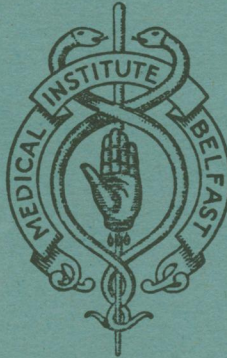


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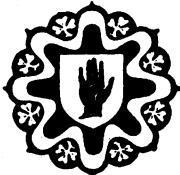
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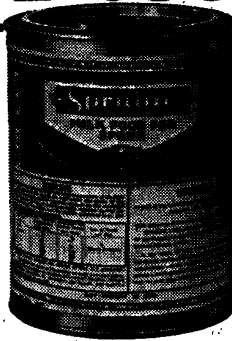
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2. Minot et al. (1928) *Amer. J. med. Sci.* 175, 599.

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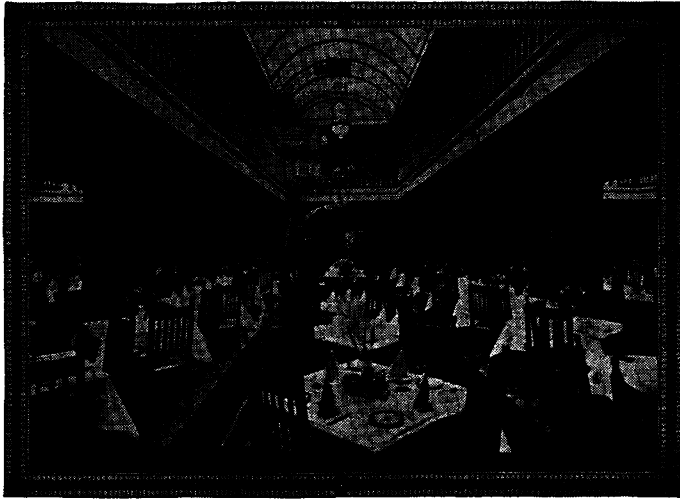
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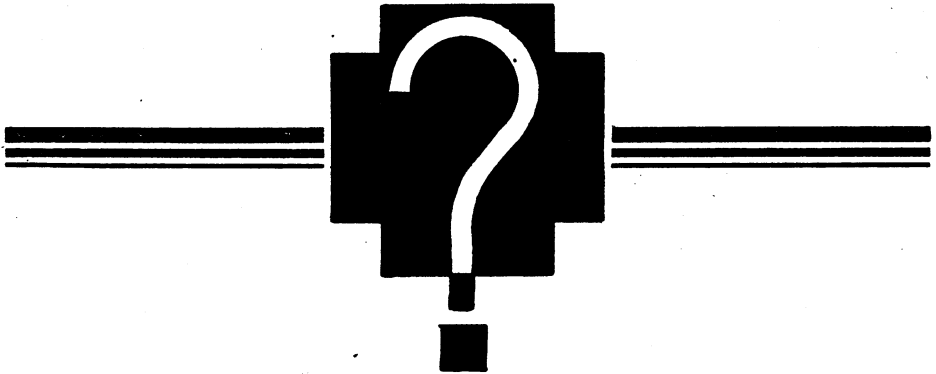
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Vol. XIV

1st NOVEMBER, 1945

No. 2

THE BELFAST MEDICAL SCHOOL AND THE WAR

WHEN Field-Marshal Sir Alan Brooke honoured the Queen's University by becoming one of its Honorary Graduates, he accorded warm and generous praise to the achievements of Queensmen and, in particular, to the response of her medical graduates both men and women. The University records, which are being compiled with assiduous care by Professor Maurice Boyd, contain 660 names of medical graduates, and we have reason to believe that there are many others who have not reported the fact of their service.

Queen's has a long and honourable association with the relief of the grievous wounds and sickness of war. In an obscure corner of the Royal Victoria Hospital, and worthy of a better place, there is a memorial tablet to David Moore, F.R.C.S.Eng. (1780-1847), which records that he was "promoted Surgeon by Lord Nelson in 1803," and was, after his retirement from the Royal Navy, Surgeon to the Hospital for twenty-six years. Nor has the call to such duties been limited to our own country's need: William McCormac served in the Franco-German War of 1870, and Joseph Nelson was so inspired by the simple and passionate political faith of Giuseppe Garibaldi, that he volunteered as a surgeon to his army. In all three branches of His Majesty's Forces, and the Indian Medical Service, Queensmen have achieved distinction. The names of Havelock Charles, John Megaw, Robert McCarrison, John Sinton, William MacArthur, John West, Brooke Purdon, William Tyrrell, Andrew Fullerton, and William McCullagh will never be forgotten.

In the war of 1914-1918 some of these and many others were awarded decorations for their gallant and distinguished conduct, and the war memorial at the University contains the names of those who did not return.

During the fateful years 1939-1945 the tradition of loyal and faithful service has been nobly maintained. So eagerly have our young doctors volunteered that it is only with the greatest difficulty that the civilian hospital services have been maintained. It is with joy that we welcome each as he returns, and it is our duty and our privilege to see to it that he is given the best chance to re-equip himself for

the tasks which lie ahead. When Field-Marshal Sir Harold Alexander became an Honorary Graduate, he appealed to the University to give every facility to the returning servicemen to enter its gates even if rules and regulations had to be broken. We are glad to know that his request was being honoured even before it was made, and that his words have not fallen on deaf ears.

There is a group of Queensmen who deserve our special gratitude: those who while still undergraduates forsook their studies to fight, and some to die, that we might live. And, although not officially members of the medical school, but of its very essence, we pay our tribute of praise to the nurses who volunteered for active service.

To the parents, the wives and sweethearts, the sisters and brothers of those whom we mourn, "those for whom life and happiness were cut to the self-same measure," we commend the kindly words of Sir Alan Brooke that we must make the memory of their splendid lives our inspiration for the future.

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Sister Doreen Pedlow.
Sister Ellen. McMillen.

*Awarded a Decoration by His Majesty the King or Mentioned in Despatches
to him, for services rendered since September, 1939 :*

ASSOCIATE OF THE ROYAL RED CROSS.
Sister Norah Earls.

MENTIONED IN DESPATCHES.
Sister Eva Caroline Daly.

War and Surgery

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At the conclusion of this, the greatest of all wars, it surely behoves us to consider the problem of war, its ætiology and consequences, what we have learnt, and how to apply the lessons of war to civil surgery. The latter applies mainly to wounds, burns, fractures, amputations, and similar conditions, leaving aside for the moment the medical side or preventive medicine, a vast subject, the success of which has been so clearly shown in this, the second great war, when, during and after a world-wide conflict under all sorts of conditions, no serious epidemic has occurred, and in which fighting strength has been conserved to the utmost, a remarkable achievement for which the medical services deserve the greatest credit.

The history of man is largely of his wars, from the earliest biblical times to our own time each important event seems to be dated by war or disease, or both, and these are man's greatest problems.

War may be considered as a disease, the most terrible of all diseases, and has been described by Pirogoff as "a traumatic epidemic" affecting people's minds and bodies, of all nations and tribes. War has always existed, nothing up-to-date has been able to prevent it. From its very nature war means wounds, and wounds need treatment, hence the development of the army medical services.

War is old and civilisation is new, so relapses into primitive savagery occur, especially among people whose ideas of civilisation are only according to their own ideas or standards, or lack of them. It has been said that "Educated men of to-day are merely primitive men who, by intelligent effort and training, have subjugated their instincts and emotions to reason. Children born of civilised peoples do not differ inherently from children born of primitive peoples. If the children of to-day were not educated and trained in the ways of civilisation they would grow up like primitive men. Every child, during its first year or two, even in the most civilised home, is nothing more than an animal, a little beast. From this stage the child develops naturally into the state of a savage. His advancement from that point onwards depends upon his training and education." This is perhaps too sweeping a statement, but it contains much of the truth, as evidenced by the Hitler youth with its Nazi training. It shows that the only hope of the future among the aggressive nations which have caused such world-wide trouble, is education and civilisation with a spiritual or moral basis.

Civilisation has been defined as self-discipline, and history has shown this to be a somewhat thin veneer, apt to crack or blister in places, or even flake off. Nevertheless, without undue flattery of ourselves and with our many faults, history again shows that Britain, from the time of Alfred the Great, who set a standard of kingship for all time, and from the time of Magna Charta, with its standard of liberty

for the people, has been the nursery of civilisation for the production and testing of the formulæ and plans of men in their affairs and ways of living. Now, with America and Russia, we, though somewhat shaken and battered, are still one of the three pillars of security against war, and of economic stability, from our history and character perhaps the most stable element, or even the keystone of this arch of civilisation.

The present state of Europe, as described by Mr. Garvin, is now worse than at any period since the Dark Ages, which was the era of misery and distress following the fall of the Roman Empire, the last years of which Hitler's Germany resembled, and which met with a like fate. A similar condition now exists over Europe, and man's greatest tragedy and curse, Civil War, will be difficult to prevent on a large scale.

It is almost incredible that a civilisation such as ours could be lost and disappear, but such has been the case before. The civilisations of Crete, Greece, and Rome disappeared, and were replaced by the misery of the Middle Ages, and what has occurred could occur again, and nearly did so. Hitler commenced his campaign by killing or interning scientists and burning the libraries, as the hostile barbarian tribes destroyed the library of Alexandria and its literary treasures, and brought a thousand years of darkness over Europe, showing civilisation to be an uncertain process, as liable to go back as to go forward. Medical science could now give the world its most healthy period, but this depends on the survival of the scientific spirit and an advancing civilisation.

Since earliest times wounds have been man's heritage, and, whether wars continue or not, industrial and other accidents will do so, and necessitate the same careful treatment, much of which has been learnt in the field of battle. It is, therefore, essential that the student should devote much more time and study to this branch of surgery, and at first, instead of learning details of rare operations, he must acquire a good working and practical knowledge of wounds and fractures and traumatic surgery in general.

The Great War established the treatment of fractures on a sound and world-wide basis, established blood transfusion, and the excision of wounds, all of which have been improved in this war and carried a stage further. New to this war, and of inestimable benefit, has been chemotherapy, i.e., the sulphonamides and penicillin, and, with all this experience and data as guides, there is now no possible excuse for bad industrial or civil surgery.

It used to be the fashion for the combatant units of the army to despise the medical services, but this branch is now recognised as perhaps the most important of all. Unless soldiers are kept morally and physically fit, they cannot and will not fight. Lord Wolseley, in his soldiers' pocket-book, described the medical officer as "the most useless officer in the army," but a more sane view is that of the late King George V, who referred to the Army Medical Service as "the one department which has never let us down." An inefficient medical service affects the morale of the troops. This was recognised long ago by the Romans, as quoted by Livy, who in his writings described the moral effects of a leader's care and interest in his

troops, and in particular in his care of the wounded. Two thousand years later, Field-Marshal Montgomery in this very city bears witness to the same principles with the same results, and extols the efficiency and value of the medical services of all ranks.

War has now lost any glamour. It is a brutal and dirty business, as shown by the relapse of the German civilisation, their concentration camps, and hospitals for human experiment. The crowning insult to medical science, as described in the Belsen trial, was the arrival of the gas for the crematorium victims in a Red Cross ambulance. In the East we have the hypocrisy, treachery, and deceit of the Japs, and their inhuman cruelty, while at the same time boasting of their honour.

Out of so much evil there has been some good. Medical and surgical progress, with its resulting benefit to humanity, has been at least expedited. "In traumatic surgery," says Crile, speaking of the Great War, "the concentrated and accumulated experience of this brief period was greater than the experience along the same lines during the past one hundred years. . . . Many new chapters were opened, some were closed and some discarded, while some were completed and their subject matter passed on to the benefit of civilian practice." War gives unlimited opportunity for experimental research and the stimulus to use that opportunity to the utmost, and this is the way to knowledge. Preventive medicine is, of course, an enormous subject, on which both war and peace depend, but at present we propose to deal mainly with wounds, their varieties and treatment.

What then do we owe to war? The creation of hospitals for the care of the sick and wounded was mainly due to the Roman Empire, which developed these, essentially from a military point of view. Between wars they also did much in the way of sanitation, water supply, housing, etc. The Crusades led to the establishment of various Orders of Mercy, the Order of St. John of Jerusalem and The Knights of Malta. The representatives of these bodies have done much fine work in the last two great wars. The Crimean War, with its tragic history of lack of medical supplies and the sufferings of the troops, nevertheless led to the foundation of the modern system of nursing, which has done as much for humanity as any other major discovery. Coming to the immediate present, war has resulted in the training of millions in first-aid, in auxiliary nursing, and general health consciousness. There have been great advances in the knowledge and treatment of industrial diseases, mass radiography, D.D.T., and penicillin, which we would probably not yet have had in more normal times.

Larrey, Napoleon's surgeon, instituted field ambulances and the excision of wounds. This latter method of treatment, however, lapsed, till it was revived during the Great War. In our own time penicillin, discovered by Fleming in 1929, was not used or developed till the stimulus of this war necessitated its use. Even the greatest wars could not continue long without an adequate medical service, and many wars have been brought to an inglorious end by neglect of this fact—witness Napoleon's campaign against Russia, when, out of the flower of the French army of half a million men, a few thousand wrecks struggled home, the remainder lost from disease and exposure.

The advance and development of science have been blamed for much of our present trouble, and certainly much of the scientist's work and achievement has been toward destruction. On the other hand, the work of Pasteur and Almroth Wright have saved more lives than wars have destroyed. This matter is being discussed in the public press at this time, with special reference to atomic energy, and suggestions have been made that scientists should not disclose their findings. This is an impracticable suggestion, as scientists from hostile nations working on similar lines would discover the secrets, and would be forced to disclose them or die in a concentration camp. Nevertheless, something must be done about the matter, and in this connection our Minister at Washington, Sir Gerald Campbell, in a recent lecture on "The Effects of Science on Humanity," says: "The scientist cannot wholly isolate himself from the rest of human affairs and remain indifferent to the wider implications of his discoveries, if civilisation is to advance into that spacious era which science is laying open to us." We must use science aright, there must be a general changing of heart, as Mr. Wells says in his "Guide to the New World," "We must now change or perish." This matter has been raised by the scientists themselves, as reported in the daily Press of 18/9/45, and which expresses their horror at the recent use of the atomic bomb, for which they blame the politicians. Certain religious elements have objected to the use of this method of war, but, when one reads of the atrocities perpetrated by our enemies, another section might think with reason that the only mistake was not to have used the method to a much greater extent. You do not discuss the moral issues with the snake or rat that bites you, you kill it as you would any deadly germ. Perhaps a demonstration might have been given first, but we all know that actual experience is usually the only effective lesson. It, however, raises the whole question of science and its relation to medicine and to human life in general.

Dr. Clark-Kennedy, in a recent lecture on "The Art of Medicine in Relation to the Progress of Thought," given at Cambridge in the early part of this year, states that "We live in an age in which scientific knowledge has outrun philosophy, narrow specialization is the order of the day, religion has ceased to be a unifying force in education, belief in the Christian revelation seems to have declined, and excessive anxiety over the health of the body has replaced preoccupation with the welfare of the soul. Humanity seems to be travelling through the night without any white line to keep us in the centre of the road. As knowledge widens, we have less and less ground in common, and our views tend to become more and more extreme.

"The art of medicine is unique in that it alone seems to occupy a middle place. Medicine has to deal with human personality, and human hopes, human fears, and human failings, in conjunction with the material human body, which is liable to so many disasters in the physical environment of our existence. Medicine could, and medicine should, be the connecting link reconciling the conflicting points of view of the humanities, on the one hand, and the sciences on the other. A purely scientific education in the arts alone is insufficient for minds compelled to live in a material world. Yet philosophy has dropped out of medical education, and the

tragedy is that medical education seems to trail along after a 'half-baked' materialism, already out of date, in an age when medicine could, and medicine must, help to integrate the arts and sciences in university education, if our sense of proportion is to be once more restored. Unless this can be done, we run the risk of losing our intellectual balance, and sinking in the sea of our own widening knowledge.

"Science looks for a definite answer to a general question. Medicine demands judgment in a particular case. That is the difference. Medicine teaches the necessity for balanced judgment, and that common sense is often a safer guide than the latest theory founded on apparent knowledge of all the facts. Medicine seems to me to teach that the white-line, though faded, obliterated in places, and always difficult to follow, is still to be found in the middle of the road."

You will say that this is neither surgery nor medicine—but war is very closely connected with both, and the soldier in his relation to his foes and the protection of his country corresponds to the doctor and his infinitely smaller but much more deadly foes—the organisms of disease and his efforts to preserve humanity. We cannot alter all these scientific and other problems suddenly, but there are at least some practical matters that we can do, and in which we can profit by past experience—that is, in the active physical treatment of wounds, and in establishing and standardising in civil life methods which have proved useful in war.

WOUNDS.

War wounds are more severe in their consequences than those sustained in civil life, the tissue destruction is greater, and the tissues are more devitalised from the heat and force of the shell or bomb fragment, more infection is blasted into the deeper layers of the wound, and the resistance to infection is diminished. The time factor between the receipt of the wound and its treatment is most important, because after six hours the wound from being contaminated becomes infected and cannot be effectively cleaned by ordinary measures. This applies more to industrial wounds, as G.S.W. are usually infected from the start, owing to the force of the projectile.

In the Great War, after a very unsatisfactory experimental period of antiseptic treatment, a fairly satisfactory basis was at last reached. This consisted in a radical excision of the wound, which was not closed by primary suture, but left open with some antiseptic gauze applied. If no sign of inflammation occurred, the wound was closed in a day or two by the method of delayed primary suture. If the wound was obviously infected and became inflamed and septic, it was left open, treated by Wright's hypertonic saline method, or the Carrel Dakin technique, and allowed to heal by granulation or secondary suture, nearly all wounds being drained.

The situation has been very much improved in this war, owing to increased experience. The wound, and especially the deep fascia is opened up to minimise tension, and the wound is trimmed rather than excised. Only devitalised tissue and a minimum of skin edge is removed, the wound is lightly packed with vaseline gauze, left open for drainage, and sulphonamides given as a routine, and penicillin

if available. The wound may not go septic; if it does the infection tends to remain local, and there is not the generalised septic infection of the Great War. The wound is often put in plaster of paris for transport, and delayed primary suture follows, or secondary suture hastened by skin grafting. The better transport in this war has improved surgical results, also the increased use of blood and plasma. This can all be done much more easily in civil surgery, where wounds are got early and radical treatment can be commenced at once.

Trueta, the Spanish surgeon, gives a good synopsis of wound treatment from his experience in the Spanish civil war. He calls it his five-point programme of basic points or principles.

(1) *Prompt surgical treatment.* Infection is proportional to the interval between the receipt of the wound and operation. This emphasised the six-hour basis between contamination and infection. He also emphasises the avoidance of numerous aid posts and frequent dressings. The patient should be rapidly transported to the main dressing station, usually in hospital.

(2) *Cleansing the wound.* No antiseptic known is equal to soap and water for wound contamination.

(3) *Excision of wound.* This must be properly done; incise, then excise dead tissue.

(4) *Provision of drainage*—by vaseline gauze and rubber strips.

(5) *Immobilise in plaster*—direct to the skin except over bony points. Without considerable experience, the plaster should be split after application.

To these should be added—

(6) *Chemotherapy*—now recognised to be a very important factor in wound surgery.

I would express agreement with Trueta's observations during the Spanish civil war that the best antiseptic is soap and water, many of the stronger antiseptics doing far more harm than good by killing tissue cells and providing a growth medium for bacteria. I have not for years put iodine, spirit, or any other violent antiseptic into or around wounds.

Another important advance is the more constant putting of wounds in plaster, although this was instituted by Lister. The plaster splint supplies the essential principle of rest to the wound, and prevents secondary infection, which has so often occurred owing to the too frequent dressing of wounds. Sulphonamides and penicillin may be given in traumatic surgery as in war wounds, when serious infection is thought possible.

Good results have recently been quoted in that most important branch of industrial surgery—finger and hand injuries and infections, which are such a steady loss to both employer and employee. Experienced industrial medical officers, using penicillin and vaseline gauze, have greatly improved the treatment of such conditions, and secured earlier return to work with hands and fingers showing a surprising degree of recovery following severe injury.

FRACTURES AND COMPOUND FRACTURES.

Here again the same principles apply, splints are more simple and consist of either the skeleton type of Thomas splint, made popular by the late Sir Robert Jones, and plaster of paris, or both combined.

