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THE CIRCULATION IN RELATION TO SHOCK *

BY

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Surgeons have long been familiar with the term "surgical pathology," but it is now apparent that surgery needs physiology to such an extent that the term "surgical physiology" is necessary. Anatomy and pathology are essential for the practising surgeon, but surgery has another side upon which its further progress must depend, and I feel sure that the day is not far distant when practical physiology will be shown to be the best training-ground for the young surgeon who seeks to advance in his subject.

In no field is the common ground between surgery and physiology seen better than in relation to shock. The surgeon sees it carry off a large proportion of his patients after operation (Mummery put it at 21 per cent.), but I do not think it is realized that an even larger percentage of experimental animals die from the same cause. I do not propose to give a textbook lecture on shock: I leave that to the writers of surgical textbooks, because it seems to me that the physiologist can be of most use in indicating the essential nature of the problem and the lines along which we need new knowledge.

Established Shock

Differences of opinion exist as to the nature of shock, and it is therefore probably best to begin with the phenomenon of established shock just before death, regarding which there is no argument. There is a low blood pressure, a rapid heart, a thready pulse, a concentrated blood, and a low temperature because the metabolic rate has fallen. Such arteries as can be studied are constricted; so are the uninjured vessels of the skin. The patient is apathetic and does not seem to feel pain; he is obviously going to die. All are agreed that at this stage a vicious cycle (shown below) is in operation which inevitably leads to death.

TABLE I.—*The Death Cycle*

It is easy to understand the mechanism of this death cycle, which is common to many fatal illnesses. Suppose we begin with the low blood pressure. This leads to a bad blood supply and to asphyxia of the tissues. Asphyxial products bring about a dilatation of capillaries, which open up like a great sponge at the periphery and soak up the blood in the body. In addition the capillaries become abnormally permeable and the blood plasma filters into the tissues. This causes concentration of the blood and still further contributes to the problem of the "lost blood." With the fall of arterial pressure there is less of reflex activity of the spinal cord; the muscles go limp and cease to support the capillaries, and this facilitates their dilatation. This point was first noted by Starling and has been more recently referred to by Yandell Henderson.

The capacity of the vessels is now too large for the blood. Less blood is returned to the heart, the cardiac output is reduced and the fall of arterial pressure accentuated, and so the fatal process goes on. All authorities agree that the heart itself is not the cause of the shock in cases of injury, and in animals it may be demonstrated that just before death it is beating vigorously but is incompletely filled. Death is due to asphyxia.

The pathological appearance varies very much according to the means by which the shock is produced, but often very little is seen. In the more typically traumatic shock the organs are pale, but, according to Moon, congestion of the lungs and liver and ecchymosis are more typical, especially of toxic shock. We need very badly a systematic study of the pathological states found related to the methods of the production of shock. I believe, however, that it is extremely difficult to obtain reliable observations from human material because of delay in securing authority for post-mortem examinations and movement of blood after death (Shaw Dunn).

Peripheral Resistance

I have referred to the problem of the "lost blood," but I should not like to leave the impression that this is the sole problem; it is only half. If it were the only problem we could simply replace the blood, and we all know that results from transfusion of blood or saline are indeed disappointing. A commonly overlooked difficulty is that the peripheral resistance of the circulation is reduced and it is no longer possible to raise the arterial pressure without raising the venous pressure enormously and the capillary pressure and thus increasing capillary filtration tremendously. Probably the liver and the heart are damaged also. This is why transfusion is of the greatest value in haemorrhage but of so little

* Summary of an inaugural lecture on surgical physiology delivered at the Royal College of Surgeons of England on May 2, 1940.

use in established shock. In haemorrhage an intense constriction of the peripheral vessels occurs. There is in existence a Medical Research Council report of the last war by McNee, Sladden, and McCartney which states that, while cases of haemorrhage did well, in all cases of shock the patient died when transfused. On going into the literature I found that Wiggers, in America, had described the fall of peripheral resistance in shock in 1918. He arrived at this conclusion from a detailed study of the shape of the pulse wave, but at that time his work had not received the recognition which it now has. The fall can, however, be demonstrated by easier methods. A similar fall of peripheral resistance is produced by histamine (Dale and Richards; Hemingway and McDowall).

