and his arm was secured to his side. He arrived in hospital about one and a half hours after the accident.

Condition on Admission.

He was suffering from severe shock, and was very restless. There was a large non-pulsatile swelling over the left clavicle, extending up into the neck. There was no pulse at the left wrist. He was markedly bloodless; the whole of the left side of the chest was dull, and respiration could scarcely be heard. He appeared to be moribund.

Diagnosis.

Injury or destruction of the subclavian vessels, with bleeding into the left pleural cavity.

Treatment.

It was a question whether to let him die quietly or to operate in the forlorn hope of being able to do something to save him. Eventually it was decided to operate. The electricity of the hospital suddenly gave out, which rendered matters more difficult, but an acetylene operating lamp was at hand, and an electric lamp was run off the x-ray plant next door by the ingenuity of Captain Cotter, R.A.M.C.

A light general anaesthesia was given. A long incision was made over the swelling above the left clavicle. As soon as the fascia was opened a large quantity of blood gushed out. A finger was at once inserted to control the artery against the first rib. Both the first and the second ribs had disappeared, and could not be felt with the exception of loose fragments of bone. The artery, however, was found at once, the end sticking up into the wound like a finger, pulsating feebly, completely severed. Whether it was bleeding or not at the time was not discovered. It was grasped at once with powerful forceps, which were left on. The distal end of the artery could not be found, and nothing could be made out with regard to the vein. Nothing could be seen as the field of operation was awash with blood. The wound was sewn up, and the artery forceps left protruding from the wound. The operation took a very few minutes. During this time saline was being given into a vein, two pints were run in, and he was left undisturbed on the table till his pulse had recovered some strength. He was then put back to bed, and more morphine given.

After-History.

More morphine had to be given during the night, but even then he did not sleep well and was very restless. Next day, however, he was much better, and we entertained hopes of being able to save him. He was very restless for the next two days. The foot of the bed was raised high upon blocks, and this seemed to worry him and keep him awake.

October 6th, 1918. He was dressed and the forceps removed from the artery. A long rubber tube was inserted into the wound and $1\frac{1}{2}$ pints of fluid blood siphoned out of the pleural cavity.

October 7th. He was dressed again and half a pint of blood withdrawn from the chest in the same manner, the bed being tilted to an extreme angle to allow this to be done more effectually. His arm was unfastened from his side and disinfected, after being washed, as gangrene of the arm was feared. The lower limbs were bandaged. He was constantly receiving saline by the rectum, and took a good deal of fluid by the mouth. Morphine seemed to have little effect in controlling his restlessness, and he was now given hyoscine in $\frac{1}{100}$ grain doses. He passed a better night, but showed signs of renewed haemorrhage next morning.

On October 8th he had torn off his bandages in spite of the special orderlies, and got his arm free, and was very restless and anxious about himself, continually asking if he was going to die.

On October 9th laudanum m 30, with potassium bromide gr. 45, were given and he passed a slightly better night, but managed again to free his arm, which he waved about wildly. The forearm was very swollen and tender. There was no sensation below the elbow. It was thought that a line of demarcation was forming below the elbow. The arm was again disinfected and put into a clean sock.

On October 10th his condition was much the same, but he was showing signs of exhaustion as he would not sleep, in spite of everything we could do. Morphine and bromide had been repeated with little effect; he was continually restless and a very bad patient.

On October 12th his condition was worse. The heart seemed pushed slightly to the right, and he was breathing badly. He again tore off the bandages from his arm, and this time from his wound as well. Hyoscine was given with very little effect.

He died of exhaustion early on the morning of October 13th. He really never gave himself a chance throughout.

Post-mortem Examination.

The left clavicle was found unbroken, as had been noted at the operation. The pole of the boathook had been thrust in below it. The first rib was broken far back, and detached from its cartilage at the sternum. The loose fragment had rotated inwards transversely. The second rib was broken and detached from its cartilage half an inch from the sternum. The artery was completely severed, evidently by the broken ribs, probably the first, as it rotated inwards. The crushed proximal end was completely occluded; the distal end was full of firm clot. The vein was not torn. The left lung was collapsed, and the pleural cavity still contained much blood.

It is my opinion that this man's life might quite well have been saved if he had been more reasonable and more amenable to treatment, in spite of the severe injuries he had sustained.