It is a matter of history, which you will no doubt remember, that the mortality of compound fractures of the femur in the early days of the Great War was about eighty per cent., and this fell to twenty per cent. by the routine application of the Thomas splint in the field, with traction from a skewer passed through the boot. Improved technique in this war has been a Thomas splint with fixed surface traction, combined with plaster of paris, the so-called Tobruk splint, which immobilised the wound and fracture and facilitated transport by ambulance or plane, the toilet of the wound being carried out as before, with routine chemotherapy. This method would, of course, be less necessary in civil practice, as the case could be got to hospital quickly and unhindered, but nevertheless the method could and is being used in hospital with skeletal traction. If the wound has been efficiently treated, it does not go septic, and the plaster of paris case prevents secondary infection, and prevents meddlesome interference. Penicillin is most useful in such cases, as a staphylococcal infection of bone is most persistent, and once established is likely to be permanent. In this connection, if penicillin has done nothing else, its beneficial results in osteomyelitis would have been of outstanding benefit to humanity. In many recent cases, it has appeared to cure the infection in a few weeks, which took as many years even to become chronic, and at the expense of gross deformity, loss of function, and permanent crippledom. This is a horrible disease, which for some reason has of late years become more frequent and more virulent, and, but for this war, penicillin would probably not have developed till much later, if at all, and many staphylococcal septicæmias and cases of osteomyelitis now recovered would have been lost or hopelessly crippled.

BURNS.

In this sphere war has provided ample stimulus and opportunity for experiment leading to increased knowledge of the treatment of burns. This has been a machine and petrol war, with enormous numbers of burns, and we have got through much trial and error to a moderately sound basis of treatment.

The classification of burns has been simplified into superficial and deep, according to the degree of skin involvement. Superficial burns only involve the superficial layers of the skin, and so are sometimes called partial. Where the skin is completely burnt through, the burn is classified as deep or complete, the skin being the important factor. Of course, the same burn may be both superficial and deep, superficial in one part and deep in another. Without going into great experimental details, I will describe briefly the treatment of a badly burnt child, which must go to hospital without delay.

First-Aid Treatment.—If the patient is going to hospital, and all bad burns should go to hospital, little is done beyond covering the part with a clean towel,

wool, and bandage. No local treatment whatever should be done (except in the case of airmen who cannot get treatment for some days: here there are various applications which may be used). The patient should be well wrapped up, kept warm, given hot drinks, and perhaps a sedative, if trained personnel is available.

In Hospital.—The general condition is assessed on arrival, the B.P., Hb., etc., estimated. If these are satisfactory and shock is not marked, suitable sedatives are given and the patient taken to the theatre. Here the surrounding skin is shaved and washed with soap and warm water, sterile towels applied, and the burnt area treated in a similar manner. Dead tissue is gently removed, blisters are snipped away, the area is frosted with sulphonamides or penicillin, or both, and dressed with squares of vaseline gauze, and covered with a thick, soft, wool dressing and crepe bandages. In bad cases, the child is nursed in a plaster shell on an abduction frame, which is convenient for nursing purposes, and sulphonamides are continued by mouth or otherwise. Subsequent dressings may be done in a bath, or under some form of anæsthesia. In deep burns, early skin grafting will be beneficial and cause more rapid healing. In a severely shocked child, the burn must not be touched till the general condition has improved, and here is the great indication for plasma. Great quantities of fluid are lost from burnt areas, and the fluid and protein must be replaced. Blood transfusion is not given here, but is most useful later when anæmia and failure of healing is common. Here blood transfusion often produces wonderful results.

With regard to tannic acid and similar fixatives, these are only used in minor domestic burns of small size and superficial type, such applications being positively contra-indicated in deep burns.

This technique has taken years to standardise, but has now reached a fairly satisfactory basis, after considerable confusion. Good nursing will pull a child through, where indifferent nursing will lose it. This is a most important factor which is sometimes lost sight of.

SHOCK AND HÆMORRHAGE.

The pathology of shock has been considerably simplified, at least from a practical point of view, which is that shock is due to loss of circulating fluid, plasma in the case of burns, blood in the case of wounds. The treatment is, therefore, early and rapid replacement of these fluids.

Blood transfusion, of course, was established as a successful procedure during the Great War, and the advance in this war has been in team-work, organisation, blood banks, the public response as donors. The use of group 0 or 4 as standard has simplified procedure, and here again the lessons learnt in war will benefit many in civil surgery. Blood is already getting more scarce and less readily available, though industrial accidents are rising, and unless some form of transfusion service remains for the giving, grouping, and storing of blood, we will to some extent lose the full advantage of this method as seen in war. There is still an enormous field for blood transfusion, both in accidents, various medical diseases affecting the

blood, and especially in maternity cases, and, if this service continues, it will ensure that such patients, who would once have died, will now live.

As an extension of this, the importance of protein replacement has been emphasised, and much work done in the giving of amino acids, hydrolysates, and so on for starvation. In this field much more remains to be done, and by these means we should be better able to prepare patients for operation and sustain them afterwards. In civil surgery during the war period we have found blood and plasma of inestimable benefit in burns, and also in the secondary anæmias following septic infections or wounds. The amount of these fluids given is much larger than formerly, and I have yet to see any ill effects from giving large quantities, provided reasonable care and judgment is used. The case of a boy with a burst appendix illustrates this. The boy had a neglected perforated appendix, the abdomen full of pus, and his general condition was very bad. After operation, which was mainly for drainage, he developed signs and symptoms of intestinal obstruction, thought to be mechanical rather than paralytic. A jejunostomy caused enough improvement to allow operation, at which a loop of small bowel was freed. The jejunostomy then began to digest his anterior abdominal wall, and he wasted to a shadow. Another operation succeeded in closing the jejunostomy, and he recovered, but the point emphasised is that he had seven transfusions during his illness, without which he would not have recovered.

CHEMOTHERAPY.

The dream of the scientist, worked for so hard by Erlich and others, was at last realised in this war, antiseptics being used to kill bacteria in the tissues without injury to tissue cells. The action of the sulphonamides and penicillin are so well known to you all that there is little fresh to add at the moment. You will remember that the discovery of penicillin followed Fleming's interest and work on antiseptics, as a result of his investigations on this subject during the Great War, when he was even then seeking for the ideal antiseptic. In 1928, he first noticed and recorded a preliminary survey on the action of penicillin, but, lacking the stimulus of war, this was not proceeded with at the time. It was, however, taken up by Florey (1940-41) and his team of workers at Oxford, but, for a considerable time, was not available in sufficient quantity, owing to the technical difficulties of its production and the enormous cost of producing it on a sufficiently big scale. Here American methods of organisation came to the rescue, and there was sufficient penicillin for the Services towards the end of the war, and we can now get adequate amounts for civil surgery. Points of interest are its effectiveness in extreme dilution, and, most important, it is perhaps the first powerful antiseptic which is non-toxic and does not injure the tissue cells. Its use has saved countless lives and limbs in the latter stages of the war, which would otherwise have been lost, and it was used to bridge the gap between the time a man was wounded and the time he reached a base hospital. In civil surgery, it must facilitate primary suture in many cases, with consequent shortening of convalescence and rapid return to function. The enduring benefits to wounds, of course, remain, and are increasingly available for civil surgery. I think, however, these drugs should be used under proper pathological

control, and after due examination of the type of organism. The practice of giving the patient, or the patient giving himself, sporadic doses is to be deprecated, and will result in the drug being ineffective when most required.

PERIPHERAL NERVE INJURIES.

I have had a large personal experience of these cases extending back to the Great War, and such injuries are also fairly common in civil surgery. Children frequently get cut with glass, and adults (often nurses) frequently get severe cuts on the wrist from crockery or milk bottles, often dividing important nerves.

From a large series of cases, the following conclusions were reached:—After any serious wound, nerve lesions should be sought for and tests carried out. Too often we find a wound sutured and a peripheral nerve paralysis only observed later, when the optimum time for successful suture has passed. Any severe wound should be opened up and investigated under local or general anæsthesia. If a doctor is not prepared to do this, he should at least make the patient carry out a few simple test movements to try the ingenuity of the main nerves of the limb. If such movements cannot be carried out, the wound should not be sutured, but referred to a surgeon for special treatment. Loss of sensation, of course, occurs in the area supplied, but in motor nerves is not very extensive and may easily be missed. From my experience in this field, I think the only hope of a good result is early primary suture. This should usually be possible in civil surgery, though often this is not possible in war from service conditions, and where large portions of a nerve are actually lost. Purely motor nerves, such as the radial or muscular spiral, recover well with good function after primary and even after secondary suture. Mixed nerves, such as the medial or ulnar, do not recover well except under the very best conditions. Recently Mr. Souttar reported good results of ulnar nerve suture in children, which is encouraging, but his two cases described were the motor branch of the ulnar, and, as I said previously, motor nerves recover well. The cases illustrate, however, that it is always worth while trying suture.

THE AMPUTATION OF LIMBS.

I have a special interest in these cases also, having been in charge of this branch following the last war, and have observed their progress since then, and in the present war. There is but little change in the amputation results other than has been described in the treatment of wounds, which, of course, is very considerable, and many limbs have undoubtedly been saved by modern methods and chemotherapy. There have, however, been many losses of limbs from the greatly increased use of mines, which produce very destructive wounds. The resulting wounds have been treated on general principles and the limbs only amputated when grossly destroyed. Amputations done in the field have been good, the surgeons following a standardised technique. That surgical horror, the guillotine amputation, has not been used in our services, some form of flaps being cut. The Americans, however, have told me that they are not allowed to use any other method, and this produces an unnecessarily bad stump. Most cases will require trimming or re-amputation, and some

of these have been bad, due to having been done by temporary surgeons in temporary home hospitals, without adequate experience in this work.

An interesting historical commentary on this subject dates back to the earliest times in Egypt. This states that the sick and wounded in campaigns are treated according to standard methods compiled by learned and experienced men. The narrative continues: "If, following the prescriptions of this sacred book, they fail to save the patient, they are absolved from all guilt; but if they run counter to its directions they are put to death, for the law-giver judged that few physicians are more competent than a system tested by time and compiled by the best." This point serves to illustrate the difference between civil surgery and army surgery in war. In the latter, standard methods of surgery were laid down by consulting surgeons of experience, from which the surgeon in the field, C.C.S., or base hospital was not allowed to depart, although the penalty for doing so was not so extreme. The rule, nevertheless, was wise, and contributed to the general good results. This is more difficult to arrange in civil surgery, where there is no limit to what a man may undertake or attempt, whether competent or not, but the efforts of such a one will become more limited with definite lists of consultants and of surgeons, outside of which, if a patient goes, he does so on his own responsibility.

The Ministry of Pensions has issued much valuable information on the subject of stumps, suitable lengths of amputation, etc., and have given four standard sites which they regard as optimum. This is, no doubt, sound in a broad, general sense, but with experience in the subject, other levels are often better in suitable cases. This is essentially a technical point, so I will not go into details, except to indicate to the surgeons that what is called an 'end-bearing' stump, i.e., one on which the patient can bear weight, always gives a much superior stump, e.g., a good Syme's amputation, or one through the knee-joint, though not artistically handsome, is often extremely good from a functional point of view. These variations, however, require personal experience, and, no doubt, standard methods and lengths are more foolproof, but occasionally waste valuable length and support.

The artificial limbs themselves are now extremely good in the lower limb. In the upper limb, appliances are used according to requirements on a short prosthesis, and a light show or dress hand kept for appearance. There is no substitute for the human hand, and the principle remains that every possible effort should be made to save even a portion of a hand or finger. Stumps should be fitted early with at least a temporary appliance, both for its physical and mental advantage.

A recent surgical report on the B.L.A. illustrates a further stage of surgery in war-time. Here maximum results were attained by team-work, efficient organisation, ample supplies of blood and penicillin, and routine standardised methods of treatment. Needless to say, the results were excellent in such conditions in an advancing army with complete air cover, ample supplies and personnel, all constituting overwhelming superiority in all forms of equipment, which, however, is not quoted to take away credit for a good job well done, but to illustrate what can be done and what should be done more often in civil life.

Much more could be said on these subjects, but this is enough to show how war surgery is related to civil surgery. We have learnt much from our comrades in the field, and the student must learn and appreciate the differences in technique in the forward areas and at the base (which areas were often less defined in this war than in the last), and we try to express a balanced opinion on what should be done at each stage in the best interests of the patient. With our wealth of scientific knowledge, and with the accumulated experience of two great wars under every variety and circumstance, it is the bounden duty of every medical officer to know at least the standard surgical principles governing the treatment of wounds and burns under war and peace conditions, and to know how to treat his patient conscientiously and well.

Coming to traumatic surgery in civil practice, recent figures from the T.U.C. show a considerable rise in cases of injury or disease incapacitating men for more than three days, as shown from the figures 1938-1943. In the latter year, the cases had risen to 173,000, an increase of 41,224, while meantime the numbers employed in the industry had fallen by 74,000. In 1938, there were 2,500 fatal and 450,000 non-fatal accidents in industry, for which six and a half million pounds were paid in compensation. In this city, in one of the big industrial firms, the medical officer, Dr. James Smiley, has done much to prevent and reduce accidents. By careful organisation, good nursing, and good technique in the treatment of wounds, he has also reduced the sepsis rate of the less severe industrial accidents, mainly involving fingers and hands, from eleven to less than one per cent., a most remarkable local improvement in the treatment of wounds.

There is one other cause of accidents—motor accidents, which constitute nearly one-half of the total accidents to the general public, and are much more numerous than those occurring in coal mines and factories, and which are now so familiar that they do not affect us much unless personally concerned. These constitute a serious loss to the community both in money and life. They are a constant drag on hospitals and a prolific source of crippling deformities. It is again a sad reflection on our state of civilisation that this should be so, and that our intelligence cannot devise some remedy. We cannot now go into the pros and cons of "Safety First" movements, and the various objections to the term as tending to inhibit the spirit of adventure, but there is no intelligence or spirit of adventure shown in being criminally careless in traffic problems and indifferent in this matter.

In this last war the safety and comfort of the troops was looked after much more carefully than in previous wars, and risks taken only after due consideration and with all possible preparation. Such methods, however, do not apply to the roads in peace-time, and we as doctors, who see so much of the results, should study the problem more, and force the civil authorities and those above them to take steps, which even now are obvious to all, to remedy this national disgrace. In this matter also we cannot dissociate ourselves from the public, and, as in food, housing, and public health, generally play a more decisive part in the life of the community.

What then of the future? Medico-political changes are in the air, and no one

quite knows what will happen next. Many Poor Law infirmaries in England have become general hospitals under the Ministry of Health, and thus, being freed from financial difficulties and with an ample supply of beds, may become the leading hospitals if a State Medical Service should come. We must not forget, however, that it was due to the failure of these state hospitals, in an earlier stage, to deal adequately with the problem, that led to the foundation of the voluntary hospital, whose record of unselfish service and teaching is indeed a glorious one. These voluntary hospitals are now often financially embarrassed, and worried by impossible waiting-lists, whereas the municipal or state hospitals are weighed down by a burden of civil sloth, lack of interest and foresight. Both tend to be understaffed and overworked. These are problems which the young surgeon and physician must take an interest in and work for their improvement. There has been too much *laissez-faire* and lack of unity in the past. Like the scientist, it will not do to dissociate ourselves from medical politics, and at least all are agreed that some change is necessary.

The country town must have one or more competent surgeons, and an adequate local hospital for ordinary and traumatic surgery. The more serious cases can be sent to a central or key hospital. In the large town there should be more accident hospitals, or, at least, accident departments, where cases are seen by senior practising surgeons who are sufficiently well paid to have time to deal with this work, which is now so often left to the newly-qualified M.O., who, with the best intentions in the world, has not had adequate experience in wound and fracture surgery. The young surgeon should earlier be able to secure a living wage, so that he is not forced to take on far more work than he can possibly do efficiently. These and other points, especially the modernised teaching of the student, the medical societies are studying at present with care and attention.

While the war was on there was one single aim—Victory, and we were never more unselfishly united as when the peril was greatest, and never achieved finer results. With the end of the war, there is no purpose, no incentive common to us all, selfish interest tends to creep in and clog our efforts. There could be an aim, purpose, and cause common to us all—the battle of health, which is the basis of life and happiness; the improvement of health services, adequate hospitals and staffs, and better traumatic surgery. We must learn and know the facts of social medicine, make these public, and interest others in the fight. This cannot be left to municipal authorities, politicians, and experts; these matters are the responsibility of every one of us. Much has been left undone, and there is much talk about guilty men; but one lesson is obvious, that there is little good blaming others. Let us blame ourselves for what we did not do to prevent war or to improve social conditions. The only thing to do is to see that this calamity of war must not happen again, and social conditions are improved. The war was fought to make the world safe for democracy; now let democracy make the peace safer for the people, and not a breeding-ground for fanatics, freaks, and financiers, while children are dirty and starved, as they are now starving all over Europe. Let us use the established facts of better health to establish this new democracy, and these facts we must

first learn, and then act on them. All such information can be easily acquired once the desire to acquire it exists.

Lieut.-Col. Nelson, in the *B.M.J.* of 22/9/45, writes on "Housing and Health," with special reference to the lot of the slum-dweller. He gives statistical proof of the ill-health and high mortality rate of the poor, and emphasises their misery, cold, hunger, and general discomfort. He points out the need for rehousing, essential foodstuffs, warm clothing, and a social security system which will provide the basic amenities of life for all those who are prepared to do an honest day's work. Housing is important, but these other factors are equally important, and this problem must be undertaken by team-work of all the different civic and medical bodies concerned. As a profession, we should have a much greater say in, at least, the health policy of the country, and should insist on many necessary reforms being carried out, not put aside. The only means to the end is a live and abiding interest for each one of us in the welfare of the community and of our own profession, and to work unceasingly to this end.

The war has been won, but the war against disease and bad social conditions goes on. Each advance, each scrap of knowledge has only been achieved through sweat and toil on the part of someone. As the Great War was largely lost by lack of imagination and foresight, let us not neglect the lessons of this one by our lack of effort and interest, and let us bring to bear on civil surgery and on the social problems of peace, the united co-operation and energy that characterised our efforts for war.

A fitting conclusion is the words of Pasteur, perhaps the greatest scientist of all time, who died just fifty years ago, and whose work was all constructive and for the good of mankind. These words were used by him at the opening of the Pasteur Institute and apply even more to-day than then: "Two contrary laws seem to be wrestling with each other nowadays: the one of blood and death, ever imagining new means of destruction and forcing nations to be constantly ready for the battlefield; the other a law of peace, work, and health, ever evolving new means of delivering man from the scourges which beset him. . . . The latter places one human life above any victory, while the former would sacrifice hundreds and thousands of lives to the ambition of one. . . . Which of these two laws will ultimately prevail God alone knows."

REVIEW

THE ELEMENTS OF MEDICAL TREATMENT. By Sir Robert Hutchison, M.D., D.Sc., LL.D., F.R.C.P. Bristol: John Wright & Sons Ltd.

A VOLUME in the classical tradition of medicine, which has become synonymous with the Hutchisonian tradition. It is a 'recast' of the author's lectures on therapeutics to The London Hospital students, and provides a useful introduction to practical everyday prescribing. The teaching is conservative, succinct, and interlarded with strong common sense. Some clinicians would cavil at Sir Robert's half-hearted commendation of sulphonamides in pneumonia; none will quarrel with his distilled wisdom in the management of dyspepsia and high blood-pressure. T. H. C.

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A Synopsis of the History of Ophthalmology

By JAMES R. WHEELER, M.B., F.R.C.S.ED., D.O.M.S.

Hon. Ophthalmic Surgeon, Royal Victoria Hospital, Belfast

Opening Address, Royal Victoria Hospital, Belfast, Winter Session, 1945-46

It is my pleasant privilege, as a member of the Honorary Medical Staff, to extend to you a warm welcome at the beginning of this session.

You are now part of a great team which is running this hospital and, as such, you will be called upon to perform your allotted tasks. This hospital may be comparatively young in years, but our forefathers have endowed us with many advantages, and our aim should be to transmit these to future generations not only unimpaired but with increased efficiency and value.

In pre-clinical days your attention has mainly been directed to your books, but in the clinical period it must be divided equally between books and men. It has been said that there is no more difficult art to acquire than that of observation.

The study of your fellow-men, their habits, character, mode of life, their behaviour under varied conditions, their vices, virtues, and peculiarities, is a vast and interesting subject.

Don't worry too much about what you will do when you qualify. As R. L. Stevenson has said, "To travel hopefully is better than to arrive, and the true success is in labour."

This session is a notable one, as after six long and arduous years of war the world is now at peace.

Four hundred and twenty members of our medical profession have gone directly from our midst to serve with His Majesty's Forces, while many others who were practising in England and various parts of our Empire have also played their part. We are justly proud of this record and the achievement of these men.

As ever in war, some have been called upon to make the supreme sacrifice. We honour their memory, and offer our special sympathy to those of our colleagues who have lost gallant sons.