Unfortunately we do not know of any satisfactory method of raising the peripheral resistance. We know of no drug which will constrict the vessels of the body generally without acting deleteriously on the heart. All drugs which in moderate doses constrict the vessels of the muscles constrict also the coronary arteries. We are in urgent need of more knowledge regarding the pharmacology of the vessels of the muscles. And now we come to the possible factors in shock which may initiate the vicious circle. I would emphasize, however, that, while each may separately produce shock, several factors may in some cases act together.

Table II gives the possible causes of shock in probable order of importance.

TABLE II.—Possible Causes of Shock

1. Haemorrhage	obvious	..	Capillary dilatation (oedema)
	concealed	..	" " "
2. Toxins	local	..	" " "
	general	..	" " "
3. Excessive vasoconstriction	..	Asphyxia—	Capillary dilata-
			tion. Muscle dilata-
4. Reflex vasodilatation	..	All vessels except skin	
5. Post-excitement, etc., depression	..	" " "	
6. Central exhaustion and injury.	..	" " "	
CO ₂ loss	..	" " "	

1. Haemorrhage

Obvious Haemorrhage.—It is apparent that in injury a possible cause of shock is severe haemorrhage, but it is quite remarkable how much blood may be lost and yet the patient survive. I need not go into the various ways by which the body compensates for the loss of blood. Suffice it to say that there is generalized vasoconstriction until asphyxia supervenes. If given in time, transfusion or salines facilitate an almost certain recovery.

Concealed Haemorrhage and Local Oedema.—There is a large amount of experimental evidence, especially that by Blalock, that when a limb or the intestine is damaged material haemorrhage and loss of blood plasma occur in the region of the injury. It is well known that if a tourniquet is placed on a limb before or immediately after an injury shock does not arise, but it appears immediately the tourniquet is removed. This had been interpreted by Cannon and Bayliss as indicating that a toxin is washed into the circulation when the tourniquet is released. On going into the matter in more detail Blalock concluded that the animal bleeds into the injured part. He found that the artery is more important than the vein and that shock does not occur if the artery is clipped and the vein left free. In part there is also what is commonly known as "reactive hyperaemia." This conclusion has been supported by comparing the weight of the injured with a corresponding uninjured part of the body. The gain in weight has been found to correspond to a loss of blood which,

it is claimed, is sufficient to cause shock. Moon, however, has attacked this thesis on the ground that it is not possible to get proper controls, for the shock reduces the amount of blood in the uninjured part, and this exaggerates the apparent gain in weight of the injured part. Blalock's results have received considerable support from Holt and Macdonald and by Charnley in Manchester and from Bell, Clark, and Cuthbertson in Glasgow. All these observers ignore the effect of a reduced peripheral resistance in the injured part, but had they done so their evidence in favour of local dilatation would be still more striking. This may be considered against the criticism of Moon. I would like to emphasize that in all such experiments there is gross damage to relatively large amounts of tissues. The pathological picture is that of haemorrhage: the internal organs are pale from deprivation of blood.

2. Toxic Shock

By this is meant shock produced by the direct action of toxic substances of different kinds on the capillaries and the setting up of the vicious circle by increasing the capacity of the circulation while at the same time there is loss of fluid from the capillaries. The evidence collected in the last war appeared to show very conclusively that this was a common variety of shock. This view was supported by practically all the official reports, and the observations on which it depends are well put forward in the writings of Bayliss, of Cannon, and, more recently, of Moon.

Previous to 1925 or so there was a general impression that the toxic substance concerned was probably histamine, because it had been shown by Dale and Laidlaw that this substance would produce shock if injected into anaesthetized cats and dogs in minute quantities. The resulting shock was in practically all respects identical with that found clinically. More recent evidence, however, has shown most conclusively that histamine is not the substance concerned, and with this conclusion Dale now agrees. Histamine can be estimated in the blood, and it cannot be found that it is increased, while it has been shown that anaesthetized man and unanaesthetized cats can cope with quite large quantities without shock being produced. It has been found, too, that, except in the skin, histamine is present in very minute amounts in the tissues of the body.