THE BALANCE OF COLLOID AND CRYSTALLOID IN CHOLERA, SHOCK, AND ALLIED CONDITIONS.

By BENJAMIN MOORE, D.Sc., F.R.S.,

DEPARTMENT OF APPLIED PHYSIOLOGY, MEDICAL RESEARCH
COMMITTEE.

THE JOURNAL of September 20th last (pp. 387, 394) contains two articles of first-class importance which come from sources so wide apart as France and India, and are recorded independently, but they shed such a light upon each other, and upon several outstanding obscure facts in the study of immunity, that it seems worth while to bestow some thought upon the underlying common cause of the whole series.

The first is a review of recent work by Richet, Brodin, and Saint-Girons¹ on anaphylactic shock, in which it is shown that such shock can be prevented by addition of sodium chloride to the dechaining dose of serum, or by rendering the blood hypertonic with saline before this serum is injected.

The second is a letter from Sir Leonard Rogers pointing out that while intravenous injections of hypertonic salines in cholera are of well-proven advantage similar injections of gum arabic as used by Bayliss so effectually in combating wound shock, or surgical shock, are here of no avail but rather appear to be a disadvantage.

Now these two sets of observations are by no means contradictory but most beautifully complementary, also both are in consonance with the findings of the French school on anaphylaxis and, as will be shown, with the earlier observations from India of Sutherland and McCay² that hypertonic salines inhibit haemolysis either in a natural haemolytic system or an actively created one with a specific haemolysin, as in the Bordet-Gengou reaction and the Wassermann test.

The common cause of all these phenomena is a disturbance of that delicate equilibrium between the colloids of the blood and cells (such as proteins and lipoids) and the crystalloids (such as sodium chloride) existing united or adsorbed in common solution or suspension.

Taking, first, the positive effect of a colloid, such as blood-proteins, gelatine, or gum acacia, in shock due to haemorrhage, surgical injury, or prolonged anaesthesia, as compared with the failure of simple hypertonic salines under these conditions, we find that the situation is one of a circulating fluid not merely defective in total volume but also relatively poor in colloid compared to crystalloid. Accordingly inorganic salts, or salines, given alone are here rapidly eliminated, having no colloid to anchor them, and so being treated as foreign bodies and thrown out by kidneys and intestine. But gum arabic, gelatine, and plasma proteins cannot be so expelled, and serve to anchor inorganic salts and so preserve the equilibrium of crystalloid and colloid not only in blood but in the master cells of brain and heart, where the state of aggregation of the protoplasm would soon become altered.

That there is such an interaction of adsorptive character between colloid and crystalloid is shown clearly by the definite changes in osmotic pressure following upon variations in the concentration of the salines in which the colloid is in solution. This osmotic pressure measures the degree of aggregation of the colloid, and the same colloid may show a ten-fold variation with varying concentrations

of the saline. Such variations can only be explained by union between colloid and crystalloid. This change was first shown for the serum-proteins by Moore and Parker³ and Moore and Roaf,⁴ and later confirmed by Lillie⁵ and others. A similar effect is obtained with gum acacia, for the measurements of the osmotic pressure of this colloid made by Moore and Roaf⁴ in distilled water gave treble the values later obtained by Bayliss⁶ in physiological saline. The obvious explanation is that given by Moore and Roaf for the serum-proteins—namely, that the solution aggregate of the colloid changes in presence of the crystalloids.

These two series of experiments upon the osmotic pressure of gum acacia in presence and absence of salt clearly demonstrate two things—(1) that a solution of gum arabic made in water, or saline, as recommended by Bayliss, and injected intravenously will at once seize upon or hold a certain amount of saline in the blood, and as a result of its presence the total salt content of the blood with which nerve and muscle cells stand in common equilibrium will rise, and (2) the most important fact, that as a result of this adsorption the state of aggregation of the injected gum will change so that the "molecular weight" or "solution aggregate" is only about one-third to one-fourth of its former value—for this is precisely what the fall in value of the osmotic pressure means on Avogadro's law.

Now the colloids of the plasma are but an intermediary to the colloids of the cells in equilibrium with them. These are still more sensitively balanced than the plasma colloids, for they are a stage more complex. Accordingly, if variation in salt concentration can alter the molecular complexity of gelatine, gum, and serum-protein, it follows that it also can and must affect the condition of complexity of cell protoplasm. There is, indeed, abundance of collateral evidence, such as incipient precipitation due to salines and the washing out of lipoids by hypotonic salines, to prove the occurrence of such changes.

