour towards acids the plasma reacts precisely like solutions of sodium bicarbonate, and so little doubt is there as to the existence of this salt in it that until recently the carriage of the carbon dioxide from the tissues to the lungs was generally believed to be effected by it. It is truly present in less quantity by weight than the proteins, but quite sufficient to neutralize the fixed acids produced in the tissues. The molar concentration, indeed, of bicarbonate is higher than that of protein on account of the enormous molecular weight of the latter. In the opinion of Dr. Moore the function of combining with excess acid is to be ascribed to the proteins, not to the bicarbonate. He gives no data for the statement that there are not enough salts to account for one-tenth of the "protective influence." But I take it that he refers to his titrations with strong acid and alkali, to be discussed below. As to the carriage of carbon dioxide, he appears to be unaware of the work of Buckmaster, who has shown that this function belongs to haemoglobin.

The proteins of the plasma are said to be responsible for at least 90 per cent. of the "protective action" of the blood. I confess that I cannot understand the meaning of the statement that "all the inorganic salts of the plasma, including even the sodium chloride, are held in union by the proteins." How, then, can the fact be explained that the electrical conductivity of the plasma is practically that of a solution of free salts? It is also inconsistent with what is pointed out in the next paragraph, namely, that the depression of the freezing point is that of a one-sixth normal sodium chloride; in other words, about that of the salts, if free. If the salts were combined with the proteins, the depression of the freezing point would be much less than this. It is true that Pfeiffer and Modelski[1] have described the formation of what they regard as chemical compounds between certain amino acids and certain neutral salts; but it is remarkable that sodium chloride was not one of the salts, and I have been unable to confirm their results, although the instructions given were followed exactly. Much less is there evidence of combination between proteins and salts. On the contrary, the freezing-point measurements of Bugarsky and Liebermann[2] showed distinctly that this was not the case. Hardy[3] also was unable to find any evidence of chemical combination between salts and globulins.

The reason why Moore and his coadjutors found serum proteins to be able to neutralize acids and alkalis was because they used *strong* acid and alkali. Such are never sent into the blood stream as products of metabolism, and the representation of the "buffer" action of blood as related to these unphysiological reagents is incorrect. There is no evidence that proteins combine with the relatively weak organic acids produced in tissue metabolism. If an indicator such as neutral red, which reacts to small changes of hydrogen ion just around the point of neutrality, be added to serum, it will be found to change colour when a very small amount of lactic acid is put in, showing that the proteins have not taken it up. The change of colour can easily be shown to be due to the carbon dioxide liberated from the bicarbonate, since it can be brought back on exposure to air. The production of the carbamino acids of Siegfried is limited to the simpler amino acids; according to this observer himself, even leucine does not form one. However, I found, by conductivity measurements signs of combination of carbon dioxide with leucine. But there is no trace of the effect with proteins. We may also call to mind the results of Fletcher and Brown,[4] who showed that the only carbon dioxide given off by muscle on heating arises from the decomposition of sodium bicarbonate by the lactic acid formed. This applies up to the temperature at which destruction of the proteins occurs. Before the view put forward by Moore can be accepted, it is necessary that experimental evidence be brought showing that a pure protein solution can take up in combination sufficient carbon dioxide to account for that given off by plasma on the addition of a strong acid. Findlay[5] shows that no carbon dioxide is taken up by egg white, a very small amount by gelatin.

But there is no doubt that proteins are able to form true salts with strong acids and bases. They can combine with the former by aid of their basic (NH_2) groups and with the latter by aid of their acidic (carboxyl) groups. The reason why they do not combine with weak acids or neutral salts is clearly that the NH_2 and COOH groups are, in neutral solutions, united together by anhydride formation. In order that any combination may take place with other substances, this internal anhydride structure must be broken down by hydrolysis, a process that requires the aid of a strong acid or base.

It is somewhat remarkable that serum proteins are, chemically, very inactive substances. They do not serve for nutrition of the tissues, and their chief function seems to be to give a colloidal osmotic pressure to the blood, so that it shall not lose water to the tissues too rapidly. They have also an important part to play in the clotting process. I venture to think, however, that the term "reactivity of the serum" is not a particularly lucid one. It is usually associated with the capacity of readily entering into chemical reaction with other substances.

The fact that salts are formed by proteins with strong acids and bases is the cause of the rise of osmotic pressure observed in such cases by Roaf and Adamson. These salts are dissociated electrolytically, and, as I have shown elsewhere, all the ions are osmotically active. Various explanations might be given of the fact referred to by Moore, that the addition of a very small amount of acid lowers the osmotic pressure. It may be due to the decomposition of a small quantity of a sodium salt of protein present in the serum owing to escape of the normal carbon dioxide and the consequent development of alkalinity.

The use of the name "buffer-salts" in application to blood plasma is to be deprecated, as it seems to me, because it is apt to give an air of mystery to what is merely a simple property of bicarbonates. The expression "sodium bicarbonate" is all that is wanted in place of "buffer-salts" in this connexion.

No satisfactory name has been suggested for the general property as possessed by many weakly dissociated electrolytes. "Tampon" is better than "buffer" in any case.

REFERENCES.

1 *Hoppe-Seyler's Zeitsch.*, vol. lxxxi, p. 329; and vol. lxxxv, p. 1. 2 *Pflüger's Archiv*, vol. lxxii, p. 51. 3 *Journ. of Physiol.*, vol. xxxiii, p. 251. 4 Ibid., vol. xlviii, p. 177. 5 *Kolloid. Zeitsch.*, vol. iii, p. 169.

THE PART PLAYED BY THE BONE GRAFT.

BY

MARCUS MAMOURIAN, F.R.C.S.E.,

SURGEON TO THE DISTRICT INFIRMARY AND CHILDREN'S HOSPITAL, ASHTON-UNDER-LYNE.

THE subject of bone grafting, which has acquired so great an importance to-day, has engaged the attention of surgeons for more than a century. Albee mentions Merren as having carried out experiments in 1809. The wonderful researches and operations of Ollier and Macewen appeared as long ago as 1867 and 1881. Singularly enough, the biology of bone and the bone graft still remains undetermined. The main views may be summarized as follows:

1. Bone is osteogenetic. The bone graft is osteogenetic and can live and grow without periosteum. (Macewen, Groves.)
2. Fragments of bone grow better than an entire piece. (Macewen.)
3. Periosteum acts as a limiting membrane and has no osteogenetic power. (Macewen.)
4. The periosteum is the principal agent of bone growth. The bone graft can live and grow by virtue of its own periosteum. (Ollier, Axhousen, and most of the American writers.)
5. The bone graft is osteo-conductive. (Murphy.)
6. Bier and others attach great importance to the cambium layer, endosteum, Haversian canal linings and marrow.

1, 2, 3. Macewen is the protagonist of the "bone from bone" theorists. His teaching is mainly founded upon his famous case (1882) in which part of the humerus of a boy was excised for osteomyelitis and restored by the implantation of small sections of bone obtained in the course of several osteotomies. The graft, therefore, was comminuted and homoplastic, and the logical inference is that the reconstruction of the diaphysis was brought about by the increase in size and coalescence of the fragments of bone. In the absence of a radiographic record all explanation as to the process of restitution must be more or less conjectural, or, at most, based upon experimental findings. The remarkable feature of the case is, that although the shaft is supposed to have been restored without the help of a "limiting membrane," yet there was limitation of size