The fact that histamine may now be freed from blame does not mean, however, that shock may not be produced by toxic substances acting as histamine would act, for there are many things which can only be explained in this way. Moon, the latest active supporter of this view, considers that much the most important fact is the finding of an increased concentration of the blood in cases of shock before the blood pressure has actually fallen—indeed, when it may have risen. This early rise of blood pressure will be discussed later. The observation that the blood may concentrate is not new. It was first made by Sherrington and Copeman in 1893, and has since been confirmed by a large number of observers, both experimentally and clinically. (Actually Sherrington and Copeman measured the specific gravity of the blood, but the blood count appears to be even more delicate.) A similar concentration of the blood is found in experimental shock (Dale and Laidlaw) produced by histamine. We have, however, yet to be certain that this increased concentration of the blood necessarily indicates toxic shock, for blood concentration occurs in shock produced in other ways. The toxic form of shock certainly occurs when minced muscle is put into the peritoneum, and in strangulated

Richter's hernia and septic conditions generally. Admittedly other factors may also assist in these states. On the other hand, we remember that individuals can survive from infarction of very large parts of organs free from organisms. It is a little difficult to see, however, why shock does not occur in infarction and absorption of blood clot. We urgently need an investigation into the exact nature of the toxic substances concerned. If this could be found, means for counteraction might be devised.

One important criticism is that it is not possible to demonstrate by cross-circulation or other methods that the blood of an animal suffering from traumatic shock is toxic. We must, however, remember that it is possible that the structures acted upon take up a certain amount of the toxic substance and that the effect is cumulative. Unfortunately cross-circulations are necessarily of short duration, and it is doubtful also if in such acute experiments the damaged tissue has had enough time to produce toxic bodies.

I have already referred to the observation that removal of a tourniquet on an injured limb may lead to the onset of shock. This, as I have said, was originally a main plank of the toxic theory, but the shock is now interpreted as due to the injured part taking up blood.

LOCAL TOXAEMIA

Since it has not been possible to find a toxin circulating in the blood it is possible that it may act locally where it is produced, and this may be considered to account for the increased concentration of the blood if the area affected is large enough. According to Blalock, who has done work on experimental burning, the local accumulation of fluid is sufficient to account for the shock. The results appear to be subject to the same criticism as similar experiments in relation to concealed haemorrhage. It is difficult, too, to imagine why patients who suffer from a rapidly filling pleurisy with effusion or ascites do not also suffer from shock.

The Nervous System in Shock

In regard to the nervous system in shock there is a great deal of confusion, and with the nervous system we must couple the medulla of the adrenal glands, which secrete adrenaline. It is quite remarkable how differently modern workers have considered this matter. Some, like Blalock and Moon, almost ignore the nervous system as a factor; others, such as O'Shaughnessy and Slome, believe that the nervous system dominates the picture. It has long been recognized that during rest the blood-vessels are kept in a state of partial contraction by the action of a vasoconstrictor centre in the medulla acting through the sympathetic. If the centre is removed or the pathways from it are destroyed the vessels supplied dilate and there is a temporary fall of blood pressure, depending on the number of vessels affected. This is the basis of much surgical treatment for spasm. If the sympathetic is stimulated there is a constriction of vessels, especially of the skin and intestine, which is enhanced by the secretion of adrenaline. Now, the chief conditions which bring the sympathetic into operation are mental stress, fear, anger, pain, and cold. It is also extremely important in the normal reaction of the body to haemorrhage, and by its activity the blood pressure is maintained in spite of considerable loss of blood. It is not, however, so well known that adrenaline causes a dilatation of the vessels of the muscles. We have become obsessed by the classical picture of the rise of the blood pressure resulting from the injection of an enormous dose of adrenaline, a dose many times that ever secreted.

It can easily be shown that minute doses of adrenaline, quite insufficient to raise the blood pressure, dilate the vessels of the muscle at the same time as they constrict the vessels of the skin. This is well seen if the changes in the volume of a skinned and unskinned limb be recorded (Fig. 1). The foregoing is only one of the

FIG. 1.—Record of the volume changes in a skinned limb, S.L.V., and of an intact limb, N.L., and of the blood pressure of a cat to which a minute dose of adrenaline has been administered intravenously. The skin constriction and the muscle dilatation are well seen, and cannot be attributed to the negligible changes in the blood pressure.

many examples of the fallacy of the blood-pressure records. But even more important is the fallacy in regard to haemorrhage or shock produced by toxins. The slightest fall of blood pressure must be considered as indicating that the compensating sympathetic activity is already in action.