Take next the case of efficiency of hypertonic salines in cholera, and inefficiency of colloidal solutions such as gums, and it is clear that this is as it ought to be, for the condition is one of excess of toxic colloids and defect of balancing electrolytes or salines. The crystalloidal balance is in this case upset in the opposite direction. Electrolytes are wanted to combine with circulating toxic colloids and with colloids of tissues and prevent these linking on to each other. Gum injected under such conditions only furnishes another claimant on that side of the balance for the already denuded concentration of crystalloids to cope with. This action robs the cells still more of their salines, and sets free adsorptive situations in which toxins attach themselves, so leading to altered aggregation of protoplasm and locking of its mobility.

On the other hand, free saline in the blood in such diseases as cholera combines with toxins to form a crystallo-colloidal union, and this is an essential factor in excretion of the poison by intestine and kidney. The unattached colloidal molecule of toxin possesses no osmotic pressure, nothing to drive it through an excreting cell. When it becomes attached to a crystalloid the combination acquires a directive force like a gas molecule within a porous pot, and like this now possesses a power of diffusion.

The unattached toxin is like a drifting hulk or barge with no motive force of its own; the crystalloid from the hypertonic saline is like the tug to this barge. The tug takes the toxic colloid out through the intestinal mucosa or renal epithelium. The tug, once attached to barge, cannot readily break the towing rope and go through alone unless there is a high gradient of fall of osmotic pressure to disrupt the adsorptive bond uniting crystalloid and colloid. Whether both go through or not will depend on the size and properties of the colloidal aggregate and the width of the lock gates in the excreting cell.

In the case of gum acacia in shock the colloidal "solution aggregate" (colloidal molecule) is too large to pass out, and this retains the crystalloid; these two together produce an osmotic pressure and keep up the volume of blood for the heart to drive round. In the case of hypertonic saline in cholera the molecule of toxin is smaller and the saline tug carries it out through intestinal and kidney cell. It is, indeed, this rapid passage out of an immense navy of crystalloidal tugs which depletes the

blood of its crystalloids; this in turn depletes the nerve cells and leads to shock and collapse.

An exactly similar explanation can be given for the results obtained in prevention of anaphylactic shock by hypertonic saline, only here the colloidal constituent, or antigen, attacked, or protected, is probably lipoidal in nature (that is, a lecithin), as it is in syphilis and the Bordet-Gengou phenomenon.

There is clear evidence that the stability, or state of aggregation, of a suspension of lipoidal nature varies with the concentration of saline or electrolytes in common solution with it. It is for this reason that erythrocytes dissolve, or haemolyze, in water or hypotonic salines.

When an animal is in an anaphylactic condition the lecithins of its nerve cells and muscle cells have been rendered sensitive to the particular serum by reaction with the first dose of this injected. These cells *in situ* within the animal's body are in precisely the same position as the colloids of the serum of an animal sensitized haemolytically by injections of a given suspension of red blood corpuscles. The Bordet-Gengou phenomenon of haemolysis happens in a test-tube, the Richet phenomenon of anaphylactic shock happens in the living body; this is the sole difference between them. In each case, as in practically every biochemical reaction of zymolysis, fermentation, and immunity, there is a similar triad of constituents to the reaction. In the Bordet-Gengou haemolysis these are (1) the red blood corpuscles, (2) the serum specifically sensitized to them, and (3) complement. In fixation, or deviation, of complement in the first stage of the Wassermann test the corresponding triad is (1) lecithin from any tissue, (2) syphilitic toxin which attacks lecithins (just as in the body it would attack the lecithins of nerve cells), and (3) complement. In the anaphylactic shock there are (1) lecithins of nerve cells, (2) the specific serum, (3) complement. In the action of oxidases there are (1) substance to be oxidized, (2) oxidizing ferment or oxidase, (3) a peroxide. In fermentation, (1) the sugar, (2) the endo-enzyme of the yeast, (3) the co-enzyme, a phosphate or phosphatide. In hydrolytic digestion, (1) the substrate, protein, carbohydrate, or fat, (2) the enzyme, (3) the co-enzyme acid, alkali, or neutral salt. In differential staining of any microscopical preparations, such as bacterium, tissue, or in selective absorption of particular salts in physiological growth there are (1) absorbing tissue (2) adsorbate, such as dye, etc., (3) the mordant, such as a salt of iron or aluminium. These examples are sufficient to show how universal is this peculiar colloidal reaction, with its triad of participants throughout all biochemistry.