To-day it gives us sincere pleasure to welcome home the following members of our Honorary Medical Staff: Lt.-Col. J. T. Lewis, Surg.-Capt. R. S. Allison, Lt.-Col. C. A. Calvert, and Surg.-Commdr. F. A. MacLaughlin. Also to welcome home, and to our Staff, two of the newly appointed members: Brigadier Ian Fraser and Lt.-Col. Howard Crozier. We hope before long to be able to welcome Major Eric McMeekin, and to-day we welcome two other newly appointed members to our Staff: Mr. J. S. Loughridge and Mr. Ian McClure.

We are glad also to see Surg.-Commdr. H. E. Halt home again, and hope that the following members of the Auxiliary Staff will soon be back with us: Majors J. C. Davidson, J. Houston, D. H. Craig, R. W. Strain, D. J. C. Dawson, and Surg.-Commdr. W. Lennon.

All realise the difficulties which the Honorary Staff have had in carrying on the routine hospital work with very depleted numbers, and in fact, it would have been impossible to do it if our Consulting Staff had not come to our aid. Although Sir Thomas Houston, Dr. V. G. L. Fielden, Mr. J. A. Craig, Mr. H. Hanna, Mr. H. Stevenson, Mr. S. T. Irwin, and Dr. J. C. Rankin had officially retired from active service on the Staff, they one and all answered our call for help and willingly returned to duty. We tender to them our sincere thanks.

To-day, as the result of war, we are living in one of those crises of history which cause a great social upheaval in human society. Steady peaceful progress is replaced by a sudden jerk forward and, as a result, we must adapt ourselves to the new environment.

The future position of our profession in its relationship to the State is being examined by our legislative authorities, and so it behoves us (the present holders of our birthright) to be certain that the public, and we ourselves, have our views clearly set out.

That great statesman, Winston Churchill, recently remarked: "The longer you can look back, the further you can look forward." And so to-day I propose to trace the history of Ophthalmology from the earliest times, race you through the Middle Ages, and so up to the present day. I will endeavour to pick out the chief actors and emphasise the part they played in unravelling the history of about 4,200 years.

The uncertainties of unrecorded history make it impossible to say where the dawn of civilisation began, but the earliest mention of any medical matter is found in an ancient work on law. About 2250 B.C. Hammurabi, a king of Babylon-Assyria, promulgated a collection of laws. A considerable number of sections of these laws relate to ophthalmology—or rather to ophthalmic negligence or malpractice; e.g., one such law states that:—

(196). If a man destroy the eye of another man, they shall destroy his eye. (In the case of a freeman he shall pay one manna of silver, and in the case of a slave he shall pay one-half his price.)

Another states:—

(215). If a physician open an abscess in a man's eye with a bronze lancet and save that man's eye, he shall receive ten shekels of silver; if the eye is destroyed, they shall cut off his fingers; if a slave's eye is destroyed, he shall pay one-half the price of the slave.

This age is obviously the Bronze Age, as bronze instruments were being used.

The practice of medicine and surgery of these times was almost wholly in the hands of priests and was mixed with the greatest superstition and magic. Apparently no patient was treated without the appropriate magic incantation being duly recited.

The scene now changes from Babylon 2250 B.C. to Egypt 1650 B.C. A priceless document was found between the legs of a common mummy at Thebes and purchased by the Egyptologist Ebers from an Arab.

This Papyrus Ebers, as it was called, consisted of 110 pages or columns, and describes all the diseases and remedies that were known to the Egyptians of that time. Of these 110 columns, eight are devoted exclusively to diseases of the eye, and treatment is advised for such troubles as pain in eye, tear in eye, pus in eye, blood in eye, turning of eye, dimness of sight, etc. Common medicaments employed were:—onions, leeks and beans, castor oil, pomegranate, copper salts, oxymel of squill, hemlock and opium.

In these days of Ancient Egypt all learning of the times was imparted in the temple schools, and so priests were doctors and doctors priests. Anatomical knowledge was generally poor, which is somewhat extraordinary when one remembers that an essential portion of the religion of the time was embalming of all bodies, both rich and poor.

These Egyptian doctors did, however, practise inspection, palpation, percussion, and auscultation, if even in a rudimentary way; while some of their public health laws were excellent.

In Homeric times there were many gods of healing, but Æsculapius was greatest of all.

Many Æsculapian temples were built which were half temple and half hospital. They were served by priests, who gave medical and surgical instruction. Possibly the subtle art of suggestion, to patients previously rendered highly liable to suggestion by want of food and drugs, was often practised by them.

In 460 B.C., in the Golden Age of Greece, Hippocrates was born, and had as contemporaries many great and immortal men such as Socrates and Thucydides. To Hippocrates, who is usually referred to as the Father of Medicine, we ascribe the oath which bears his name and the many writings which are said to be his. It is almost certain that the oath was in use before his time, and also that all these writings were not those of Hippocrates the Great. Nevertheless the title "The Hippocratic Art" is well justified, because Hippocrates completed the separation of scientific medicine from temple practice and magic. He introduced into medicine the science of observation and inductive reasoning. Finally he taught that "The physician is a servant, not a teacher of nature"—do enough, but never too much.

What Hippocrates failed to understand was that there were various sorts of disease. His crude pathology made treatment a question of influencing his four cardinal humours—blood, mucus, yellow bile, and black bile. This was attempted by restrictions in diet, hot foot-baths, irritant gargles, cupping, venesection, the cauterising of blood vessels in the neighbourhood, multiple incisions down to bone, and even trephining of skull.

In the treatment of ocular affections the acute variety were treated by venesection and cupping, with local counter-irritation, at some remote distance, to draw the humours away from the eye. The chronic affections were treated mainly with local application of milk of women and gall of goats, but various preparations of copper, iron, and lead were also used.

Greek medicine was practised not only in Greece but extended also to Alexandria

and Rome—this period extends from the time of Hippocrates to the end of the fruitful era of the Roman Empire (about eight hundred years).

The Alexandrian school introduced collyria for treatment of eye diseases. The collyrium was a solid medication (not a liquid) containing multiple secret ingredients made up in a cake, the basis being gum. Seals or stamps used to imprint inventor's names, ingredients, etc., on the collyrium have been recovered in large numbers. A fragment of cake was dissolved in water, oil, milk of women, urine, bile or saliva before use.

The disease which was such a scourge to eyes was trachoma. It has been described as "as old as the Nile and the desert," and certainly caused tremendous suffering and much blindness.

Three famous men's work was accomplished in this period of Greek medicine—Celsus, Pliny, Galen. Celsus of the Alexandrian school wrote "De Medica" in A.D. 29. It is mainly a compilation, but written in excellent Latin. Out of a historical void he gives a detailed description of couching for cataract. The name cataract was adopted later by Constantinus Africanus—the Greek name was "hypochyma" and the Latin "suffusio." The names all express the humoral implication—in "suffusio corrupt" the humour was supposed to collect in a space between the pupil and the lens, thus obstructing visual spirits. When suffusio was fully formed it could be displaced into a part of the eye rather than in front of the lens by means of an operation. Operation consisted of entering a sharp strong needle into the eye and gently working the suffusio away from the pupil.

Roman writers of this period were interested in the problem of why the pupil is black. Pliny made the observation that the eyes of nocturnal animals were brilliant in the dark; but the fact that no animal radiates light it has not received was not appreciated for many years to come.

Galen (A.D. 131-201). Next to Hippocrates this old Roman master of medicine has been called the greatest of all physicians. Unfortunately, his books on optics and diseases of the eye have been lost in the tide of time. He did, however, add to the knowledge of the anatomy of the eye. He declared nature created nothing defective and nothing in vain. He describes the eye as the most divine of organs, and admires the wisdom of the creator who took such care of brain and retina. Like Hippocrates, he thought the crystalline body (lens) to be the essential organ of vision; and his ideas on cataract were the same as Celsus'. He believed the function of the retina was to perceive the alterations which occur in the crystalline body and to communicate them. He used hyoscyamus to dilate the pupils for cosmetic purposes.

It is interesting to note that in this era Julius Caesar raised the status of physicians who were permanent residents in Rome by granting them citizenship. These physicians were mainly Greeks or slaves, as the better-class Roman only took up legal or administrative posts.

THE ARABIAN PERIOD (A.D. 850-1375).

About A.D. 630 there appeared the Prophet Mohammed. By 1050 the Turks

under the banner of Allah began a reign of conquest and Christian persecution in the then-known world of the Eastern Mediterranean. One unfortunate result of this was the burning of the famous library at Alexandria : this has created a gap in these ancient writings which can never be refilled. The Arabians did, however, translate some Greek writings into Syriac and later into Arabic. Unfortunately they revered the authority of tradition and did not learn the crowning wisdom that fact is greater than dogma. And so, alas, many mistakes were perpetrated in these translations.

The Crusades against the banner of Islam (1096-1272) had one advantage, that, as a result of travel, some Eastern learning began to filter west.

Before decay overtook the Arabian Renaissance the torch had been handed on to Western Europe by the translations into Latin from the Arabic version of the Greek masters. Also, at this time we have the work of an Arabian genius Alhazen, whose Optics were the earliest basis of our present science.

Interlocking with the Arabian era there began a period of systematised intellectual effort in the schools of Salerno and Montpellier.

The famous monk Constantinus Africanus translated Arabic writings into Latin, and thus began a movement which gathered speed with years. Later Beneventus Grassus wrote a book giving a good summary of Greek and Arabic teaching. It is important historically, as it is the only book of its kind which was translated into many different languages.

In this era there appeared an interesting treatise on the hygiene of the eye by one, Peter the Spaniard, who later became Pope John XXI.

The conception of contagiousity of ophthalmia was offered by John Yperman.

It is hard to say exactly when the genius of man discovered the fact that glasses relieve the ocular defects of nature. In the days of the Roman Empire short sight diminished the market value of a slave. The old Roman patrician's only means of overcoming his presbyopia was to make a slave read to him.

The observation that segments of spheres can be used as magnifying glasses was not original to Roger Bacon, but this English monk, physicist, mathematician, and philosopher was the first person to recognise clearly the use of lenses for old people and for those with weak sight. In 1268 Roger Bacon in his *Opus Magnus* treats of the science of optics in general and lens in particular. He recommends the use of a plain convex lens, with the thickness smaller than the radius, as an aid for seeing for the old. Such lenses were to be used resting on the page to magnify the text.

Bacon had shortly afterwards to flee before Papal wrath, but before doing so he probably passed his ideas on (indirectly) to Alexander de Spina—a Dominican monk at Pisa. The latter is generally accepted as the inventor of spectacles.

The existence of rock glass was known from the earliest times, but the evolution of spectacles parallels the evolution of civilization.

There is no doubt that rock crystals were probably used by prehistoric man to make tools and as a burning-glass. Placed opposite the sun's rays, the crystal is a most useful contrivance to produce heat and as a remedial agent for cauterising

the human body. The ancient Egyptians, Greeks, and Romans knew well the art of polishing rock crystals.

There is a common belief that glass-making and spectacles came from China, but this is not so. There are records of Confucius (551-479 B.C.) and earlier Chinese writers containing various stories to which claims are attached. It is more probable that glass-making and spectacles were introduced into China via India by trading Israelites coming from highly advanced nations settled along the Mediterranean.

Pliny, the historian (A.D. 23-79), credits the discovery of glass-making to the Phœnicians, who rested their cooking-pots on blocks of natron (subcarbonate of soda). The heat of their fire fused this alkali with the sand of the shore to produce glass.

Amongst the earliest existing examples of glass is a small lion's head of opaque blue glass of very fine colour. The example is in the British Museum, and is of Egyptian origin dating to about 2500 B.C. Records of Assyrians in the Near East about that time give a detailed process for making glass and also the actual material used. The glass of these early periods was used for decorative purposes or objects of art. Remains of window-panes were found in the ruins of Pompeii, as were also some convex lenses with very short focal lengths.

It has long been established that primitive tribes devised light protective goggles before contact with civilisation. The Eskimos have long used wooden goggles hollowed out to fit over the eyes, and held in place with string or a leather thong tied round the head. Small horizontal slits served to admit the minimum of light, while the back of the wood was blackened with smoke, black paint, or graphite.

For centuries masks were devised for treating squints, forcing the faulty eye to assume a normal position in looking through a small aperture. Coloured glasses were made in the latter half of the sixteenth century, chiefly green, blue, or smoked glasses, or amber lenses, etc.

The invention of printing in 1440 established spectacle-making as an industry, as many persons now found it necessary to correct their visual errors.

The similarity of spectacle frames about this time indicates a common source of origin. In 1465 the Spectacle Makers' Guild took part in a review before the French king.

The earliest known lenses were for the correction of presbyopia, but they were first used as a hand-glass. It was only later that methods were devised to support the lenses before the eyes.

It is interesting to note that men of dignity and learning were always portrayed wearing spectacles. Amongst the Chinese, frames, even without lenses, were a badge of superior social status and learning. Also the tortoise was a sacred reptile to the Chinese and, therefore, tortoise-shell rims were thought to be conducive to good fortune and long life.

The next lenses developed were for the correction of hypermetropia. It was not until the sixteenth century that myopic lenses came into use. Little is known as to how the power of the lenses was designated during this period, but probably the age of the wearer was the basis of classification.

The seventeenth century marks the beginning of a new era in progress in the optical field. In 1623 Daza de Valdes, a notary of the Inquisition at Seville, mentioned cataract lenses. In 1608 Galileo Galilei constructed his telescope on the model of Hans Lippershey of Holland, and discovered four satellites of Jupiter, demonstrating the fact that they revolved round the planet. This gave a new impetus to the lens-grinding profession. During this century Newton conducted his famous experiments on the composition of light. He was the first to decompose light by prisms and recombine it again. This definite knowledge paved the way for further experiments in optical lenses and apparatus.

About the same time as the telescope was being constructed the microscope was also coming into use. A Dutchman called Leeuwenhoek was studying his "little animals," as he called them, and in 1673 first published his observation to the newly formed Royal Society in London. It is interesting to note that England was still at war with Holland at this time, and until 1874, but the historian records that the nations had been at war without being angry. Now Leeuwenhoek has been given the title of "Father of Bacteriology and Protozoology," and he was undoubtedly the first to see and describe his "little animals," but he made no attempt to carry his findings any further. The super-excellence of his lenses, which he taught himself to grind, polish, and mount, together with the exceptional keenness of his eye, puts him at least a century ahead of all other microscopists. Surely there must have been a want of an inquisitive genius in the following age?

The theories enunciated by Galen persisted for centuries, but about the year 1500 Leonardo da Vinci, the famous Italian painter who produced the "Mona Lisa," was the first to discover that the retina, and not the lens, was the essential organ of vision. He also realised the principle of the "camera obscura" as applied to the eye.

During the sixteenth and seventeenth centuries the facts of physiological optics began to be slowly accepted, and one Robert Hooké first measured the minimum visual angle (the basis of our present-day test-types).

Clinical progress had, however, not made much headway, and it was not till the beginning of the nineteenth century that Brisseau convinced the Academie Royal des Sciences that cataract was really an opaque lens.

It is said that Susruta of India in 3000 B.C. had described the true pathology of cataract, stating it was due to derangement of intraocular fluids. It is also said that this surgeon practised antiseptic surgery—fumigating his room prior to operation and insisting that hands, nails, hair, and beard were kept clean.

In 1748 Daviel (France) first published his planned operation of extracting the opaque lens from the eye through the anterior chamber. It took about one hundred years for this operation to be accepted as far superior to the old operation of couching with all its resulting complications.

Daviel's principle of extracting the opaque lens from its capsule is still employed up to present times, but of course the technique has been much improved. To-day the intracapsular extraction of the lens (i.e., removing the lens complete with capsule) is rapidly gaining ground. It was invented by De la Faye in 1753, but

it was only after 1890 when Herbert of Bombay, and Mulroney and Smith in the Punjab (all members of the Indian Medical Service) published their results that it began to be accepted.

With the intracapsular extraction of the lens good results are brilliant, but the operation is more difficult to perform, and if accidents do occur the resulting consequences are more serious.

The last great ophthalmologist of the pre-scientific era was William Mackenzie of Glasgow, whose textbook on Ophthalmology was the book of the day, translations being used both in Germany and France. He is credited with the earliest recognition of the fact that increased intraocular tension was the essential factor in glaucoma.

I now come to the three factors which so greatly contributed to revolutionise medicine in general, and surgery in particular.

1. *Bacteriology by Pasteur*.—Leeuwenhoek observed yeast-cells, but did not appreciate that these structures were living organisms. Pasteur confirmed that putrefaction and fermentation have their origin in germs.
2. *Antiseptic surgery introduced by Lister in 1869*.
3. *Anæsthesia*.—The ancients tried vinegar, mandragora and other plants, as well as ice and snow, to try to render surgery painless. In 1842 ether was first used as a general anæsthetic by Long in America, and shortly afterwards Simpson of Edinburgh introduced chloroform.

Cocaine was first used in ophthalmology in 1884 by Carl Koeller of Vienna, but it had been used some years previously for nose and throat work.

To-day it is difficult for us to imagine what surgery was like prior to these days. Now operations could be performed painlessly, and especially with delicate operations as on the eye without the patient moving at the critical moment. Also, the first battle had been won against that dreadful enemy of the surgeons—sepsis.

In spite of these three major discoveries the ophthalmic surgeon had still one great nightmare, which is present even to this day; i.e., sympathetic ophthalmia—an inflammatory reaction in an injured eye spreading to the non-injured eye, with resulting loss of vision. In 1818 Waldrop noted the fact that veterinary surgeons destroy the injured eye of a horse, with lime or with a nail, so that the good eye may be saved. To-day we can prevent sympathetic ophthalmia occurring, but we are unable to cure it when once it is established.

The application of the principle of the magnet in removing metallic foreign bodies from injured eyes has preserved sight in an untold number of cases. In 1842 Nicholas Meyer first removed a foreign body from inside an eye by applying a magnet to the scleral wound. Later Dickson of London and McKeown of Belfast further improved upon his technique. In 1875 Hirschbeg invented the powerful electromagnet which is used to day.

The outstanding invention of the ophthalmoscope by Herman Helmholtz was destined to make ophthalmology the most exact of all clinical sciences. In 1851

he published his paper describing the apparatus which enabled him to do what for centuries had baffled his predecessors—view the inside of the living eye. Apparently one; Baggage in England, had done the same thing a few years previously, but unfortunately had failed to publish the fact.

The great ophthalmologist of this day was Albrecht Von Graefe of Berlin (1828-1870). In this age of "clinical intuition" he took full advantage of this new ophthalmoscope by examining the interior of the eye and describing the normal and pathological pictures which were revealed to him thereby. Von Graefe laid the foundations of a scientific and practical clinical ophthalmology. It is, however, with glaucoma that his name is most frequently associated.

The term glaucoma goes back to Hippocratic times, and was generally accepted to mean a greenish or bluish appearance of the eye. It was then supposed to be an affection of the lens as opposed to cataract, which was a perverted humour in front of the lens. The term was probably applied loosely to all forms of blindness, other than cataract, in which the pupil changed colour.

The essential feature of glaucoma—a rise in the intraocular tension—was only generally appreciated about 1840, but Von Graefe was the first man to measure clinically the intraocular tension, to describe the cupping of the optic disc and the pathological changes in the visual fields.

Von Graefe noted that corneal staphyloma regressed when an iridectomy was performed, and in 1857 he described his classical operation of a broad iridectomy to relieve the congestion in cases of acute glaucoma. His pathological conceptions may not have been quite correct, but his operation was to be the means of preserving much vision and the saving of untold suffering.

Since his day various operations have been devised to establish extraocular drainage in order to relieve increased intraocular tension, notably Leger's sclerectomy, Elliott's trephine, and Holt's iridencleisis.

The drugs which are used to-day in the conservative treatment of glaucoma—those producing an artificial contraction of the pupil—were not discovered until 1862. In this year the miotic effect of calabar bean was noted—later Eserine (1864) and Pilocarpine (1875).

The fact that extracts of hyoscyamus and belladonna produce artificial dilation of the pupil had been known for centuries, but it was only in 1831 that Mein isolated the atropine alkaloid (Homatropine 1879).

To Von Graefe is given the credit of establishing the proper clinical use of these two groups of drugs.

In this wonderful scientific age many countries produced men equal to the occasion. Sir William Bowman (Britain) was not only a distinguished ophthalmologist and scientist, but he has been described as the greatest of all anatomists. De Schweinitz (U.S.A.), Fuchs (Vienna), De Weckers (France), and Danders in Holland, are names that will certainly remain in history, as will also Credé for his method of preventing ophthalmia neonatorum, and Hutchinson for his classical description of inherited syphilis.