In considering the role of the nervous system in shock there are several possibilities. The vasoconstrictor adrenaline system may be excessively stimulated; it may be inhibited and a depressed state may succeed stimulation; it may be exhausted or damaged. Experimentally all four states may be produced.

Hitherto the most important view of the neurogenic production of shock was that the vasoconstrictor centre was exhausted. This idea was originally put forward by Crile and was extensively supported by Lockhart-Mummery in a Hunterian Lecture. It has, however, been quite clearly shown that in the majority of cases the centre is not damaged or exhausted in shock, because it will react to suitable stimuli and often the arteries are constricted. It has been taken for granted, therefore, that the nervous factor was of little importance. With a fuller understanding of the control of the circulation it has become evident that shock may be produced in several other ways through the agency of the nervous system.

3. Excessive Sympathetic Stimulation

The possibility that the sympathetic adrenal system may be over-stimulated now receives most serious consideration, because we know that this is a normal compensating process in haemorrhage and in shock produced by toxic substances. It is a new idea that the compensation may be harmful or excessive. The possibility is based on the work of Freeman, who showed that if adrenaline is infused into an animal at the rate it is normally secreted the animal passes into a state of shock associated with a concentration of blood and low blood volume. Similar results have been obtained by Britton and Cannon in decorticated animals, which pass into shock after a short period of so-called "sham rage." Quite independently G. A. Clark of Sheffield has found

that the organs of animals so shocked present the congestion and ecchymosis which Moon has found typical also of toxic shock.

Freeman suggests that in the production of shock the sympathetic by its activity causes intense vasoconstriction, a peripheral asphyxia, and capillary dilatation, and thus sets up the vicious circle. Such an asphyxial dilatation I have produced in the ear of a rabbit by prolonged sympathetic stimulation. I am, however, inclined to think that the driving of the blood into the relaxed vessels of the muscles may be just as important and allow loss of the blood plasma, for shocked patients do not become blue, as might be expected in asphyxia. It is of special interest to remark that Freeman has found that the shock is prevented, and even that from haemorrhage reduced, by removal of the sympathetic or its paralysis by ergotoxine. In this connexion it is of some interest that Lockhart-Mummery recommended the use of ergot in 1905, before its effect in reversing the action of adrenaline was known, and it may be that keeping the patient warm also reduces sympathetic activity. He also recommended the use of adrenaline!

We must, then, ask ourselves, Is it possible that similar states occur clinically? Certain facts are very suggestive. We know, of course, that in injury and in operation there is a considerable element of fear and pain; we know that cold is detrimental to shocked cases. It has been stressed, in this country particularly by Zachary Cope, that the state of established shock is commonly preceded by a period during which the blood pressure is above normal, and Moon emphasizes that the blood concentration occurs before the blood pressure begins to fall. It is stated that painful superficial burns are much more likely to give shock than deep burns which damage nerves. It may be, of course, that the toxins from damaged skin are more poisonous than those from deeper structures.

It is important at this stage to realize that the acceptance of the significance of this factor of overaction of the sympathetic does not necessarily make it impossible to hold that there may not at the same time be concealed haemorrhage into muscle; indeed, it is quite possible that the excessive contraction of the vessels elsewhere will cause an exaggeration of the haemorrhage. Certainly in the case of muscle injury it must be admitted that if, for example, the skin vessels did not constrict and drive out their blood less haemorrhage would take place. At the same time most, I think, find it difficult to believe that Nature should provide a protective mechanism against haemorrhage which so easily does harm when its help is most needed.

The importance of this factor in shock lies in the possibility that the administration of adrenaline and similar substances—for example, ephedrine—may do harm, and in the possible desirability of reducing sympathetic activity by pharmacological agents. The effect of pituitary extract on blood distribution is similar to that of adrenaline.

4. Inhibition of the Vasomotor Mechanism

Experimentally a profound fall of blood pressure may be produced in animals by mechanical stimulation, but experimentalists know that for reasons not completely understood cats vary very much in this respect. It has been found that the animals are particularly sensitive to such stimuli in spring, when the sympathetic is most active. Also, the cats must be in a certain depth of anaesthesia, and the fall is apt to occur more readily under certain

anaesthetics. The trauma necessary to produce shock is often quite small: sometimes merely repeatedly tapping the tibia or muscles is sufficient to cause shock.