Now, such an adsorptive reaction can be locked up or prevented either by the absence, or by the chemical fixation, of one of the partners to the reaction. Many years ago Moore and Roaf showed that this formed the physico-chemical basis of anaesthesia. Here the anaesthetic locks in with the cell colloids and reduces metabolic activity. The same happens in many poisonings, such as cyanide poisoning, where the cyanide locks into the colloid and prevents oxidation, although the blood is fully charged with oxyhaemoglobin. Similarly, locking of enzymes and prevention of their action can be shown in the test-tube, even with inorganic colloids such as colloidal platinum.

This is the explanation of absence of anaphylactic shock in presence of excess of saline, which binds in with the reacting crystallo-colloidal system and destroys that delicately poised lability which is necessary to the adsorptive reaction. Similarly McCay and Sutherland showed that the haemolytic reaction did not occur between a specific haemolysin, corpuscles, and complement if the saline content were made about double that of the animal's serum.

No doubt for each type of reaction more sensitive crystalloids than common salt may be found, and we are here at the very heart of experimental therapy. The preventive crystalloid at any given concentration will be efficacious according to the reaction constant of its affinity for one or other of the reacting substances, or, in other words, upon its specific adsorptive power, or its mordanting power. This will differ from one pair of colloid and crystalloid to another, and is the basis of that property whereby one type of cell takes up one crystalloid and another selects another. This is the reason why the main ions of the plasma are sodium and chlorine, while

those of red blood corpuscles are potassium and the phosphatic anion. It enables diatoms to take out silica for their skeletons from the minutest traces in sea or pond water, and the osseous tissues similarly to adsorb calcium phosphate.

The most striking instance of all of this delicate equipoise between colloids and crystalloids is the regulation of the amount of saline in the cells and circulating fluids of the body. From the evolutionary point of view this regulation is much more ancient than that of body temperature, and its pathological variations are probably more important than those of the temperature could we only discover as ready a means of studying them as is the clinical thermometer in the case of temperature.

This equipoise of salt concentration started in evolution at the level of the fishes, with the teleostean, and up that long range of evolution to man, through countless types and channels, there is scarcely a flutter in its value. The variations in all species may probably be said not to lie outside the limits marked in isotonic saline by 0.7 and 0.9 per cent., and in any one given species the physiological range is many times narrower.

What is the mechanism of this exquisite adjustment throughout such a wide range of the animal world, and with any variation in the external environment, from fresh pond water, or the very hypotonic fluids daily in use by man and other animals, up to the salinity of sea water, which is manifold hypertonic to the blood of all teleostean fishes? The answer is that this amount is that which is in equilibrium or colloidal adsorption with the colloids of cells and plasma. Any additional amount becomes free in the circulation, and is promptly removed by excretion. In other words, isotonic saline expresses the balance between colloids and crystalloids.

The union between colloid and crystalloid is very slight; it is a molecular union in which the units are molecules not atoms, and there are no atomic linkages. It much more closely resembles the union of salts to their water of crystallization, and such physical properties as electrical conductivity are not interfered with. Nevertheless, the union is quite definite, and without it life as it now exists would be impossible.

REFERENCES.

¹ *Compt. rend. de l'Acad. des Sciences*, Tome 169, 1919, p. 9. ² *Biochemical Journal*, vol. v, 1909, p. 1. ³ *Amer. Journ. of Physiology*, vol. vii, 1902, p. 261. ⁴ *Biochemical Journal*, vol. ii, 1906, p. 34. ⁵ *Amer. Journ. of Physiology*, vol. xx, 1907, p. 127. ⁶ *Proceedings Royal Society*, vol. 89 B, 1916, p. 384.

THE TREATMENT OF INCIPIENT MENTAL DISEASE.*

BY

SIR ROBERT ARMSTRONG-JONES, M.D.,
F.R.C.P., F.R.C.S., C.B.E.,

FORMERLY LIEUT.-COLONEL R.A.M.C. AND CONSULTING PHYSICIAN
IN MENTAL DISEASES TO THE LONDON AND ALDERSHOT
COMMANDS; LECTURER ON MENTAL DISEASES,
ST. BARTHOLOMEW'S HOSPITAL.