The twentieth century opens with advantage being taken of the improvement in

the microscope, which afforded greater accuracy in histological studies. In 1904 Sir John Parsons gave the world a complete monograph on "The Pathology of the Eye." The year 1911 marked the climax of 150 years struggle to find a satisfactory clinical method of illumination of the anterior parts of the living eye. Alvar Gullstrand of Upsala, Sweden, had produced his "slit-lamp microscope," so that one could now view the anterior structures of the eye with a high binocular magnification.

The greatest triumph of this century in ophthalmology has been a method of treating retinal detachment. Gonin of Lausanne published his method of closing the retinal rents and searing the loose membrane back into position, by means of thermal and chemical irritants applied to punctures in the sclera. His technique has since been improved upon by Larsson, Safar and Weve, who used diathermy, and Vogt who used electrolysis.

Previous to Gonin's time all these eyes went completely blind, while to-day in over fifty per cent. of cases the sight is preserved.

For over one hundred years attempts had been made to regain the transparency of an opaque cornea by means of grafting. In 1922 Tudor Thomas of Cardiff, after a long series of experiments, succeeded, the secret of his success being that he applied grafts from animals of the same species.

The intellectual supremacy of man is a result of appreciating and interpreting complex visual patterns. In many modern achievements it is frequently some optical device that contributes to the final result—without optical instruments, clinical and scientific laboratories, motion picture studios and observatories, etc., would be almost helpless.

Prior to the eighteenth century the use of glasses was unnecessary to the majority of individuals, as the ability to read or write was the possession of the learned few, and the costliness of the glasses made them prohibitive to the average individual.

Astigmatism was demonstrated by Young in 1801, and in 1827 Airy designed suitable cylindrical lenses.

A trial case of lenses was arranged in 1843, while test types were devised by Jaegar in 1854.

For a long period the art of fine optical glass-making was shrouded in secrecy, and passed along from father to son.

The main constituent of optical glass is sand, or silica. Sand makes up 12 per cent. of the earth's crust, yet only a few known deposits will furnish a suitable quality for optical glass. In general this glass contains about 70 per cent. sand, 11 to 13 per cent. calcium oxide of lime, 14 to 16 per cent. sodium oxide or soda, with a small percentage of potassium, borax, antimony, and arsenic to aid in improving quality. The raw materials are united by fusion or melting at relatively high temperatures in special crucibles made of burnt clay. In order to obtain the high standard of optical glass to which we are accustomed to-day an accurate control over the entire manufacturing process must be maintained.

It is over fifty years since the first attempt was made to make a contact lens.

i.e., a lens which fits between the lids in actual contact with the eyeball. The idea is to abolish a faulty corneal refracting surface by substituting an accurate one. In certain cases with high or difficult refractive errors the visual improvement to the patient is tremendous. The great difficulty, however, is for the patient to tolerate a glass in contact with the eye for any length of time, but by the modern method of obtaining an accurately fitting glass this tolerance time-factor is being extended.

The last decade has seen our pharmacopeia re-written by the introduction of the sulphonamides and penicillin. The former made possible a great advance in the treatment of trachoma, and in the cure of ophthalmia neonatorum. Penicillin has demonstrated its wonderful power in external eye infections, and ocular wounds, but up to date has been disappointing in deep intraocular infections. It is too early, however, to arrive at definite conclusions.

To-day we here, the members of the Staff of this Hospital, are helping to plan a new Health Service for the nation in general and for our own Medical School in particular.

Our prayer is that we may be enabled to "think clearly," as it is only by clear thinking that real progress can be achieved.

It is exactly one hundred years ago (1845) that the first permanent ophthalmic unit was established in Belfast. Dr. Samuel Browne, R.N., J.P., who later became Mayor of Belfast, opened The Belfast Ophthalmic Institute at 35 Mill Street, Belfast.

About twenty years later this unit became the present Belfast Ophthalmic Hospital. Sir John Walton Browne, who succeeded his father on the Staff of the Ophthalmic Hospital, was also a surgeon on the Staff of the Royal Victoria Hospital. He said he was going to make the Ophthalmic Hospital his hobby and that some day he hoped to see established in Belfast an Eye Hospital worthy of the city. Being a practical man, he left a large sum of money* with that end in view.

Two years ago, in a presidential address to the Belfast Medical Students' Association, I suggested that the Belfast Ophthalmic Hospital, the Benn Ulster Eye, Ear, Nose and Throat Hospital and the Ophthalmic Department of the Royal Victoria Hospital should combine and build a new unit in the vicinity of the Royal Victoria Hospital and the Institute of Pathology.

Thanks to the helpful co-operation of the various Boards of Management concerned, this idea has materialised, and concreted plans for such a unit are now under consideration.

The practice of medicine has now become so complex, it is essential that all branches combine to pool their knowledge in order to obtain the best results.

With this end in view it has been decided that there should be established a large out-patient or diagnostic block attached to the main hospital which will be common to all units. Here a free interchange of knowledge between various departments will be readily available.

When it comes to rendering special in-patient treatment and further research

each unit will have its own pavilion or hospital within the colony where this work can be carried out.

This should ensure more adequate material and better facilities for the teaching of, not only undergraduates, but also post-graduates.

But when our new organisation is completed will we be in Utopia? That depends as always on us as individuals.

In the highly scientific age of the last century perhaps the machine has had more attention than the man. Perhaps disease has had more attention than the patient. Let us remember that the microscope does not observe nor do our books think.

The reputation of a Medical School will depend not so much on its hospital and laboratories as upon the character and ability of both its students and teachers.

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REVIEW

MODERN TREATMENT YEAR BOOK, 1945. Editor: Surgeon Rear-Admiral C. P. G. Wakeley, C.B., D.Sc., F.R.C.S., F.A.C.S. London: The Medical Press and Circular.

THIS Year Book has won a well-deserved place in the affections of many practitioners, and the current volume will enhance its reputation. The galaxy of brilliant contributors is a guarantee of the authenticity and interest of the work. The subject matter has been chosen with some care, and there is not a single dull page in the volume.

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T. H. C.

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T. H. C.

Some Aspects of Nutrition in War-time

By H. E. MAGEE, D.SC., M.B.

FOR many years physiologists have recognised that the basic food requirements for similar types of persons living in similar environments are in a broad sense equal. The factors which determine food requirements are sex, age, climate, and amount of muscular exercise. Income and social status have nothing to do with requirements. The war has given practical application to this principle; our rations and priorities take no account of income or social status.

REQUIREMENTS.

The first really authoritative and comprehensive statements of dietary requirements were made by the League of Nations Technical Commission on Nutrition from 1935 to 1938.^{1, 2} These recommendations of the Commission were not published in a form directly applicable to any given country. Before applying them it was necessary to take into account the age and sex distribution of the population, average weights and types of occupation. George and I did this for the population of Great Britain in 1938, and the result, shown in Table I, was published in 1939 and 1943.^{3, 4}

I would emphasize that the values in this table are statistical averages and that they are not necessarily applicable to individuals within a given age group. For reasons which, in our ignorance, we must call constitutional, there are variations even among individuals of the same age, sex, weight, and occupation, in regard to food requirements, just as there are variations between individuals in blood pressure, pulse rate, concentration of hydrochloric acid in the gastric juice, and other physiological phenomena. That there are variations amongst individuals is one of the most fundamental of all the biological laws. It is, nevertheless, frequently forgotten by medical as well as lay people, and failure to take account of the principle can cause much bother in the administration of a national scheme such as that for our national dried milk. The average size and number of feeds for infants are printed on the packets of milk, as a rough guide, but often they are interpreted as being rigidly applicable to individual infants.

Some figures in the Table require further comment.

CALORIES.

The daily calorie requirement of the average man in Great Britain is given as 3,000. This does not mean, for example, that a group of farm labourers will be satisfied with 3,000 calories; they would require about 4,000. Nor does it mean that a group of sedentary workers require 3,000 calories; they would be satisfied with, say, 2,700. The same qualification would apply *mutatis mutandis* to other selected groups.

PROTEIN.

The requirements for protein depend more than anything else on whether new tissue has to be formed. It is high for children, adolescents, expectant and nursing

TABLE I
LEAGUE OF NATIONS COMMISSION.
STANDARDS FOR ADEQUATE DIET.

YEARS	1-3	3-7	7-12	12-15	15-17	17-21	Males 21+	Females 21+	Expectant and Nursing Mothers
Calories -	1100	1500	2100	2900	3000	3000	3000	2400	3000
Protein (gm.) -	42	50	65	95	100	90	70	60	80
Calcium (gm.) -	1.1	1.3	1.4	1.5	1.4	1.1	0.8	0.8	1.5
Ferrum (gm.) -	5.0	8.0	13.0	16.0	15.0	13.0	10.0	10.0	13.0
Vitamin A (I.U.) -	3000	3000	3000	3000	3000	3000	3000	3000	5000
Vitamin B ₁ (mg.) -	0.55	0.75	1.03	1.45	1.00	1.00	1.00	0.83	2.00
Vitamin C (mg.) -	30	30	30	30	30	30	30	30	45
Cost weekly in 1942 -	4/0½	5/7½	7/6	9/5½	9/6½	9/-	9/-	8/4	9/6

mothers, and highest of all for adolescents and mothers. The same applies in general to all constructive nutrients such as calcium and iron. The British rations and priorities are in conformity with these requirements. Expectant and nursing mothers, children and adolescents can obtain relatively and absolutely (for mothers and adolescents) more constructive and protective foods than other consumers. The requirement of protein for the adult depends on weight, 1 gm. per kilo is regarded as adequate. The weight of the average man is usually taken to be 70 kg., but it is in fact less than this in these islands. The requirement does not vary with occupation. A man engaged in muscular work does not need any more protein than a sedentary worker of the same weight, nor does he require as much as his wife if she is pregnant or nursing, or as his adolescent son. The practical application of this principle cuts across old established but quite erroneous customs.

It is customary for the housewife to give a larger proportion than he needs of protein-rich foods, such as meat, eggs, and cheese, to the bread-winner. Children and adolescents are also often deprived of similar articles of diet for the benefit of the father. It does not do the father any good to over-feed at the expense of other members of the family. There is no physiological justification for this custom, and the sooner it is stopped the better for the health of communities. It is a good rule and in accordance with scientific evidence that, if there must be sacrifices in the family, they should be made for the expectant or nursing mother and not by her.

ANIMAL PROTEIN NEEDS.

It is frequently stated that the requirements of animal protein, or so-called first-class protein, are so and so, and that given diets provide such and such proportions of the requirements. There is, however, no evidence indicating how much animal protein is necessary or even desirable for good health. In fact, perfectly good health has been maintained on a purely vegetarian diet. What is important is that the diet should contain all the essential amino acids in digestible form and in sufficient amounts. A mixture of animal and vegetable proteins is the most suitable and acceptable to most people, but in precisely what proportions they should be is not known.

NUTRIENT REQUIREMENTS OF THE NATIONAL RESEARCH COUNCIL.

The National Research Council of the U.S.A.⁵ drew up new food standards in 1941 (see Table II). Apparently they were dissatisfied with the vitamin requirements given by the League of Nations Commission, because these have been very considerably increased. Their standards for calories, protein, and minerals are practically the same as those of the League of Nations. The requirements for vitamins given by the N.R.C. are, for the most part, quite unattainable in Great Britain, having regard to prevailing food habits. The National Research Council have not published any convincing reason that I know of to justify these high values. The League of Nations standards will almost certainly be improved as knowledge increases, but there is little doubt in the minds of many experts in this field that the N.R.C. values for vitamins, however true they may be for U.S.A.,

TABLE II
RECOMMENDED DAILY ALLOWANCES
OF THE NATIONAL RESEARCH COUNCIL (U.S.A.)

	Calories	Protein (gm.)	Calcium (gm.)	Iron (mg.)	Vitamin A (I.U.)	Thiamin (mg.)	Ascorbic Acid (mg.)
CHILD							
Under 1 year -	900	36	1.0	6	1500	0.4	30
1—3 years -	1200	40	1.0	7	2000	0.6	35
4—6 years -	1600	50	1.0	8	2500	0.8	50
7—9 years -	2000	60	1.0	10	3500	1.0	60
10—12 years -	2500	70	1.2	12	4500	1.2	75
Boys							
13—15 years -	3200	85	1.4	15	5000	1.6	90
16—20 years -	3800	100	1.4	15	6000	2.0	100
GIRLS							
13—15 years -	2800	80	1.3	15	5000	1.4	80
16—20 years -	2400	75	1.0	15	5000	1.2	80
MEN							
21+ -	3000	70	.8	12	5000	1.8	75
WOMEN							
21+ -	2500	60	.8	12	5000	1.5	70
Pregnant -	2500	85	1.5	15	6000	1.8	100
Lactating -	3000	100	2.0	15	8000	2.3	150

are far too high for Great Britain. This is particularly so for vitamins A and C. For instance, the adult man is said to require 5,000 I.U. of vitamin A and 75 mg. of vitamin C daily. Our present rations and allowances only give about 1,700 I.U. of vitamin A daily. To get the remainder, a man would require to eat 55 oz. of cabbage or 2.2 oz. of carrots daily! In regard to vitamin C, we may take it that the rations provide none of this vitamin to speak of. To get 75 mg. per day a man would, for example, have to eat 13 oz. of potatoes and 17 oz. cabbage, swedes, and carrots, allowing a 60 per cent. loss for cooking, which is usual (Table III)

Individual determinations of the consumption of vitamin C by 250 schoolchildren were carried out in two industrial towns in England in 1943-44, and the average daily consumption was 23 mg. per head daily over a month in winter. (Individual figures for consumption are not available.) The average amount provided by the school meals taken over a period of a month varied from 2 to 16 mg. per day in different schools. With very many schoolchildren under present circumstances, particularly in industrial areas, the school meal provides practically the entire intake of vitamin C. It therefore follows that many children get, and for years have been getting, only a fraction of their requirements as recommended by the N.R.C. It may be argued that the intake, although sufficient to prevent deficiency disease, is nevertheless too low for optimum health. The fact is, however, that scurvy is practically non-existent in Great Britain. In nutritional surveys, which I shall speak about later, carried out by expert clinicians during 1942-45, and covering over twenty thousand people of both sexes, all ages, and varying occupations, scattered all over Great Britain, we found no evidence of anything resembling scurvy. If 75 mg. is in truth the daily requirement for a child aged 12 years, then scurvy ought to develop rapidly when the intake amounts to only 2-16 mg. We have yet to see a school child, whether or not it eats school meals, showing any evidence whatever of scurvy.

The use of the word "sub-clinical" has been used for some time in nutritional literature. The term is mere hypothesis. "Clinical" indicates an objective reality; something we can appreciate with the senses. "Sub-clinical" then must mean something that we cannot appreciate with the senses, and if we cannot appreciate it, how do we know of its existence? If there were any objective evidence of its existence it would be "clinical" and not "sub-clinical." "Pre-clinical," it seems to me, is what is meant, namely, undetectable derangements of function which, if they are allowed to persist become detectable, and therefore clinical, but "pre-clinical" is just as much hypothesis as "sub-clinical."

STANDARD REQUIREMENTS : HOW ARRIVED AT.

Energy needs have been established by determining the energy output by direct and indirect calorimetry in different physiological states on people of both sexes, varying ages, and occupations, during sleeping, lying, standing, and working at various occupations. From the determined output of energy the amount required can readily be calculated. For protein, calcium, phosphorus, iron, and other minerals balance experiments have been employed. The general procedure is that

TABLE III
 AMOUNTS OF VITAMINS A AND C IN RATIONED FOODS
 AND ESTIMATED QUANTITIES OF UNRATIONED FOODS REQUIRED IN ADDITION TO
 SECURE 5,000 I.U. OF VITAMIN A AND 75 MG. OF VITAMIN C.

VITAMIN A, I.U.			
RATIONED FOODS, February, 1945.			
Meat	- -	12 oz.	- 144
Cheese	- -	3 „	- 1,107
Milk	- -	2 pts.	- 1,600
Dried egg	- -	4 oz.	- 3,408
Butter	- -	2 „	- 2,272
Margarine	- -	4 „	- 2,272
*Sardines	- -	3 „	- 231
Herrings	- -	3 „	- 27
*Prunes	- -	4 „	- 785
*Dates	- -	2 „	- 16
		—	
TOTAL (per week)	-		11,862
		(per day)	- 1,695
		*"Points" goods.	

VITAMIN C, MG.			
Rationed foods	- - -		0
Potatoes	- -	13 oz.	- 52
Swedes	- -	6 „	- 42
Carrots	- -	5 „	- 10
Cabbage	- -	6 „	- 84
		—	
		17 „	188
Cooking loss 60%	-		113
		—	
			75

DATA ON VITAMIN C CONSUMPTION
 FROM TWO LARGE COUNTY
 BOROUGHES IN ENGLAND.

Average daily consumption for 250 schoolchildren in winter of 1943-44 = 23 mg.

Vitamin C content of school meals over a month in 1943-44 = 2.16 mg. per meal in different schools.

the intake and output are determined over varying lengths of time and the intake is varied; the point at which balance occurs is taken to represent sufficiency of the nutrient in question. These procedures are quantitative and results are predictable with a fair measure of accuracy.

Vitamin standards are not arrived at in the same quantitative fashion. Partly they have been determined from the doses required to cure actual human deficiency disease, partly from human feeding experiments, and largely by the application of the results of animal feeding experiments to man. Obviously balance experiments with vitamins, which are required in such tiny amounts, are out of the question.

Precisely because vitamin standards have not been arrived at by a strictly quantitative procedure, the standards cannot be regarded with the same degree of confidence as those for other nutrients. There is a large element of speculation about them, and every statement of requirements of vitamins, therefore, has to be interpreted with much latitude on the plus and minus side. They should be regarded merely as giving rough indications of requirements.

PRINCIPLES OF WAR-TIME FOOD POLICY IN THE UNITED KINGDOM.

This was based broadly on the science of nutrition. Before the war there existed statistics of food production, of imports, of exports, and of the amounts of different foods which went into human consumption; dietary surveys had given us much knowledge of the amounts of different foods consumed by different sections of the population and also of deficiencies which existed.⁶ There also existed much detailed information about family budgets, including expenditure on different items, such as food, rent, and clothing.⁷ This background was, of course, of inestimable value in planning food policy for war. I cannot go into all the details; I shall only attempt to give you a few examples of the measures taken so as to illustrate the scientific principles underlying the War Food Policy.

Milk.—Milk has been called the keystone of the nutritional arch and demanded first attention. It was obviously essential to ensure that production should be maintained, and increased if possible. The commonest dietary deficiency before the war was in respect of calcium, and the deficiency was most marked in poor families with young children. Milk and cheese are the chief sources of calcium. Therefore, it was desirable that a scheme should be devised to ensure sufficient milk to those most in need of it, namely, mothers and children. Supplies had to be ensured in the first instance. This meant giving priority in animal feeding stuffs to dairy cattle. They were placed before beef cattle, poultry, and pigs. Dairy farmers were urged to produce more milk, farmers who had not produced it before were urged to take it up, and all farmers were urged to produce more and more of their own feeding stuffs. Pigs and poultry, as competitors with man for human food, had to be reduced. It should be remembered too that the ratio of conversion of vegetable into animal food varies with the animal. In this sense milk is the most economical and beef the least. For instance, the dairy cow converts into energy in the form of milk 60 per cent. of the energy in its fodder; the figure for the beef animal is only about 10 per cent.⁸

National Milk Scheme.—This scheme first of all defines physiological needs for milk and then establishes measures to supply them. Expectant mothers, children, adolescents, and certain classes of invalids, called the priority classes, were given first call on available milk supplies, and the cost of such milk was much reduced or, in case of need, supplied free. To each class of priority consumer certain quantities of milk were allocated, and everyone in these classes, irrespective of income or social status, was entitled to receive his appropriate allocation. Mainly because of the operation of the scheme, consumption of milk and therefore of calcium, protein,

and other nutrients in milk, has gone up in the poor families with young children, but has gone down in the small wealthy families compared with pre-war times.

Skimmed Milk.—Before the war practically every authoritative body that made pronouncements on nutrition deplored the improper use, and especially the waste, of this valuable food which went on in many countries of the world. Before the war large quantities of skimmed milk were fed to pigs and poultry, and large quantities of it were also run to waste. At the same time in Great Britain, we were importing large quantities of skimmed milk in condensed form for human consumption. Very little skimmed milk is produced in Great Britain now, but large quantities of it are imported and consumed as “household milk.” The high nutritive value of skimmed milk for children has been proved beyond doubt by Orr,⁹ Aykroyd,¹⁰ and many others. It is an interesting reflection on the mentality of modern man that elaborate series of feeding tests were required to convince him of a truth which is at once obvious by reflecting on how skimmed milk promotes the growth of rapidly growing animals like the pig and fowl, and on its composition relative to whole milk. I hope we have seen the end of the stupid waste and improper use of this excellent food, for it is unquestionably improper use to give any skimmed milk to pigs or poultry so long as there is a human being who would benefit by it.