Most observers use anaesthetics which unduly depress the reflexes and are therefore unable to produce this type of shock. These facts regarding anaesthetics have given critics of the neurogenic hypothesis of shock production a basis for their criticism, but I would emphasize that the same results can be obtained in decerebrate animals—the nearest imitation of the unanaesthetized patient we can obtain.

In Fig. 2 is shown the record of an animal under dial in which a fall of blood pressure was produced by driving a sharp object a few times through the muscles of the thigh. It is seen that the fall of blood pressure is

FIG. 2.—(For description, see text.)

profound and sustained. Faradic stimulation of the sciatic nerve caused a temporary recovery, but etherization of the animal resulted in complete recovery, during which puncturing of the muscle was without effect. Such a record shows most clearly that afferent impulses were responsible for the fall of arterial pressure and the state of the centre. I am not prepared to say whether the fall is due to a local or general dilatation of vessels; but such experiments, together with those of O'Shaughnessy and Slome and of Bell, Clark, and Cuthbertson, who found that shock from mechanical injury to a leg was much more difficult to obtain if the nervous pathways were blocked, again show beyond doubt the importance of the nervous system. It may be that a local vasodilator reflex like the nutrition reflex of Hess is concerned. Again we ask ourselves, Does this form of shock occur clinically? It seems most probable that it is this kind of shock which occasionally accompanies apparently trivial wounds or which may occur almost immediately after severe wounds or operations. It is stated also that shock is most likely to occur in patients who are ill and exhausted. John Hunter records two instances of men who died quite soon after having their testes bitten off by horses, and such cases of death from trivial injury are well recognized in medico-legal circles. A difficulty in the acceptance of this possibility may be the fact that we know that in shock the arteries are constricted and the skin pale, but we must remember that once the vicious circle is in operation an increased capacity effect due to capillary dilatation predominates and the vasoconstrictor centre may then compensate by causing constriction. We know that in ordinary fainting the vessels of the skin are constricted.

Whether or not central inhibition is important as a primary cause of shock requires further clinical study, but if it occurs at all it must contribute to failure of the circulation in haemorrhage and toxæmia by reducing the power of compensation.

Anaesthetics in Shock

We have, then, two clear possibilities in regard to shock produced by stimulation of afferent nerves. In one the sympathetic system may be stimulated and in the other it may be inhibited. We urgently want to know what is

happening in the sympathetic efferent nerves. According to Gaylor, there is in shock complete "silence" in sympathetic nerves, but so far it appears that only the accelerator nerves to the heart have been studied. Both types of case would obviously be benefited by anaesthesia, but, because of the well-known danger of giving anaesthetics in toxic shock, so far no one has dared to give anaesthetics as a routine to shocked cases unless it was really necessary, and then the blood pressure is not often taken. I do not think there can be any doubt that some kinds of shock are prevented by anaesthesia. This is certainly true of some varieties of experimental traumatic shock in animals, in which it has been shown that there is a great increase in the number of impulses passing up the afferent nerves from the shocked area (Beattie and Slome).

In these modern days we can scarcely contemplate operation without anaesthesia, but we have it on no less authority than that of Lister that the introduction of chloroform materially reduced post-operative shock. This is confirmed by a large number of surgeons. Some of these, like Cushing, follow Crile and prefer local blocking of nerves to general anaesthesia. This subject was referred to extensively by Lockhart-Mummery in his Hunterian Lecture. This blocking is considered to be specially important in weakly persons likely to go into shock. In experimental work there is much discrepancy on this point, largely because different workers have used different amounts of trauma and animals in different states of anaesthesia (cf. Holt and Macdonald; O'Shaughnessy and Slome).