THIS subject is a matter of great public importance, because the cost of maintaining the insane and the mental defectives of this country implies a vast financial burden upon the rates and taxes, now amounting to about four million pounds a year, and this burden has been gradually increasing for many years. So far as reliable lunacy statistics could inform us the total number of insane persons in England and Wales had reached, at the end of 1914, the alarming total of 140,466 persons, or 1 to every 266 of the estimated population. These were the exact numbers on January 1st, 1915. Since the commencement of the war no official record of the total numbers has been obtainable, because soldiers and sailors and airmen, as well as others serving with the forces, who may have become insane or who may have suffered from a temporary mental and nervous breakdown and who required care, have been treated in war hospitals, and have not been regarded as insane. They have not been certified, and therefore have not come under the jurisdiction of the Board of Control (Lunacy Commissioners); consequently accurate statistics of official insanity in England and Wales have not been possible. Naturally, since the above

date the total officially recorded in asylums and private establishments has considerably diminished, but the numbers must be misleading and unreliable if they are taken to reflect the exact incidence of insanity among the people.

The special point dealt with here is the treatment of insanity in its early stages, and every medical practitioner must have had experience of the difficulties presented by mental cases in private practice—not only in their actual treatment of the disorder, but also from the strong feelings aroused and expressed by the certificate and the consequent compulsory removal and detention of those certified into the various mental hospitals or into the private asylums which are recognized by the law and are the most suitable curative establishments. In order to obtain the best remedial treatment in these places, it is obligatory and compulsory for all, except the voluntary boarders, which only applies to private or paying patients, to be first certified as insane, and every doctor, as well as all the friends and relatives of a mental patient, realize the hardships which the certificate of insanity imposes upon the person certified, as also the undeserved stigma which is reflected upon him and his friends by its issue. A few of these disabilities are that the medical certificate of insanity separates the sufferer from his friends, it removes him from his home, it cuts him off from all social privileges, it removes from him his domestic rights, it takes away all his former financial control over his own affairs, it disfranchises him so long as he is under its ban, and it practically dispossesses him of all the rights and liberties which men hold dear. No other illness is more dreaded nor more costly, yet no other illness under skilled care is recovered from more quickly. The need for skilled care was so well insisted upon by Sir Henry Hallford when he was called in to treat His Majesty King George III after the failure of Dr. Willis that he was fully justified in the statement made that the care and control of a mental patient was the most responsible duty imposed upon any physician, and success in treatment depended upon qualities of head and heart such as no other disease demanded from the nurse and doctor; but success in mental cases is attended with infinite satisfaction and credit, and he was enabled by it to gain the confidence and respect of his sovereign in four reigns, for he became the confidential adviser in turn to King George IV, to William IV, and to Queen Victoria, thus exercising for himself as well as for the medical profession a reputation of distinction as well as gratitude for personal service, marked skill, and steadfast devotion.

The first cry that one hears when called upon to advise or to treat a case of mental disease is "Please don't put mother away"; "Please don't send her away to an asylum to associate with lunatics"; "I couldn't bear the idea when she got well that we should have been a party to having her certified as insane." And these are real grievances, especially to the lower middle classes, who are the real workers in the State, who bear their ills without revolt, and who often suffer in silence. The rich or the well-to-do can be received as voluntary boarders into any mental hospital or into any private establishment, but the less financially favoured, who constitute the great majority in the State, must be certified insane and detained until they have shown their right to be free, if they desire to undergo treatment, or their friends wish it. There is no place wherein to send the poor unless previously stigmatized by the certificate as lunatics.

Before the war it was so fully realized that even if recovery occurred the painful memory of association with cases worse than themselves, and the recollection of an illness with its distressing consequences would tend to precipitate a relapse, and that the stigma of a mental illness would remain for the whole of life and would be a blot upon his record, so that he would have no chances of success in the future. His detention as a lunatic would cause him to be shunned and avoided by all his former friends, and on leaving the asylum he would be isolated in a world of his own and viewed with suspicion and distrust. Owing to the nature of his illness he would be left without friends, without work, and without sympathy, even though, as in most instances, he was not to blame for his illness or misfortune. However short the detention, the disastrous consequence of certification remained; and not only did the undeserved reproach adhere to him, but it reflected also upon members of his family

* Communication to the West London Medico-Chirurgical Society during the latter part of the session 1918-19.