Potatoes and Vegetables.—The dearth of shipping made restrictions on imports of fruit unavoidable. The first question to settle was whether to concentrate on the import of one or two varieties and prohibit others, or whether imports of all varieties should be uniformly reduced. It was decided to import only the orange, because in all-round nutritive value it is superior to other fruits. Later on, imports of oranges also had to cease. To compensate for this deficit in the national dietary, it was necessary to increase the production and consumption of potatoes and vegetables. The chief concern was over the adequacy of vitamin C, but it was, of course, fully realised that potatoes and vegetables are very valuable for other nutrients besides vitamin C. Potatoes are important sources of calories and protein, and vegetables of carotene, vitamin B and mineral salts, as well as of vitamin C. Farmers were accordingly urged to increase the production of these foodstuffs; farmers who had not previously produced them were urged to do so. In addition, allotments on the outskirts of every town and village in the country were vigorously developed.

Bread.—Bread is the most important source of energy in countries of western Europe. This is derived from its carbohydrate and, to a lesser extent, from its protein content. In order properly to utilise the calories from carbohydrate, corresponding amounts of the B vitamins are required. These, in so far as we understand their function, are concerned primarily with physiological oxidations. Wholemeal is a rich source of these vitamins as well as of iron, but it also contains a substance, phytin, principally in the bran, which immobilises calcium, forming an insoluble and unabsorbable salt. If the diet contains only a minimal quantity of calcium, then absorption and metabolism of calcium would be disorganised, and rickets or osteoporosis would ensue. A diet rich in calcium from any source will neutralise this effect of phytin. Abundance of milk or cheese would have this effect, but when,

as was the case in Great Britain, the milk supply was insufficient and the intake of calcium uncertain, then it was a wise precaution to fortify bread made from higher extraction flours with calcium. Calcium also improves baking qualities.

From the beginning of the war experts on nutrition and others had been advocating on health grounds the raising of the milling extraction above the 75 per cent. then prevailing. Up till April, 1942, the bulk of the bread consumed was made from white flour of 75 per cent. extraction. This is very poor in vitamin B and in iron, but contains little or no phytin. In April, 1942, 85 per cent. extraction flour for bread-making became compulsory. This, while very rich in B vitamins and iron and other protective nutrients, also contains fair amounts of phytin. It was therefore essential to neutralise the effect of phytin by the addition, to all flour used for bread-making, of a certain proportion of chalk.

The Medical Research Council had recommended this extraction rate as giving the maximum nutritive value of the wheat grain with the minimum of indigestible fibre (bran), and also the addition of calcium. The present rate of extraction is 80 per cent.

These examples will, I hope, give you some idea as to the basic principles underlying our war-time food policy.

RESULTS OF WAR-TIME FOOD POLICY.

The war-time food policy is the first application of the science of nutrition to the national dietary; not, however, in the fullest sense, for our consumption of milk is too low, especially for the ordinary consumer, so also are the consumptions of fat, of fruit, and certain other things; but, within the limits imposed by available supplies, we can say that the people of Great Britain have been fed during the war in accordance with the principles of nutrition. The effects on the health of the country that have been observed, have gone a long way towards proving that the application of the new knowledge of nutrition is a powerful factor in determining the well-being of communities.

NUTRITION SURVEYS.

Since 1942 the Ministry of Health has been conducting systematic surveys of the nutritional state of samples of the population all over England and Wales. These surveys were begun by Dr. Sydenstricker and were continued by Drs. Hawes and Stannus, and then by Drs. Adcock and Fitzgerald. All of these clinicians had previously had many years' experience in the recognition and treatment of deficiency disease; the first in U.S.A. and the other four in various parts of the Colonial Empire. Table IV gives a summary of the results up to the middle of 1944. These surveys were of the so-called rapid type. They were designed to give a rough picture of the state of nutrition of large groups of the population. It is not claimed that they give a full and complete picture of the state of nutrition of the people, but there can be little doubt that few signs or symptoms of deficiency disease were or could have been passed over. The technique consists briefly in a search for definite evidence of deficiency disease and then of an assessment, in so far as our present

TABLE IV
 CLINICAL NUTRITION SURVEYS—1942-44 SUMMARY.
 GENERAL STATE OF NUTRITION, BOTH SEXES, ALL AGES.

CLINICIAN		STATE OF NUTRITION					TOTAL
		Good	Fair	Poor	Good	Fair	
Sydenstricker -	June, 1942, to January, 1943	No. 3,456	971	66		4,493	
	% 77	22	1.5				
Hawes and Stannus -	January, 1943 to July, 1943	No. 2,126	432	33		2,591	
	% 82	17	1.3				
Adcock and Fitzgerald -	October, 1943, to May, 1944	No. 5,209	268	33		5,510	
	% 94	5	0.6				
TOTALS -		No. 10,791	1,671	132		12,594	
		% 86	13	1.1			

TABLE V
 EXPECTANT AND NURSING MOTHERS.

CLINICIAN		STATE OF NUTRITION					Folliculosis	Gingivitis	Corneal Vascularisation
		Good	Fair	Poor	Good	Poor			
Sydenstricker -	No.	803	115	2	12	174	14		
	%	87	13	0.2	1.3	19	1.5		
Hawes and Stannus -	No.	176	14	—	3	45	15		
	%	93	7	—	1.6	24	7.9		
Adcock and Fitzgerald -	No.	292	4	1	27	34	3		
	%	98	1.3	0.3	9	11	1		
OTHER ADULTS AND ADOLESCENTS, MALE AND FEMALE, INCLUDING FACTORY WORKERS, MINERS, SHOP ASSISTANTS, CIVIL DEFENCE, YOUTH ORGANISATIONS, AND OTHERS.									
Sydenstricker -	No.	1,047	168	9	92	157	20		
	%	86	14	0.8	7.5	13	1.6		
Hawes and Stannus -	No.	436	64	3	39	37	6		
	%	87	13	0.6	7.7	7	1.2		
Adcock and Fitzgerald -	No.	2,867	49	2	407	518	95		
	%	98	2	0.1	16.2	17	3.4		

knowledge makes possible, of the nutritional state of the individual. This, as is well known, is a most difficult subject, and the results of the surveys have been subjected to some criticism.^{11, 12} The answer to these critics is, that if they can provide a more reliable method, we shall be very glad to have it, but, in fact, there is no other method. The method of survey used at present is essentially the same as that adopted by Sydenstricker in 1942. All the clinicians engaged on these surveys have had, and still have, ample opportunities of checking each other's methods and criteria. Essentially the same method is being used by Sydenstricker and others at present in the examination of people in and from the liberated countries of Europe.

These surveys (Tables IV and V) of the Ministry of Health have shown that the state of nutrition of the population has been reasonably well maintained during the five and a half years of war. The results that have been obtained since the tables were completed tell essentially the same story. Certain signs frequently associated with deficiency disease were observed in variable numbers of subjects. The commonest of these were folliculosis and follicular keratosis, gingivitis, and, to a lesser extent, stomatitis, cheilosis, and corneal vascularisation. Only when three or more signs characteristic of a given condition were observed, was a diagnosis of deficiency disease given. Sydenstricker found one case of pellagra and eight cases of deficiency of riboflavin amongst almost five thousand persons of different ages. Neither Hawes and Stannus nor Adcock and Fitzgerald found any case of definite deficiency disease amongst about ten thousand persons. Corneal vascularisation used to be regarded as definitely pathognomonic of riboflavin deficiency, but recent work on the condition has thrown much doubt on this interpretation.

For several months Hawes and Stannus have been investigating the etiology of some of these conditions, particularly follicular keratosis. By some, this condition is considered to be due to deficiency of vitamin A, and by others to deficiency of vitamin C. Using therapeutic tests, Hawes and Stannus have shown that the condition is not affected by the amounts of either of these vitamins consumed. Indeed, both have reason to believe that the good effects frequently attributed by some investigators to vitamin A therapy may well have been due to factors other than the vitamin present in the oil, e.g., unsaturated fatty acids. Cod-liver oil, for instance, contains some of these and also appreciable amounts of iodine. It is too early yet to come to any definite conclusion about the cause of follicular keratosis. A discussion on the condition was held recently at the Royal Society of Medicine.¹³

GROWTH OF SCHOOL CHILDREN.

My colleague, Dr. Bransby, has been systematically studying since 1940 the rate of growth of schoolchildren, and has been making comparison with pre-war schoolchildren. It can be said that the rate of growth is not less, and in many places, notably Glasgow, greater than in pre-war days. Food is unquestionably the most important environmental factor determining the rate of growth, and it seems reasonable to assume that this satisfactory state of affairs is attributable mainly to the adequacy of the national dietary.

TABLE VI
ENGLAND AND WALES.

YEAR	Maternal Mortality Rates (inc. abortion) per 1,000 live and still-births	Infantile Mortality Rates per 1,000 related live births	Still-births Rate per 1,000 live and still-births	Neo-natal Deaths (0-4 weeks) Rate per 1,000 live and still-births
1939	3.1	50.6	37.8	27.0
1940	2.60	56.8	36.1	27.8
1941	2.76	60.0	34.4	27.5
1942	2.47	50.6	33.0	26.1
1943	2.30	49.2	30.2	25.3
1944	1.95*	46.0*	27.7*	24.5*

*Provisional figures

MORTALITY RATES.

It has been shown by Ebbs, Tisdall, and others¹⁴ in Toronto, by an investigation carried out in London on behalf of the People's League of Health,¹⁵ and by other observers, that the health of mother and child before, during, and after labour is influenced for good or ill by the nature of the diet. The statistical returns (England and Wales) for the years up to 1943 (Table VI) show that there has, on the whole, been a fairly steady decline in the rates of maternal mortality, infantile mortality, neo-natal mortality, and still-births. These criteria of the public health are unquestionably also influenced by other than dietary factors, but that they are influenced by the nature of the diet is equally beyond question. All this evidence, and there is more that could be mentioned, such as diminution in the incidence of anæmia during the war,¹⁶ in the opinion of many well qualified to judge, indicates that the people of Great Britain, notwithstanding the trials and stresses, psychological as well as physical, of five years of war, have been reasonably well nourished and sustained by a diet which, although often monotonous, has, nevertheless, provided in fairly adequate amounts all the essential nutrients.

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The Pathology of Rheumatic Fever

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ONE of the most important steps in establishing the ætiology of any given disease is the production of similar specific lesions experimentally. In the case of rheumatic fever the precise causation has not yet been clearly shown, and preparatory to some experimental observations, it was decided to examine in some detail the lesions found in this condition.

In the early days the presence of rheumatic fever was recognised by the occurrence of small vegetations on the valves of the heart, accompanied sometimes by myocarditis and pericarditis. The association of acute rheumatism with a specific pathological lesion was first described by Aschoff in 1904, who observed that small nodules composed of large histiocytic cells occurred in the vicinity of the coronary arterioles. These have since been called Aschoff nodules, and their presence in the heart is the hallmark of active rheumatic infection. Their distribution is widespread, occurring in the valves, the endocardium, the interstitial and septal connective tissue of the myocardium, and in the pericardium.

More recent observations on the pathology of rheumatic fever suggest that although the Aschoff nodule is essentially the specific lesion of rheumatism, there are other less commonly recognised lesions which, though not specific in themselves, may be regarded as such when accompanied by Aschoff nodules. Attention has been drawn to the occurrence of rheumatic arteritis, aortitis, rheumatic pneumonia and nephritis, and the conception is growing that rheumatic fever is a disease process which may have widespread visceral manifestations. Pappenheimer and Von Glahn (1926) described lesions of the peripheral blood vessels in ten out of forty-seven cases of acute rheumatism, while Friedberg and Gross (1934) noted in several cases extensive involvement of the arterial system resembling polyarteritis nodosa.

Eighteen cases of acute rheumatic fever and eighteen cases of mitral stenosis were available for study, and an examination of these was undertaken, first of all to analyse the structure, evolution, and distribution of the Aschoff nodule in the heart; secondly, to observe the degree of involvement of the coronary arteries, and lastly to decide, by an examination of all the organs from these cases, in what measure the pathological findings afford evidence that rheumatic fever is not only a disease of the heart, but of the whole vascular system.

Since the cases available presented considerable variation in the clinical duration of the disease, there was accordingly great variation in the histological picture, and it became possible, by correlating the morphological findings with the duration of the symptoms, to trace the stages in the evolution of the specific rheumatic lesion.

It is intended to discuss the findings in these eighteen cases in the following sites—

1. Myocardium.
2. Endocardium.
3. Valve, valve-ring, and angle.
4. The coronary arteries.
5. Aorta.
6. Viscera.

THE ASCHOFF NODULE OF THE MYOCARDIUM.

This was found to be present in the myocardium in fifteen out of eighteen cases. From a study of the cases in which symptoms had been present for a very short time, it became apparent that the first stage in the development of the Aschoff nodule was swelling and fibrinoid necrosis of connective tissue fibrils in small focal areas, usually in the vicinity of the coronary arterioles (plate 1).

It was then observed that the appearance of fibrinoid necrosis was followed by an inflammatory reaction composed chiefly of polymorphs, with a few lymphocytes and eosinophils. These cells surrounded and infiltrated the damaged area (plate 2). As yet the nodule was a non-specific lesion and only assumed its characteristic mature form when the large mononuclears or multinucleated cells appeared. These gradually replaced the polymorphs, many of which became pyknotic, and nuclear fragments could be recognised in the centre of the nodule (plate 3). The mononuclear cells were present first at the periphery, but eventually were situated more centrally as they became the predominating cell type, and were generally surrounded by a mantle of lymphocytes and an occasional Anitschkow cell, showing the nuclear characters, to which attention was first drawn by Anitschkow (plate 4).

In the fully developed nodule necrosis of collagen was not so conspicuous a feature. The nodule at this stage was observed to be one of two types, coronal or reticular. The coronal Aschoff body, found mainly in the interstitial connective tissue was composed of large mononuclear cells, arranged in rosette fashion around a central zone of necrotic collagen. In the reticular type, which occurred principally in the connective tissue septa of the heart, the cells tended to lie in an irregular manner between swollen collagen fibrils. The large mononuclear, or Aschoff cell, merits further description. It was observed to be of considerable size, frequently multinucleated, with basophilic cytoplasm. The nucleus was relatively large, lobular or 'budding,' and when multinucleated the number of nuclei was small, and they were located centrally in close proximity to each other. The nuclear membrane was well marked, while the chromatin formed fine dust-like particles or irregular concentrations in the centre of the nucleus. These cells are probably histiocytes, which become active following damage to the myocardial connective tissue.

The next stage in the evolution of the Aschoff nodule was seen to be the stage of repair or organisation. Necrotic collagen disappeared from the centre of the nodule, and polarisation took place. The cells became elongated, and were

eventually arranged parallel to one another along delicate strands of fibrous tissue, which were directed in the long axis of the connective tissue septa of the heart (plate 6). This process of polarisation may well be dictated by mechanical factors. The mononuclear cells became more and more spindle-shaped, and eventually appeared as fibroblasts. At this stage the lesion resembled a rather cellular scar (plate 7). As healing proceeded the lesion became quite acellular, and terminated in a fine fibrillar paravascular scar.

From these observations it was possible to divide the whole process from necrosis of collagen to paravascular scarring into definite time periods and to draw conclusions as to the duration of the lesions. These stages of development were recognised by Gross and Ehrlich (1934). Thus in the early weeks and up to the end of the first month focal necrosis of connective tissue followed by an inflammatory response is probably as far as the process advances. During the second month the mature Aschoff nodule is present, and towards the end of this period, i.e., about the eighth week, polarisation commences. The later phases are represented by polarised Aschoff nodules, and these are likely to be found during the third to the fifth month. The fibrillar Aschoff nodule occurs after the sixth month, and complete healing is generally established by the ninth month, after which period it is impossible to age the Aschoff lesion.

It was interesting to note that in many cases various stages of development of the nodule were present in the same heart, indicating that what appears clinically to be one attack of rheumatic fever, consists in successive episodes of myocardial injury, and with each episode there develop fresh foci of connective tissue damage.

The occurrence of paravascular scarring is also of importance, for its presence in the myocardium may be the only indication of a previous rheumatic carditis. The frequency with which it is found in routine post-mortem material, especially in cases which give no history of previous rheumatic infection, suggests that in this country, at any rate, subclinical attacks of rheumatic fever must be of common occurrence.

ENDOCARDIUM.

Endocarditis was present in eight out of eighteen cases. As elsewhere in the heart, the characteristic lesion of rheumatic endocarditis was seen to be the Aschoff nodule (plate 8). It was most commonly found in the endocardium of the posterior wall of the left auricle. It usually occurred in the middle or outer layers and frequently in the subendocardial tissues. It was generally of the coronal type and, as in the myocardium, it passed through certain stages of development. Necrosis of collagen in the acute phase was a prominent feature, and this was accompanied by a polymorph reaction, which later gave way to large mononuclear cells. Two other types of lesion were observed. In the first type, Aschoff cells were present, but were not arranged in node formation. The cells tended to lie in palisade manner along bands of necrotic collagen. This change was confined mainly to the middle layer of elastic and connective tissue, and was quite extensive throughout the length of the endocardium. In the second type of lesion, the band of necrotic collagen was subendothelial in position, while on either side of this band were

darkly staining cells, spindle shaped and intermingled with polymorphs, which, on the inner aspect, replaced the surface endothelium (plate 9). This lesion is not in the generally accepted sense specifically rheumatic, but has been described by Pappenheimer and Von Glahn (1927), who believe it is as characteristic of rheumatic endocarditis as is the Aschoff nodule. When no nodules were present in the endocardium, there was frequently a generalised inflammatory infiltration with lymphocytes and polymorphs.

As healing proceeded, Aschoff nodules and inflammatory cells disappeared, capillaries penetrated into the outer half of the endocardium, and fibroblastic proliferation occurred. In recurrent cases it could be seen that previous episodes of endocarditis had led to a great thickening of the endocardium, most marked in McCallum's patch (posterior wall of left auricle), where it was possible to appreciate the thickening and wrinkling of the endocardium even on naked-eye examination.

VALVE RING, VALVE ANGLE, VALVE.

In the present study, the mitral valve was involved in twelve cases, while occasionally there was an accompanying aortic and tricuspid valvulitis.

Gross and Friedberg (1936) have drawn attention to the importance of the valve-ring lesion in rheumatic fever, which almost always accompanies a lesion of the valve leaflet. And so, brief mention will be made of the type of lesion which was encountered in this region.

Vascularisation was a common feature, sometimes by capillaries or vessels showing intimal muscular hyperplasia. The extent of the inflammatory infiltration depended on the stage of the rheumatic process. If early, polymorphs, eosinophils, and lymphocytes were present. Plasma cells and Anitschkow cells occasionally predominated, while Aschoff cells, either singly or in nodules, occurred frequently. Areas of necrotic collagen were observed sometimes communicating with similar necrosis in the valve angle. On one occasion the arterioles showed fibrinoid necrosis of their walls and were surrounded by areas of hæmorrhage.

If recurrent attacks of rheumatic carditis had occurred, there was extensive fibrosis of the valve ring with excessive vascularity. In several cases it was noted that in the absence of an active valve ring lesion there was an acute valvulitis of the leaflet distal to the ring.

Valve-angle lesions were also noted. These were always accompanied by some degree of infiltration of the valve ring. Extensive endocardial and subendocardial accumulations of cells were present. Large mononuclears, lymphocytes, polymorphs, eosinophils tended to project from the endocardial surface, the endothelium having disappeared. Sometimes the cells were arranged in palisade to the surface. More frequently, however, the cells infiltrated the subendocardial layer diffusely. Sometimes deeply basophilic cells with multiple nuclei were present, especially in association with necrosis of collagen in the valve angle (plate 10). Necrotic collagen occasionally extended right to the surface of the valve angle and projected as a small verruca. As healing occurred fibrosis followed. In recent cases this

was represented by cellular fibrous tissue, which projected like a 'spur' from the valve angle, later proceeding to hyalinisation and even calcification.