Anaesthesia does not tell, however, if the shock is due to excessive stimulation or to inhibition of the sympathetic. But, what is still more difficult, are we justified in giving some form of anaesthetic to patients who are shocked? If morphine is beneficial would some other nervous depressant be even more valuable? These are all clinical problems that can only be solved by experiment. If the nervous factor is not a contributory factor then all anaesthetics, and even morphine, should be avoided where possible, because they reduce the normal compensatory mechanism to haemorrhage and capillary dilatation. Through the courtesy of Mr. Clark, at the Glasgow Royal Infirmary, I have tried to find out if the pulse rate in burns gives any clue regarding sympathetic activity, but so far I cannot discover anything definite. Some patients are recorded as being severely shocked with pulses of 130, which suggests increased sympathetic action, but others are also shocked with pulses of under 90. I have, however, found that practically all the patients who die are shocked from the moment they are admitted, and that death occurs on the first or the second day. I have since found that Mitchiner says that 80 per cent. die in the first two days and only 20 per cent. are septic. The type of patient suffering from burns who was admitted unshocked and died about the third or fourth day seems to have disappeared under modern treatment, although there are still a few, especially old people, who die from pulmonary complications at the end of a week. So far as burns are concerned I would agree with O'Shaughnessy that the old differentiation of primary and secondary shock is obsolete. Either the initial shock is fatal or it is evanescent.

I do not wish, however, to leave the subject of anaesthetics without again emphasizing the fact that the individual who gives an anaesthetic such as ether or chloroform in obviously toxic shock is guilty of little short of homicide. I believe Wilson has found that such anaesthetics are harmful in shock from burns.

5. Depression of the Sympathetic following Stimulation

Whenever the sympathetic is stimulated there follows a period when it is depressed or resting. This we see in the slowing of the heart and the fall of blood pressure which occur after sensory stimulation or exercise. Clinically the depression which follows intense excitement is well known. It is commonly called exhaustion; but, experimentally, during the depressed period it is quite possible to cause stimulation. It is not practicable to discuss here the possible cause of the depression (see McDowall, 1931). This type of shock may occur as a sequel to the overstimulation referred to under the heading "Excessive Sympathetic Stimulation."

On searching the older literature I found two very interesting examples of this depression given by John Hunter. He writes: "Lord Eglinton informed me that whenever two soldiers are condemned to be shot but one was to be pardoned and they were to throw dice for their lives, that commonly the successful one fainted while the other remained calm." He also records the case of a lady who awoke one night to find a man with a revolver entering her bedroom. She managed to get outside and lock the burglar in the bedroom, whereupon she immediately fainted.

Those of us who have had an operation can realize the intense relief there is at finding oneself alive and relatively free from pain when the event is over. I believe, too, that depression is quite common in airmen after a period of intense excitement. It is notorious that patients who fear operations are liable to go into shock afterwards. There are also patients who do very well in a ward but who would turn their faces to the wall and die if put into a private room. They need the stimulation of seeing others. This type of fall in blood pressure cannot obviously be considered in dealing with the shock that follows immediately upon an injury, but it might quite readily add to the effect of toxins and thus contribute to the fatal result.

6. Loss of Carbon Dioxide

The possibility that a loss of carbon dioxide consequent on a stimulation of respiration by afferent impulses might be an important cause of shock was particularly emphasized by Yandell Henderson, and it appeared to receive support from the observations of Dale and Evans that the vasoconstrictor centre was thrown out of action by over-ventilation. This observation is true of etherized animals but does not apply to all animals anaesthetized in other ways, and it is not true of unanaesthetized man. J. S. Haldane was able by overbreathing to produce in himself an apnoea of two minutes without at the same time having a fall of blood pressure (Boothby).

Clinically it has been found that the administration of carbon dioxide is not of marked value, but here again we are in difficulty. If the vasoconstriction is already excessive, like that produced by adrenaline, carbon dioxide may even do harm.

Relation of the Adrenal Cortex

Of recent years we have heard much about the use of adrenal cortex in combating shock. I will deal shortly with the rationale of this treatment. We know that removal of the cortex results in a condition very much like shock and we know that such a procedure greatly enhances the sensitivity of animals to histamine (Dale, Kellaway, and Cowell). Our knowledge of the subject is as yet scanty, but the cortical hormone appears to exercise some

effect over capillary permeability and salt balance of the body. Because of this its use has been strongly advocated in shock with a view to increasing the capillary permeability. It is, however, evident that it cannot be expected to be efficacious in every type of shock. A few successful experiments have been published by Wilson and his co-workers, but here again there is urgent need for extensive investigation.