Valve.—The first stages of valvulitis were recognised by a generalised swelling and œdema of the valve substance, especially in the spongiosa layer. Frequently the valve was infiltrated by polymorphs, lymphocytes, and an increased number of Anitschkow cells, an inflammatory reaction quite non-specific in character. This was particularly noticed in the tricuspid, pulmonary, and aortic valves, in the absence of any other more specific valvular lesion. The ingrowth of new capillaries from the valve ring along the spongiosa layer was an almost constant accompaniment of an acute valvulitis, and occurred at an early stage. Occasionally vascularisation of the ventricularis was also seen, while in recurrent attacks of valvulitis, muscularised vessels were constantly present. Aschoff nodules were of common occurrence. As in the myocardium, all stages of development were encountered. When these were present near the surface of the valve, they led to changes in the overlying endocardium, but when well within the valve substance they were associated with œdema and generalised inflammatory infiltration, but the endocardial cells remained intact. Fibrinoid necrosis of collagen occurred, giant cells were frequently seen, usually in node formation, but sometimes, as in the valve ring, there was a diffuse infiltration. The Aschoff nodules sometimes showed polarisation, generally in relation to small blood-vessels in the spongiosa layer.

A special study was made of the rheumatic vegetation to try to determine what changes within the valve led to its formation. Of importance in this respect was the presence in the valve of Aschoff nodules in which necrosis of collagen was a conspicuous feature. Since these were associated with œdema and increased tension, they tended, as any inflammatory process does, to spread along the line of least resistance, that is, towards the surface of the valve, and eventually to project above it. Aschoff nodules in all stages of extrusion were seen. Eventually the nodule, which was once subendocardial, became well elevated above the surface, and what was originally the central zone of necrotic collagen, was observed to form a hyaline 'cap' to the vegetation, while in its base Aschoff cells were still recognisable (plate 11). In its early stages the vegetation still preserved its thin covering of endocardial cells, but eventually this became necrotic, and with the deposition of platelet thrombi the vegetation rapidly increased in size. Other vegetations showed evidence of healing, fibroblasts and capillaries being present in their base. Organisation took place, and as contraction and shrinkage of the fibrous tissue occurred, the vegetation was drawn into alignment with the valve surface.

In the past a great deal of stress has been laid on the formation of a rheumatic vegetation by deposition of blood platelets on the surface of the abraded endocardium. It seems, however, that the primary mechanism is an extrusion of necrotic collagen on to the surface of the valve. These small verrucæ are present, not only along the line of closure, but almost anywhere on the valve surface, auricular or ventricular. They are mostly microscopical in size, and it is only when they occur along the line of closure that the additional factor of mechanical impact

contributes to the deposition of large platelet thrombi, which render them visible on naked-eye examination.

An uncommon type of valve lesion was occasionally seen, in which Aschoff cells were arranged in palisade manner beneath the valvular endocardium. Their presence in this position was associated with necrosis of collagen on the surface, and with the deposition of a thin layer of platelet thrombi.

Extensive vascularisation of the valve, especially in the auricular layer, was a constant feature of the healing stage. In mitral stenosis the valve was found to be grossly thickened by hyaline fibrous tissue which sometimes had undergone calcification. Vascularisation with vessels of the intimal musculo-elastic hyperplastic type was always present, and the persistence of these in a valve which showed fibrosis was always found to be evidence of a past episode of rheumatic valvulitis.

CORONARY ARTERIES.

With the growing recognition of rheumatic fever as a disease of the whole vascular system, attention has been drawn in recent days to the lesions which may occur in the main coronary arteries and their branches. Passing reference has been made in the older literature to the possible presence of such lesions, but their significance as part of the rheumatic process was not always appreciated. It was, therefore, considered of importance in this study to examine with care the coronary vessels to determine the frequency and extent of their involvement and to decide whether the type of lesion is essentially rheumatic in origin.

In all of the eighteen cases it was possible to find some degree of involvement of the coronary arterial system. The lesions varied greatly in their severity, but the more acute the rheumatic attack the more easily was their presence recognised. The main coronary arteries, as well as the smaller arterioles were equally involved. A common finding was a generalised infiltration of the arterial wall by polymorphs, eosinophils, lymphocytes, and Anitschkow cells. Sometimes the inflammatory infiltration was confined to the adventitia, while elsewhere there was a well-marked panarteritis, accompanied by extensive proliferation of the subendothelial tissues, and œdema of the media.

Fibrinoid necrosis of the media was a very characteristic finding. In its earliest stage the affected media assumed a hyaline eosinophilic appearance with absence of nuclear staining, swelling, and loss of definition of the individual muscle fibres (plate 12). This sometimes was segmental in its distribution, affecting only an arc of the circumference, but frequently the whole arterial wall became necrotic. If very extensive, fibrinoid necrosis of the adventitia occurred, associated with an accumulation of fibrin, red cells, and large mononuclears beneath the endothelium. and in one vessel thrombosis had developed. At first, fibrinoid necrosis of the artery was unaccompanied by any cellular reaction, but eventually polymorphs appeared in large numbers in the adventitia and invaded all coats of the vessel (plate 13). This acute type of lesion was present in five out of eighteen cases, and the pathological process which it most closely simulated was polyarteritis nodosa.

A third type of lesion, and one which can be regarded as entirely specific, was

the frequent occurrence of Aschoff cells in the adventitia or actually within the vessel wall. When in the adventitia the infiltration was either diffuse, focal, or in palisade arrangement, and was quite distinct from the paravascular Aschoff nodules. It was quite common to find Aschoff nodules in the media of small arterioles, and here they were associated with focal areas of fibrinoid necrosis (plate 14). Occasionally the Aschoff cells were present as a diffuse infiltration and extended into the subintimal layer.

As healing proceeded, scarring of the media was a prominent feature. This was quite distinctive and consisted in fibrous replacement of muscle usually only in a segment of the circumference, and perhaps only in the inner or outer third of the media (plate 15). Intimal and adventitial fibrosis also occurred. Some vessels showed evidence of recurrent involvement, the muscle being replaced by fibrous tissue and the adventitia thickened, while recent fibrinoid necrosis was present in the media with perivascular infiltration of polymorphs and Aschoff cells. Gross *et al* (1935) reported that in inactive cases of rheumatic carditis, previous arterial involvement can be recognised by the earlier development of intimal hyperplastic and fibrotic layers, and by the appearance of heavier elastification and scarring of the media.

Eighteen cases of mitral stenosis (inactive) were therefore examined to determine if possible the nature and degree of arterial change resulting from previous rheumatic arteritis. As would be anticipated from a study of the arterial lesions of the acute stage, medial fibrosis was a common finding and occurred in sixty per cent. Muscularisation of the intima was another frequent lesion, but as intimal change is more or less a physiological ageing process, it therefore would seem that scarring of the media is of more significance. However, muscularisation, fibrosis, and elastification of the intima were occasionally found in the very early age group, at an age when such lesions would not normally be present and therefore can be accepted, especially in association with medial change, as a result of involvement of the arteries in a previous rheumatic process.

In conclusion, it appears that the coronary arterioles are regularly involved in acute rheumatism. All degrees of arteritis are encountered, the commonest being a panarteritis with inflammatory infiltration of all coats of the vessel. Although this is not specifically a rheumatic process, it has been described in only one other disease—polyarteritis nodosa.

Then there is the more specific type of lesion where Aschoff cells and nodules occur in close association with the coronary arterioles. As healing occurs there is an earlier development of the normal age period changes in the artery, but probably of greater significance is the presence of fibrosis of the media.

AORTA.

While the occurrence of lesions of the coronary arteries in rheumatic fever has frequently passed unrecognised, it has for some time been realised that rheumatic aortitis is one of the manifestations of this disease. Pappenheimer and Von Glahn (1924, 1926, 1927) have published several papers on this subject, and they frequently

observed the occurrence of Aschoff nodules in the adventitia with perivascular infiltrations of Aschoff cells in the media, later proceeding to the formation of wedge-shaped scars around the vasa vasorum.

In this study, aortic lesions were present in six out of eighteen cases. There was a diffuse inflammatory infiltration of the intima in five aortas. The cells present were mainly lymphocytic with occasional polymorphs. No Aschoff cells were seen. In one aorta the inflammatory cells were arranged in palisade manner beneath the surface endothelium. In the media lymphocytic cuffing of the vasa vasorum occurred, with prominence of the endothelial cells lining these vessels. Occasionally large mononuclear cells of the Aschoff type were seen. Underlying areas of intimal proliferation, the media frequently showed extensive necrosis, recognised by absence of muscle nuclei, and sometimes cystic degeneration.

The type of lesion in the adventitia depended on the duration of the rheumatic process in the heart. When this was in the acute stage, fibrinoid necrosis of collagen was present in the adventitial fibrous tissue. Polymorphs, lymphocytes, and large mononuclears were found in large numbers. In four cases Aschoff nodules were seen (plate 16). These were larger than the nodules found in the myocardium, their arrangement was reticular and coronal, and they terminated in polarisation and fibrillar scarring (plate 17). In cases in which no active lesion was seen, there were certain findings which suggested a previous rheumatic aortitis. Fibrous thickening of the intima was observed frequently, by itself of no significance, but its almost constant association with healed lesions of the media and adventitia suggested that the whole pathological picture might be the result of a specific type of arterial damage. In the media there were large areas devoid of muscle nuclei. In one case this was accompanied by compression of the elastic lamellæ and disappearance of muscle cells, while around the vasa vasorum were wedge-shaped scars. A common finding in the adventitia was a peculiar laminated fibrosis which resulted in dense adventitial thickening. When this was present there was no lesion of the vasa vasorum which might suggest a syphilitic origin.

In conclusion, the presence of the Aschoff nodules in the adventitia in the acute stage may be accepted as evidence of active rheumatic aortitis, but in the healed stage intimal, medial, or adventitial lesions occurring alone are of no significance. However, when there is a combination of all three lesions, intimal fibrosis, medial scarring, and adventitial thickening, it is suggestive that rheumatic fever may have been responsible for their development.

RHEUMATIC PNEUMONIA.

The recent intensive pathological study of the pulmonary changes in rheumatic fever can be considered to have started with Paul (1928), who found that in fifty per cent. there was a focal hæmorrhagic lesion which could be considered characteristic though not specific. At about the same time Naish (1928) described what he called a new type of pathological consolidation of the lung in rheumatic fever, and termed the condition 'rheumatic lung.' Even more emphatic about the specificity of rheumatic pneumonia was Fraser's report (1930), in which he

described vascular changes, proliferation, necrosis of alveolar walls, and typical Aschoff nodules in the interstitial tissue of the lung.

There is much conflicting evidence regarding the specificity of the histological findings in rheumatic pneumonia, but the evidence so far tends to suggest that there is a pneumonia which is characteristic but not entirely specific.

PULMONARY LESIONS.

In seventy-five per cent. the most characteristic feature was widespread proliferation of large mononuclear cells, these filled the alveolar spaces and were unaccompanied by any other inflammatory cell type. Occasionally they contained hæmosiderin, but the picture was not that of chronic venous congestion. There were usually extensive pulmonary oedema and alveolar hæmorrhages. Septal cell proliferation, oedema, and hæmorrhage generally occurred together, and presented quite a characteristic microscopical appearance. Associated with pulmonary oedema was the formation of hyaline membranes. These were bright eosinophilic bands which lined the alveolar ducts and alveoli. They stained more deeply and were quite distinct from the oedema fluid with which they were associated (plate 18). In two cases there was fibrinoid necrosis of the walls of the pulmonary arterioles, and in one vessel in the interlobar septum there was perivascular necrosis of collagen. Focal alveolitis was observed in three cases. This consisted of fibrinoid necrosis of a small segment of the alveolar capillary wall with subsequent thrombosis, exudation of fluid, and infiltration by inflammatory cells (plate 19).

The microscopical appearances suggest an inflammatory type of oedema, in which there is an increased permeability of the alveolar capillaries with exudation of fluid and red cells, proliferation of septal cells, and formation of hyaline membranes.

In conclusion, it may be said that a specific type of rheumatic lung cannot be considered to exist, but a characteristic pulmonary picture is often present.

SPLEEN.

Occasionally it has been observed that the spleen and lymph glands are enlarged during an attack of rheumatic fever. No microscopical changes, however, have been described in the spleen in this condition.

In the search for possible visceral manifestations of the rheumatic process, there were observed in three cases splenic lesions which might be considered specific. The central arterioles of the Malpighian bodies were surrounded by numbers of polymorphs. These were confined mainly to the adventitia and were distinct from the adjacent zone of lymphocytes. The lesion was a periarteritis quite like that described in the coronary vessels. As healing occurred, extensive periarterial fibrosis resulted. In support of a possible rheumatic ætiology for this splenic lesion, it was frequently noted in cases of healed rheumatic carditis and mitral stenosis that there was an excessive degree of periarteriolar fibrosis in the spleen.

KIDNEYS.

Klotz (1913) was the first to draw attention to the constancy with which widespread lesions occur in the arterioles of the viscera in rheumatic fever. In the

kidney he observed a non-suppurative perivascular infiltration in relation to the smaller blood-vessels. Pappenheimer and Von Glahn (1926) describe extensive lesions of the renal arteries, with swelling of the endothelium, fibrinoid necrosis of the media, and periarterial infiltration by polymorphs and large mononuclear cells. They believe that the vascular lesions most closely resemble polyarteritis nodosa, from which they differ in only very fine detail.

Renal vascular lesions were present in only one of the cases under examination. These included fibrinoid necrosis of arteries, afferent arterioles, and glomerular capillaries. Necrosis of collagen in the adventitia was sometimes present. This was a case of early acute rheumatic fever, so that the absence of any periarterial inflammatory reaction was explicable on account of the short duration of the rheumatic process.

CONCLUSIONS.

This morphological study of eighteen cases of acute and eighteen cases of healed rheumatic fever indicate that the lesions of this disease are more widespread than is generally appreciated.

In the heart, the specific lesion, the Aschoff nodule, occurs in the paravascular, interstitial, valvular, and subendocardial tissues. It has been shown to undergo a remarkably constant evolution, beginning as a necrotic lesion of the fibrous tissue, it is soon manifested by an acute non-specific inflammatory infiltration, which in turn gives way to the focal aggregation of a rather peculiar form of histiocyte—the Aschoff cell. These cells appear to undergo an evolution into fibroblasts with the production of collagen, the process eventually terminating in the formation of a fibrillar scar, the only characteristic of which is its site.

Accompanying this specific lesion is an arterial damage which, though consisting of a non-specific fibrinoid necrosis and associated inflammatory infiltration, is remarkably constant. The vascular lesion is usually, but not always, confined to the coronary system. In the present analysis it has been encountered in the lungs, spleen, aorta, and kidneys.

The changes in the valve are of predominant importance. In this study it has been revealed that the formation of vegetations is a more complex process than is generally appreciated. Necrotic foci of collagen may, by reason of the associated oedema and swelling, project from the surface of the valve, and with the subsequent loss of the covering endocardium become coated with platelets and a film of fibrin. A similar end result may develop upon an immediately subendocardial Aschoff nodule. The development of macroscopic verrucae is, however, partly dictated by mechanical factors, and it is these which appear to be of importance in the determination of the common site of these lesions on the lines of valvular closure.

The frequent implication of the aorta in the rheumatic process was of interest, for it strengthened our evidence in favour of the conception that rheumatic fever is essentially a disease of the whole vascular system. Of further importance in this connection was the occurrence of pulmonary arterial lesions and occasional involvement of the splenic and renal vascular system.

It is generally believed in rheumatic fever that the heart is the site of maximum

damage, but from these observations it is suggested that all tissues of mesenchymal origin, especially the vascular mesenchyme, are liable to be involved, and no matter where the rheumatic lesion occurs, and no matter what ætiological agent is responsible for its production, the nature of the tissue damage is fundamentally the same, the process being constant in its histological appearance, showing modification in different sites, dictated by the essential structure of the tissue involved.

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THE PATHOLOGY OF RHEUMATIC FEVER

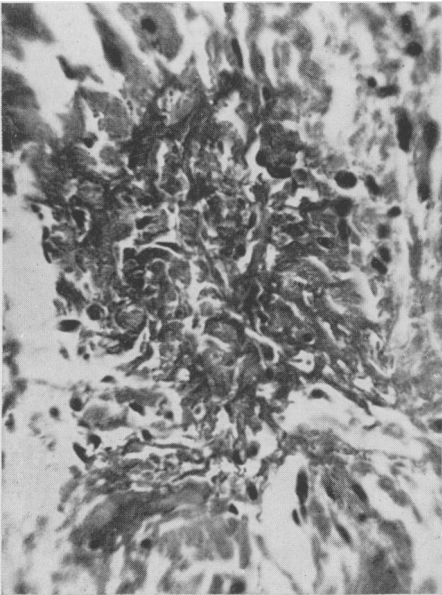


Plate 1

Aschoff nodule: first stage showing fibrinoid necrosis of collagen.

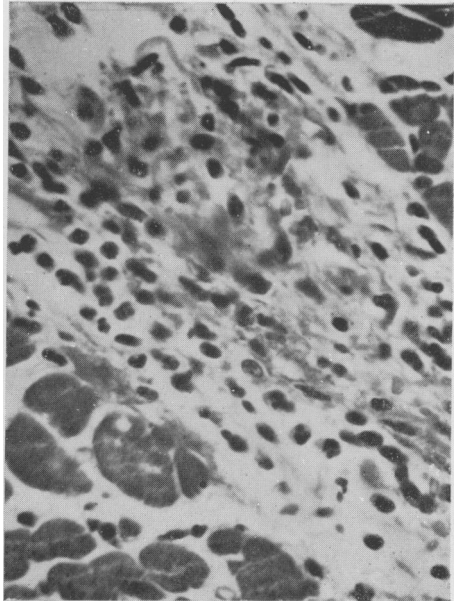


Plate 2

Second stage with focus of necrotic collagen infiltrated by polymorphs.

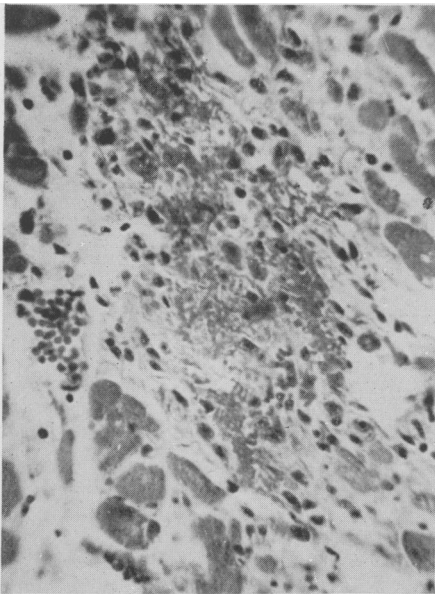


Plate 3

Polymorph reaction subsiding and mononuclear Aschoff cells appearing.

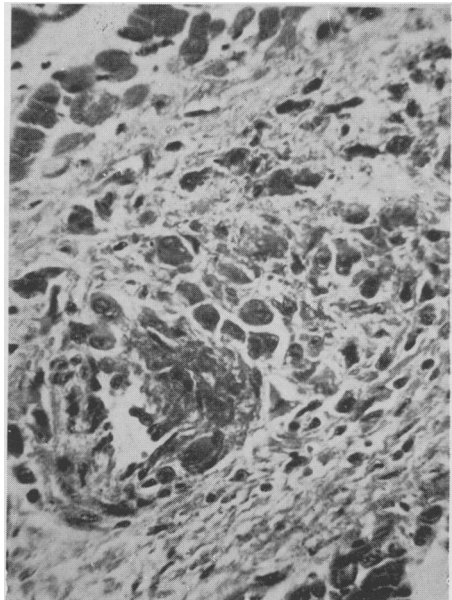


Plate 4

Mature nodule: focal aggregation of Aschoff cells, necrosis of collagen less conspicuous.

THE PATHOLOGY OF RHEUMATIC FEVER

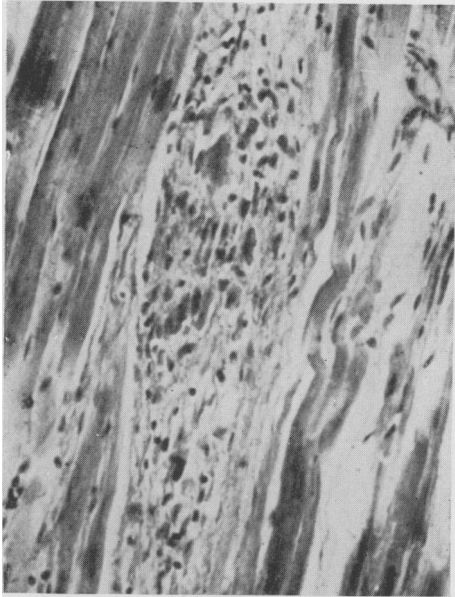


Plate 5
Early polarisation, cells becoming oval and orientated in parallel lines.

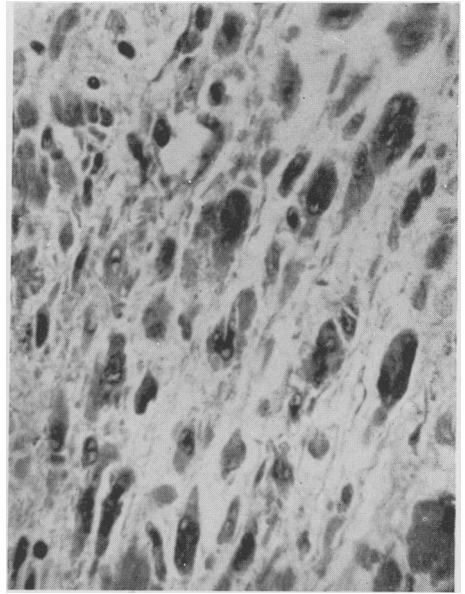


Plate 6
Higher power: showing the typical Aschoff cells becoming fusiform.

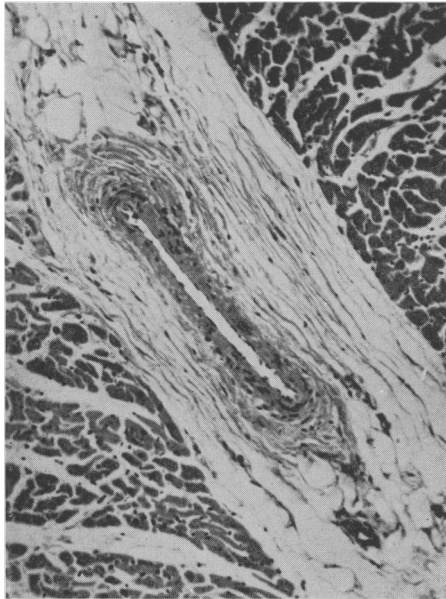


Plate 7
Aschoff nodule: almost healed, forming a slightly cellular fibrillar paravascular scar.

THE PATHOLOGY OF RHEUMATIC FEVER

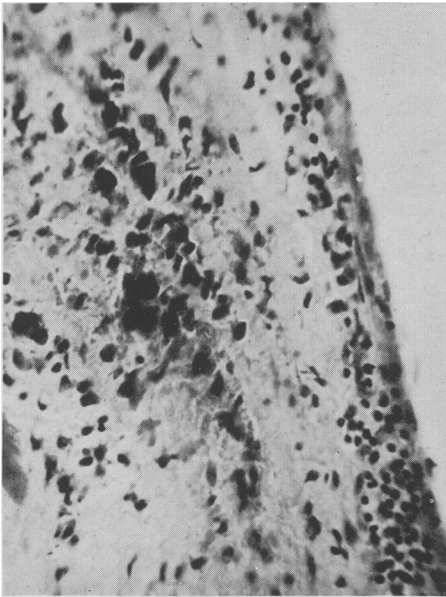


Plate 8
Aschoff nodule in endocardium.

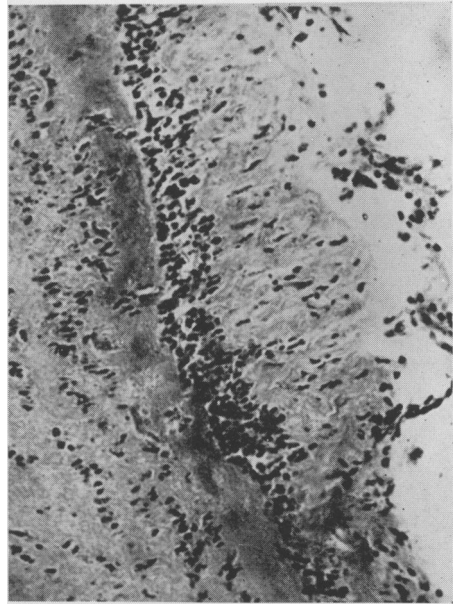


Plate 9
Endocarditis: subendothelial band of necrotic collagen with surface proliferation of cells.

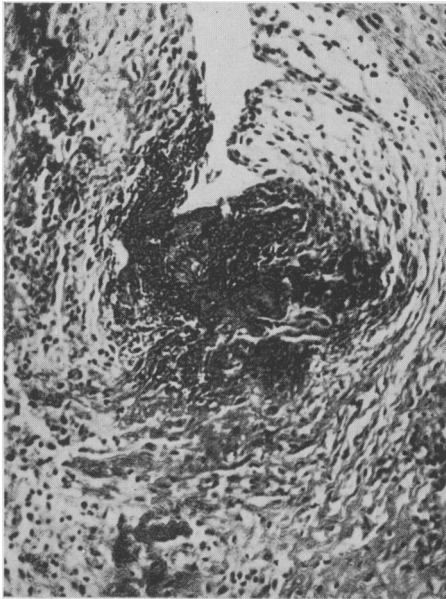


Plate 10
Valve angle: showing necrosis of collagen and infiltration of adjacent valve ring.

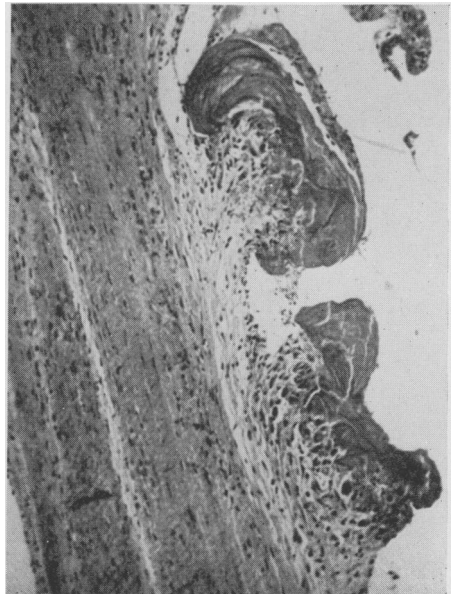


Plate 11
Mitral valve: verrucae composed of hyaline cap of collagen with covering of endothelium, and Aschoff cells in base.

THE PATHOLOGY OF RHEUMATIC FEVER

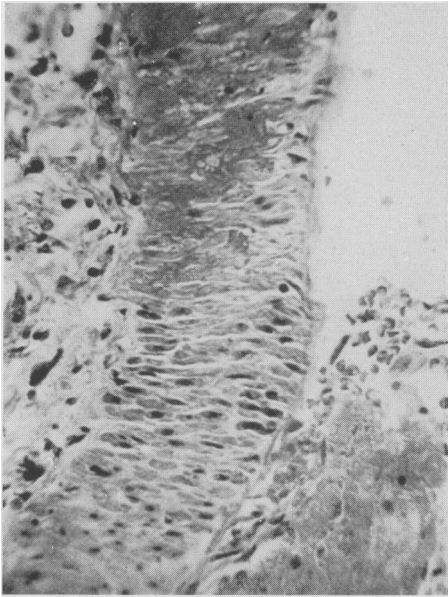


Plate 12

Coronary artery: fibrinoid necrosis of segment of vessel.



Plate 13

Coronary artery—acute panarteritis.

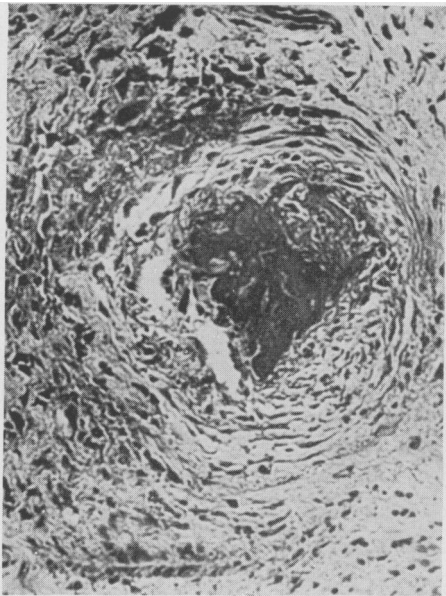


Plate 14

Arteriole showing subendothelial accumulation of fibrin, Aschoff cells in adventitia and in media.

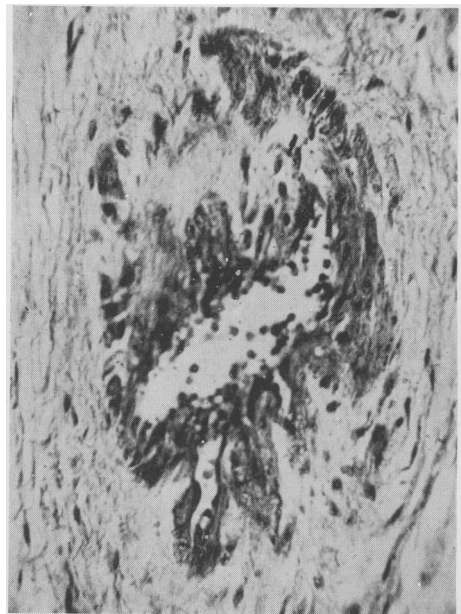


Plate 15

Healed arteritis—patchy fibrosis of the media.

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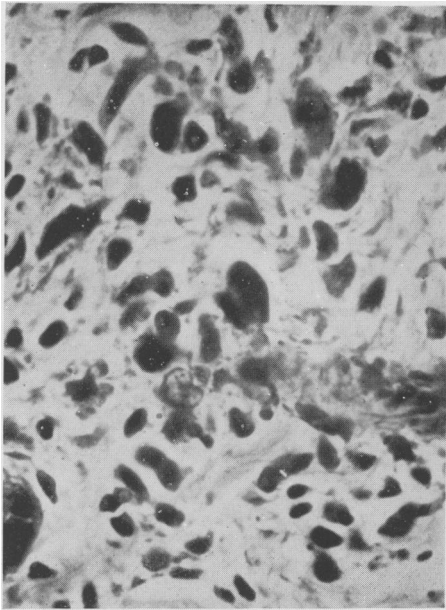


Plate 16
Aortitis: Aschoff nodule in adventitia.



Plate 17
Aortitis: nodule in adventitia undergoing polarisation.

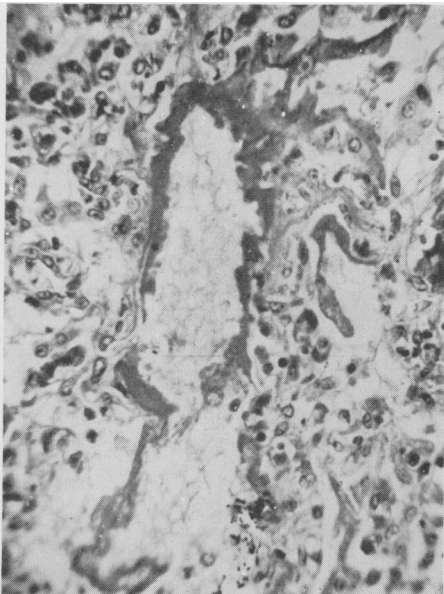


Plate 18
Rheumatic pneumonia: hyaline membrane lining alveolus.

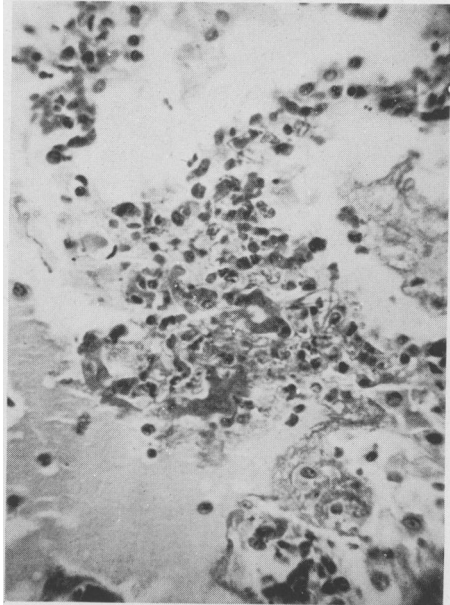


Plate 19
Alveolitis: thrombosis of capillary with inflammatory infiltration.

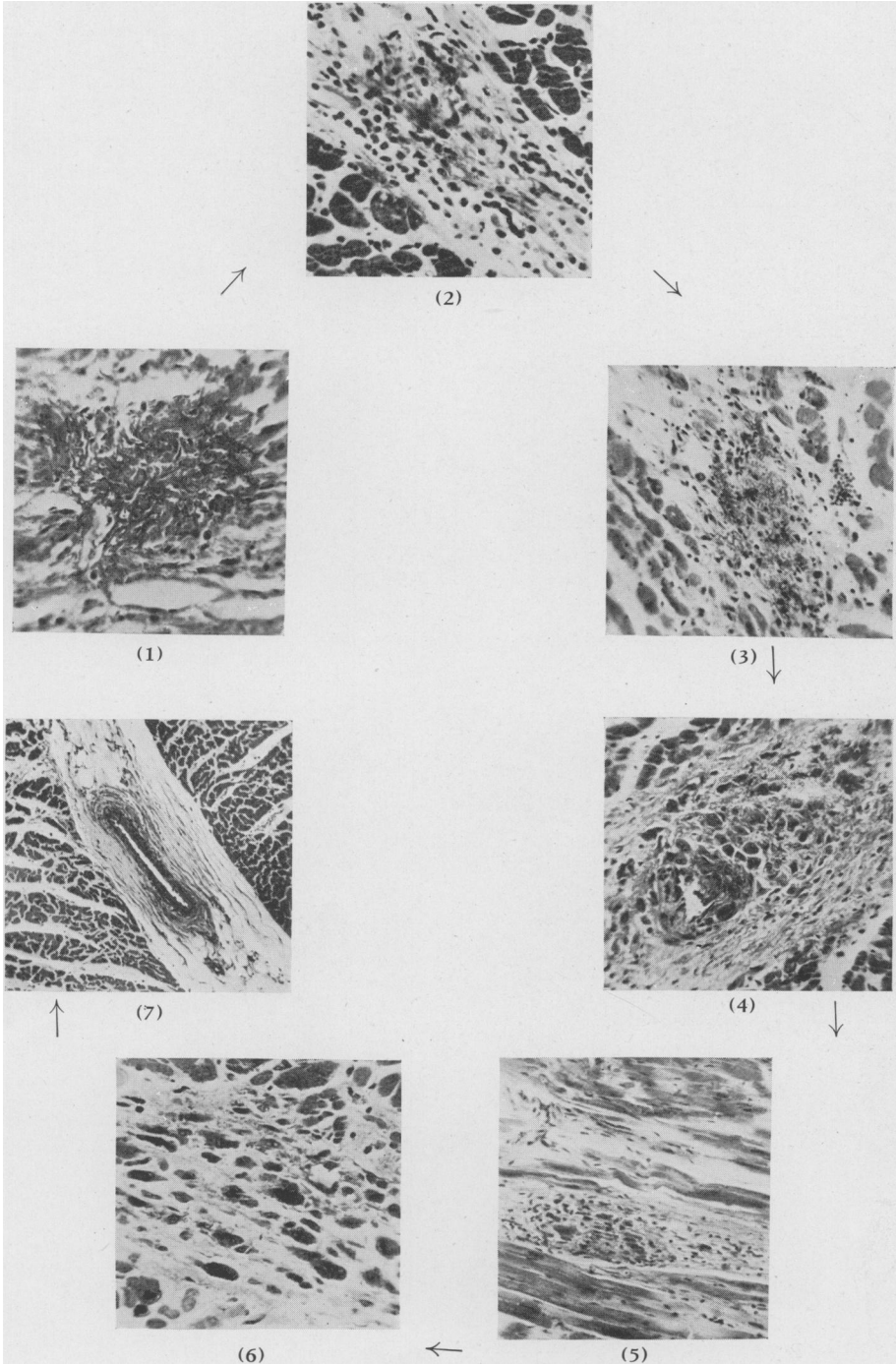


PLATE 20

The Evolution of the Aschoff Nodule

damage, but from these observations it is suggested that all tissues of mesenchymal origin, especially the vascular mesenchyme, are liable to be involved, and no matter where the rheumatic lesion occurs, and no matter what ætiological agent is responsible for its production, the nature of the tissue damage is fundamentally the same, the process being constant in its histological appearance, showing modification in different sites, dictated by the essential structure of the tissue involved.

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The Pathogenesis of Subacute Bacterial Endocarditis

By YVONNE MACILLWAIN, M.D.

Department of Pathology, Queen's University, Belfast

THE first clear reference to the sub-acute form of bacterial endocarditis was made by Senhouse Kirkes in 1852. Osler, in the Goulstonian lectures of 1885, was the first to give a really comprehensive picture of the disease, using the title "Malignant Endocarditis." He was particularly impressed by the frequency with which it was associated with rheumatism or chorea, and by the number of cases in which there had been previous damage to the cardiac valves.

This relationship is one which has been noted over and over again by almost all workers who have studied the disease. There is general agreement that in about fifty per cent. of the cases there has been a previous history of rheumatism. In post-mortem material the evidence is even greater, over eighty per cent., according to some authors. Of those cases with no apparent rheumatic basis, congenital cardiac malformations are noted in many instances. Others, though few in number, present evidence of syphilitic or atherosclerotic changes in the valves. In still others there is no relevant clinical history or underlying valvular change.

The congenital abnormalities most frequently associated with bacterial vegetations are patent ductus arteriosus and bicuspid aortic valve. Lewis and Grant (1923) were the first to recognise clearly that a bicuspid aortic valve may be an acquired rather than a developmental lesion. Gross (1937), and more recently Koletsky (1943), have made intensive histological studies of hearts showing this abnormality. Both these authors noted that in adults, as opposed to children, the affected valves show obvious thickening and fibrosis and are rarely associated with other congenital defects. Koletsky made the further generalisation that in infants and children bicuspid aortic valves are apparently not susceptible to bacterial disease. Both he and Gross formed the opinion that in many instances (forty to fifty in Koletsky's series) the lesion is acquired, generally as the result of a rheumatic valvulitis. In other cases where there is a true congenital defect, care must be taken to exclude a superimposed rheumatic infection. In the post-mortem records of the Royal Victoria Hospital are five cases of subacute bacterial endocarditis occurring in congenitally malformed hearts. Two of these also show the presence of rheumatic stigmata. Equal care in this respect is required in the heart, which is the site of a syphilitic valvulitis. It is emphasized, both from the literature and personal studies, that the examination of only one routine heart block is insufficient evidence for the exclusion of rheumatic stigmata. The available evidence thus suggests that the role of rheumatic carditis in the ætiology of subacute bacterial endocarditis is of even greater importance than generally recognised.

The important question appears to be the mechanism by which the diseased valve favours the deposition of organisms. Some of the older writers believed that

infection occurred as a result of embolisation of the vessels in the scarred valves. The modern idea is that localisation occurs on the valvular surface. The mechanisms suggested are many and varied. Some depend on the interpretation of the ætiology of rheumatic fever itself. Thus Poynton (1920) and others believed that both diseases were bacterial in origin, and that ulcerative endocarditis was "malignant rheumatism." Schlesinger (1935) suggested that rheumatism is a virus disease which predisposes the valves to secondary bacterial invasion. Others consider that it is the structural alterations, such as roughness and calcification, which are of importance. Allen (1939) considers the question of localisation to be dependent on mechanical factors. He believes that in rheumatic valvular deformities, the force of impact, and the duration of contact, of the infected blood with the surface of the valve are increased, and that the brunt of this impact is borne by the line of closure. In the majority of cases of congenital abnormalities Allen considers that there is an obvious self-explanatory defect in mechanics whereby abnormally great tension and impact are transmitted to a region not designed for their reception. The exception is the bicuspid aortic valve. He too considers that in many cases this is an acquired lesion, and that as such valves are fibrosed and deformed, the principles of increased impact and contact are applicable to them. The evidence presented is convincing, but Allen himself emphasizes that his theory attempts to explain, not why implantation occurs, but why it occurs at a particular site. He feels that in all probability localisation takes place after the stage has been set by a generalised altered reaction of tissue or immunity. The latter suggestion is supported by Held and Lieberson (1943), who attribute the peculiar pathological changes and clinical course of subacute bacterial endocarditis to local tissue re-activity caused by hyper-immunity. They suggest that in chronically diseased valves the usual responses to infection do not occur. Instead there is a deposition of fibrin and blood platelets, which constitute the soil on which circulating bacteria implant themselves.

Though not suggesting a similar mechanism for their formation, the presence of such platelet thrombi on diseased valves was noted by Grant, Wood and Jones (1927-9). They found the thrombi particularly frequently on those valves most prone to develop bacterial endocarditis. Their belief is that they occur in response to changes in the underlying valve. They feel that they have demonstrated that it is these platelet thrombi, rather than the crevices and pockets of the scarred valves, which are of importance in bacterial localisation.