Conclusion

At the present stage of our knowledge we must conclude that shock is a clinical state that may be produced by several processes which are initially quite different and which may act separately or in conjunction. It is, however, quite unnecessary to assume that all shock is produced in the same way. It would therefore be quite wrong to dogmatize regarding treatment; much less should we attempt to apply the same treatment to all. We must know more accurately what factors are concerned in the particular case we are attempting to treat. To obtain this knowledge detailed investigation of large numbers of cases must be studied. To make all the necessary observations a great deal of labour is needed, and I suggest that at the present time those responsible for our medical services should consider the possibility of organizing on a wide scale the study of this subject, which may soon become a primary consideration of many of these doctors.

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NOTES ON RUBELLA WITH SPECIAL REFERENCE TO CERTAIN RHEUMATIC SEQUELAE

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During the epidemic of rubella in February and March, 1940, more than 300 cases were observed. It was noticed that in a large number of these the onset and course did not follow the lines usually considered to be normal in this disease. It is thought, therefore, that these notes may be of interest in view of the fact that, as rubella does not ordinarily attract much attention and no observations have to our knowledge been published regarding it for some time, its course may have changed in some respects. Our observations may be divided into three parts: (1) differences in its onset and course; (2) differences in the complications from those described in most textbooks; (3) the question of relapses.

Onset and Course

In four cases the onset of rubella had been very acute. There had been a period of malaise lasting from twenty-four to forty-eight hours, during which a swelling of the

mucous membranes of the nose, palate, and gums, without catarrh, was noticed, giving rise to considerable trouble. After that the patients experienced a sudden rigor with high temperature, and had stiff necks and occipital headache. They also complained of considerable muscular pain at this time, and one stated that the right wrist had swelled up. A diagnosis of meningitis was made in two of these cases, and appeared to be confirmed in the morning by the appearance of a rash of the type seen in cerebrospinal fever. Within a few hours, however, these symptoms had passed off, and the correct diagnosis was made. Another such case was diagnosed as "encephalitis," while the fourth was labelled "influenza." It is worthy of remark that all the cases seen during 1939 and also the first two weeks of the present epidemic were of an exceptionally mild type.

A progressive increase in the severity of the cases as the epidemic proceeded was noted, however. We had particular facilities for observing this fact as one of our hospitals was made the clearing-station for the British Expeditionary Force, and from the beginning of February until the end of March two batches of patients were admitted each week. The severer cases all occurred towards the end of the epidemic.

Rheumatic Sequelae

Osler (1939) states that there are no special complications of rubella, but mentions that in rare instances certain symptoms may occur, among which is arthritis. Ker (1934) states that rubella differs from other infectious diseases in that it shows a remarkable freedom from complications.

During the course of the epidemic described we have been much impressed with the occurrence of various "rheumatic" symptoms. Their grades of severity range from transient muscular pains that disappeared after twenty-four to forty-eight hours (15 per cent.) to cases that were indistinguishable clinically from severe rheumatic fever, one of which is described in detail below. The muscular pains appeared on the third day of the disease (taking the average of ten unselected cases), although two patients complained for the first time on the ninth day. These pains affected the shoulder-girdle in a majority of cases, and were most noticeable on movement of the arms or on turning in bed. In some cases, however, the onset was in the gluteal and thigh muscles. Occasionally, where the patient gave a history of having suffered from fibrositis in the past, it was the site of this old trouble which became reactivated. In one case fibrositis of the lumbar region had been experienced two years previously, and on the ninth day of rubella this returned and spread down the leg as "sciatica," which did not improve in spite of treatment. On account of this the patient was ultimately transferred to England. The patients who showed rheumatic complications were not always those who had had the septic throats referred to later, although in some cases this was so.

The following cases are chosen as being typical of the mild type of temporary muscular pains encountered.

Miss A., aged 29.—Admitted 3/3/40; discharged 14/3/40. Rash appeared 3/3/40. Throat and gums normal; swelling of occipital glands. Pains in joints began 4/3/40 in wrists, knees, and ankles. No swelling of joints. Rash disappeared in three days and pains in joints improved on disappearance of rash. Temperature 99° on admission; normal since.

Miss B., aged 24.—Admitted 8/3/40; discharged 17/3/40. Rash appeared 8/3/40, with severe pains in gums. Throat normal; occipital glands enlarged; gums appeared normal. Pains in joints 10/3/40—in wrists and ankles—which kept