Gross and Fried (1937) described a peculiar eosinophilic necrosis of collagen, which they consider to be particularly apt to occur at the line of closure of old rheumatic valves, and in those showing sclerosis of the Mönckeberg type. They also found proliferative changes in the valvular endothelium. These were most marked at those sites which are subjected to the greatest pressure. They believe that it is these valvular changes which predispose to the surface deposition of material from the blood stream, leading to the occurrence of thrombi. These, in turn, act as foci for the implantation of bacteria from the circulating blood. These authors made a study of forty-two cases of subacute, and twenty-eight cases of acute, bacterial endocarditis. Evidence of a previous rheumatic process was found

in seventy-five per cent. They did not consider activity of the rheumatic infection to be a necessary precursor to the development of the bacterial lesions.

This is entirely contrary to the findings of Pappenheimer and von Glahn (1935). They claim to have demonstrated that subacute bacterial endocarditis, rather than attacking valves with old healed lesions, develops on valves bearing recent rheumatic vegetations, and during the existence of active though sub-clinical rheumatism.

From this survey of the literature it has been possible to draw several conclusions. The areas on which vegetations develop have generally been the site of a previous pathological process. In a small number of cases this has been congenital or syphilitic in type. In the vast majority, the underlying lesion has been a rheumatic carditis. In this latter group must be included many of the bicuspid aortic valves seen in adults, which were formerly believed to be congenital in origin. In valves already involved by any of these lesions mechanical factors are important in dictating the site of bacterial localisation. The evidence available suggests that vascular embolisation plays no part in the latter. It is believed that localisation is dictated by changes on the surface of the valve. These surface lesions develop in response to the underlying pathological process, whether congenital, syphilitic, or rheumatic. The nature of these changes, the mechanism of their production, and in particular their relation to rheumatic fever, are all problems which require further elucidation.

With this object in mind, a study was made of the valves of twelve patients dying during an acute attack of rheumatic fever. Many showed evidence of previous attacks, so that varied stages of the rheumatic valvulitis were seen. The findings are in general agreement with those of McKeown, published elsewhere in this Journal. Only those changes considered relevant to the initiation of the bacterial vegetations will be discussed here.

The initial lesion appeared to be a deep valvulitis, possibly spreading from the valve rings to the more distal parts of the leaflet. In its most acute form the valvulitis consisted of a generalised non-specific swelling and oedema, and infiltrations by leucocytes and large mononuclears (plate 1). Later, Aschoff bodies—the specific lesions of rheumatic infection—appeared. These consist of necrosis of collagenous tissues and aggregation of the peculiar large mononuclears known as Aschoff cells. The latter were arranged either as nodules or as a more diffuse reaction. The lesions were most marked in the spongiosa of the mitral valve. When such a reaction occurred deep in the valvular tissues, the appearances and evolution were analogous to those which occur in the myocardium. There were no surface changes with these deeply situated lesions. When intermediate in depth, the rheumatic nodule was often associated with swelling and infiltration of the sub-endocardial tissues on its superficial aspect, so that a cellular “palisade” was formed (plate 2). In other cases there was no true palisade, but merely a “bristling” of the surface layer of cells, which were usually swollen and prominent. In even more superficial Aschoff lesions there was no intervening cellular reaction, so that the necrosis extended to the surface, from which the swollen and oedematous

material often projected as a definite nodule (plate 3). Such areas were sometimes covered by intact endothelium (plate 4). More often the endothelium was either degenerate or had disappeared (plate 5). No other essential difference could be found between the two types, though the areas which had lost their endothelial covering often projected as definite verrucæ. Sometimes such an area was covered by a thin deposit of platelets and sometimes there was also a layer of fibrin (plate 6). On the deeper aspect the typical rheumatic cellular reaction was readily seen.

In view of these findings, the suggestion is made that the rheumatic verruca consists essentially of necrotic collagenous material derived from the valve itself. Deposition of platelets and/or fibrin may occur as an epiphenomenon, but is not the initiating factor. Given the presence of a rheumatic lesion, two processes are concerned in the evolution of the actual verruca. Firstly, œdema and the seepage of fibrin into the necrotic material through the thin covering layer. This may be due to increased permeability of the valvular endothelium, such as is known to occur in damaged capillary endothelium anywhere in the body. Secondly, trauma and mechanical factors, resulting from closure of the swollen valve leaflets, may increase the tendency to protrusion. In this connection it may be noted that microscopic verrucæ were observed on various parts of the valve surface. Macroscopically the characteristic feature of the lesions is that they occur specifically along the line of closure. The explanation may well be that, provided there is present a minute verruca composed of necrotic tissue on the line of closure itself, the traumatisation occurring along this line will favour the deposition of platelets and fibrin. The result will be a verruca readily visible on naked-eye examination. This would account for the more frequent occurrence of the verrucæ on valves where the pressure is greatest, and along the line of closure of such valves.

Two further types of surface necrosis were noted. In one there was an underlying diffuse type of infiltration of the sub-endocardial tissues associated with the presence of cells of the Aschoff type. In the second there was no reaction in the adjacent tissues, but merely a linear superficial collagenous necrosis. A somewhat similar series of surface changes in relation to alterations in the deeper layers of the endocardium was noted in the wall of the left auricle. In lesions regarded as being of longer duration there was often a persistence of the necrotic material after the active cellular reaction had been replaced by granulation tissue. Eventually healing by fibrosis and vascularisation of the valve occurred.

Though not of primary importance in the rheumatic process per se, it was felt that the verrucæ characteristic of its active phase might be the decisive factor in the pathogenesis of bacterial endocarditis. They present a raw area to which any circulating element might readily adhere. That this occurs in the case of platelets and fibrin has already been indicated. The resulting thrombus must surely provide an excellent site for bacterial implantation. With these facts in mind, a study was then made of the valves of thirty-four cases of subacute, and twelve cases of acute, bacterial endocarditis. In many of these the only valves available were those showing massive bacterial vegetations. In them the extent of the latter was often such as to mask any underlying rheumatic lesion. Nevertheless, in eight out of

the thirty-four subacute, and three out of the twelve acute cases, typical rheumatic, bacteria-free vegetations of one or other of the types previously described were seen. A similar observation was made by Gross and Fried (1937). They considered that since the incidence of typical rheumatic verrucæ was lower than that of myocardial Aschoff bodies, and since they were unable to demonstrate even the presence of Aschoff bodies in all cases, they could not conclude that bacterial infection of the valves in rheumatic patients is due to the implantation of bacteria on unhealed rheumatic verrucæ. Nor did they consider that one is justified in interpreting all such verrucæ as evidence of an active rheumatic process. Their explanation was that, as a result of toxic irritative effects of the bacterial infection, non-bacterial verrucæ may form on the valves. If the suggestion be justifiable that the development of verrucæ is dependent not only on the mere occurrence, but also on the site, of the rheumatic valvular lesion, then one would expect the incidence of verrucæ to be lower than that of the incidence of myocardial Aschoff nodules.

With regard to Gross and Fried's hypothesis of the bacterial origin of such vegetations histologically identical with those of rheumatic endocarditis are found: Secondly, all the cases examined by them were examples of bacterial infection, and if the latter is capable of producing a bacteria-free vegetation, one would expect to see a relatively high incidence of such lesions. On their own showing, this was not so. Conversely, Pappenheimer and von Glahn (1935) noted that bacteria-free vegetations histologically identical with those of rheumatic endocarditis are found:

- (a) On the same valves as the bacterial vegetations.
- (b) On other valves, in the same heart on which there are no vegetations containing organisms.
- (c) On the left auricular wall.

They expressed the view that active rheumatic vegetations are, in persons who have had rheumatism, a necessary and almost constant prerequisite for the implantation of bacteria. It has already been shown in the present study that typically rheumatic, bacteria-free vegetations were seen in hearts showing bacterial endocarditis. It is believed that the former are the sites of implantation of the organisms. It is further believed that transitional forms were seen, in which the original localisation of the organism to the fully developed typical bacterial vegetation could be followed. At first there is merely the deposition of a few organisms on the surface of the rheumatic verruca. As the lesion progresses, these organisms multiply, and there is marked deposition of fibrin and platelets. Often, at a slightly later stage, there appears to be a further process of bacterial implantation and multiplication, and the accumulation of more fibrin. In the early stages the rheumatic nature of the underlying lesion is quite clear. With time and the evolution of the bacterial infection this specifically is lost, and the base of the vegetation consists of granulation tissue (plates 7-10).

In order to assess the likelihood of a patient with an acute rheumatic valvulitis developing an infected vegetation, it is necessary to make some estimate of the frequency with which organisms may enter the circulation. The procedures found

by various workers to result in at least a temporary bacteræmia are shown in Table I.

The most comprehensive reports are those of Okell and Elliott (1935). They obtained positive cultures following dental extractions in seventy-five per cent. of cases with marked oral sepsis. In general, they found that the incidence of bacteræmia depended on the degree of sepsis and amount of operative trauma. One of their most significant observations was that in ten per cent. of 110 persons with gross dental sepsis organisms were recoverable from the blood before any operative interference. Murray and Moosnick (1941) showed clearly that the organisms recovered from the blood in such cases are in fact derived from the gingival area. Fish and MacLean (1936) demonstrated streptococci in the blood and lymph spaces in the peridontal membrane and pulp of pyorrhetic teeth. They were able to prevent infection of the blood stream by cauterisation of the gingival area before extraction.

It is thus clear that focal sepsis, particularly of the oral region, may frequently result in bacterial invasion of the blood stream. Before attempting to correlate such bacteræmias with the onset of subacute bacterial endocarditis, one must determine whether the organisms concerned are the same in both instances. In most cases of endocarditis the organism found is a relatively non-pathogenic streptococcus of the viridans type. Most of the remainder are due to the bacillus influenza. Of thirteen cases in the present study giving positive blood cultures, eleven were due to the streptococcus viridans. One yielded a hæmophilus para-influenzæ, and the other a hæmolytic streptococcus.

Rosebury (1944) states that streptococci of the viridans type are generally, though not always, the organisms found in the blood stream in cases with transient bacteræmia. He also states that the most complete serological classification of the greening streptococci is that of Solowey (1942), who studied over two hundred strains. Of these, 108 had been isolated from the blood of patients with endocarditis lenta; 99 were obtained from human throats and infected teeth, 15 were vaginal in origin. No less than three-quarters of these, other than those of vaginal origin, were streptococcus salivarius. In this connection it may be mentioned that Horder (1908-9) found that in sixty-six per cent. of forty cases of subacute bacterial endocarditis, blood culture yielded "saprophytic" streptococci of the type common in the alimentary tract.

Hadfield and Garrod (1942) state that the organism responsible for most cases of subacute bacterial endocarditis is a non-pyogenic streptococcus. In their opinion such organisms exhibit almost endless variety in morphology, colonial characters, and fermentation: they consider that the disease may, in fact, be due to any of a number of nondescript streptococci whose normal habitat is the mouth. They suggest a similar origin for the other accepted causal organism, the hæmophilus para-influenzæ. It thus seems apparent that the organisms concerned in both transient bacteræmias and ulcerative endocarditis of the subacute type are the same.

Recently there have been several reports linking chronic focal sepsis, with the

ever-present opportunity for bacteræmic episodes, with the initiation of infected cardiac vegetations in susceptible patients. Rushton (1930) was one of the first to note this association. He also pointed out that the relation to oral sepsis may often be overlooked, due to omission of any dental examination from the case reports. This is probably true also of many other possible antecedent causes of bacteræmia, which may often be subclinical in their manifestations. Another factor which renders difficult the association of a possible bacteræmic episode with subacute bacterial endocarditis is the very insidious onset of the latter, which makes it difficult to date with accuracy.

It has already been concluded that acute rheumatic valvulitis offers a suitable focus for the implantation of bacteria. The chances of a coincident bacteræmia at this stage appear to be such as to render the superimposition of an infected vegetation a practical possibility.

Corroborative evidence of the importance of activity of the rheumatic process was afforded by study of the myocardial lesions of cases of bacterial endocarditis of the subacute type. Twenty-seven out of thirty-four (seventy-nine per cent.) showed recent rheumatic stigmata of various types. Similar findings were obtained in several of the acute cases. An even more significant finding was that in those cases in which the clinical duration of the bacterial endocarditis could be estimated, the apparent histological age of the rheumatic lesion was comparable.

Moreover, it was demonstrated that the administration of horse-serum to rabbits resulted in myocardial and valvular lesions very similar to those of acute rheumatic carditis in man. In animals showing these lesions the intravenous inoculation of a culture of streptococcus viridans resulted in the development of a bacterial endocarditis of the subacute type. In a control series of normal rabbits receiving an exactly similar dosage of organisms, no evidences of bacterial localisation was found (MacIlwaine, 1945).

This theory of active rheumatic lesions as the ætiological basis for subacute bacterial endocarditis is in accord with many of the recognised features of the disease. The valves on which the bacterial vegetations are prone to develop are those on which the incidence of rheumatic lesions is maximal. Mural implantation of bacteria is uncommon except on the posterior wall of the left auricle. This is a very common site of rheumatic lesions (plate 11). Changes in the valve angle are occasionally noted in rheumatic endocarditis (plate 12). These were also seen in the experimental reproduction of the valvular changes. Both in man and in the rabbit bacterial vegetations were occasionally noted in this situation. None of the other hypotheses suggested for the initiation of the bacterial lesion appear to explain the occurrence of the vegetations on either the left auricular wall or the valve angle, where mechanical stresses are minimal. Clinically, the onset of bacterial endocarditis is unusual in cases with long-standing valvular lesions or in whom auricular fibrillation has supervened. This is interpreted as being due to the fact that the tendency to recurrence of the rheumatic attacks diminishes with increasing age.

In addition, the pathological process described can be utilised to explain at least in part the curious paradox of a comparatively innocuous organism, such as

the streptococcus viridans, as the cause of a disease which is almost, if not always, fatal.

It has been pointed out that the rheumatic verrucæ often show a surface deposition of fibrin, on which it is believed that the organisms settle. The process is regarded as being cumulative, with the laying down of more fibrin and organisms, till finally the large vegetation typical of subacute bacteria endocarditis is formed. The streptococcus grows luxuriantly in fibrin. Friedman (1938) pointed out that a fibrin mass is very impermeable, and that this impermeability is augmented in the presence of serum. He noted that "an infected fibrin mass suspended in serum is the actual pathological picture encountered in subacute bacterial endocarditis." He and his associates believed that persistence of the organisms depends on two factors—

1. The sluggish inflammatory reaction of the valve, so that the focus is not sterilised and walled off, as occurs in other parts of the body.
2. The presence of the fibrin, which not only acts as an excellent culture medium, but also prevents leucocytic infiltration.

The organisms also seem to be unaffected by specific antibodies, which are frequently present in the blood during the course of the disease. This is possibly because they too are unable to pass the fibrin barrier to reach the organisms. The persistence of the infection cannot be attributed to a general lowering of resistance and septicæmia. This is evident from the fact that when particles of the vegetations break off to form emboli, the resulting infarcts are not septic, and heal rapidly. Also, reports in the literature indicate that when it is possible to isolate the infected focus, cure often results. Hamman and Reinhoff (1935) reported a case in which a traumatic arterio-venous aneurysm became the site of an infected vegetation. Complete cure of the viridans septicæmia followed ligation of the affected vessels. There have also been an increasing number of reports in recent years, showing that bacterial endocarditis associated with patent ductus arteriosus has been cured by ligation of the infected segment of the vessels.

The factor responsible for the continuance of the infection must therefore be inherent in the valvular lesion itself.

Many workers, but in particular Libman (1923), have emphasized that healing may occur. This is noted in two types of patient. One is the person who, from showing all the clinical signs and symptoms of the fully developed disease, gradually returns to comparatively normal health. In the second, more common variety, the patient though showing a remission of infection, dies as the result of mechanical alterations in the general circulation, or of embolisation, or even uræmia. At post-mortem of such patients Libman states that there are often evidences of healing.

A point which appears to be of importance in this question of progression or retrogression of the valvular lesion, and which has been relatively neglected in the literature, is the possibility of re-infection. It has been shown that focal sepsis may result in a bacteræmia. Chronicity is usually one of the outstanding features of any focal area of infection. If one bacteræmic episode can occur, there seems

no reason why the process should not be repeated. The large rough bacterial vegetation, with its superficial coating of fibrin, surely presents an even more favourable site for bacterial invasion than the original rheumatic lesion. If this is so, then one can visualize a cumulative process in which the very presence of the bacterial vegetation is the dictating factor in its persistence. Obviously in such circumstances any attempt at healing by the formation of granulation tissue in the base of the vegetation will be frustrated by the superficial deposition of new zones of bacteria and fibrin.

It is felt that this hypothesis may account for those cases in which definite remissions, with obvious improvement in the clinical condition, are followed by the return of all the signs of infectivity, with a fatal termination. When the original and re-infecting organisms are the same, this sequence of events will be almost impossible to prove. There are, however, scattered reports in which re-infection with a different organism has been demonstrated.

Libman (1923) stated that in cases of subacute streptococcal endocarditis, secondary infections with pneumococci are occasionally found. He also noted that following a bacteria-free phase in a case of influenzal endocarditis, re-infection with an anhaemolytic streptococcus occurred. Libman felt that such recurrences of the disease are much more frequent than recognised. Orgain and Poston (1942) presented six cases of classical endocarditis in which two or more organisms were repeatedly isolated from the patient's blood during life.

Although the presence of mixed infection has been noted by several authors, there has been very little comment on this finding. Obviously such an occurrence is of importance, not only in the maintenance of the valvular lesion, but in the therapy of the disease. The main difficulty in effective use of chemotherapeutic agents is generally considered to be the presence of the impermeable fibrin mass which surrounds and protects the bacteria. It has been suggested that heparin may be effective in dissolving this barrier. The reports on sulphonamide therapy, with or without the additional use of heparin, are conflicting, but on the whole disappointing. Some of the reports on penicillin are more promising, but it is too early yet to assume that a reliable and constant therapeutic measure has been found. No bactericidal agent capable of use in the human subject has yet been proved effective against every organism. Therefore, even if some method is found which is universally effective even in the presence of the fibrin barrier, the ultimate test of its value will be whether the organism—or organisms—concerned be susceptible to its action. The recognition of mixed infections thus becomes of practical importance in the treatment of subacute bacterial endocarditis. It is suggested that until the cure of the bacterial lesions becomes a practical reality, chemotherapeutic and other measures should be used in the elimination of all chronic foci of infection elsewhere in the body. These appear to be the initial cause of the bacteræmias without which bacterial endocarditis could not develop, no matter how susceptible the state of the valve. It is wished to emphasize particularly that such prophylactic measures are appropriate in the rheumatic patient. In the absence of a bacteræmia the acute rheumatic valve progresses through the various stages

TABLE I
REPORTED OCCURRENCE OF BACTERÆMIA.

AUTHORS	PROCEDURE
OKELL AND ELLIOTT (1935) - -	Extraction of teeth.
BURKET AND BURN (1937) - -	Extraction of teeth.
PALMER AND KEMF (1939) - -	Extraction of teeth.
MURRAY AND MOOSNICK (1941) -	Extraction of teeth.
FAILLO (1942) - - -	Extraction of teeth.
NORTHRUP AND COWLEY (1943) -	Extraction of teeth.
ROUND, KIRKPATRICK, AND HAILS (1936) - - -	Ten minutes mastication in patients with pyorrhœa.
ELLIOTT (1939) - - -	Movements of a tooth in its socket before extraction.
MILLET AND VAN EYK (1940) -	Operation or curettage for chronic tonsillitis or enlarged adenoids in children.
ROMER (1913) - - -	Uterine curettage.
RICHARDS (1920) - - -	Manipulation of arthritic joints.
BROWN (1923) - - -	Appendectomy.
SIEFERT (1925) - - -	Various surgical procedures.
LEHMAN (1926) - - -	Uterine curettage.
SCOTT (1929) - - -	Operations on the urinary tract.
BARRINGTON AND WRIGHT (1930) -	Operations on the urinary tract.
RICHARDS (1932) - - -	Manual massage of infected areas.

of healing to fibrosis, and the end result is often a well-compensated valvular lesion. If, on the other hand, bacteria enter the blood stream in the active stage of a rheumatic valvulitis, the end result may well be a fatal bacterial endocarditis.

Further, the evidence suggests that waves of bacteræmia may lead to the additional deposition of bacteria in the vegetations. If so, then it becomes a matter of some importance to eradicate all foci of infection, even in the patient who is already suffering from bacterial endocarditis. It is clear that it is of little avail to sterilise the blood stream, or even the vegetations, if new bacteræmic episodes are permitted to occur before there has been time for healing. Until re-epithelialization of the valvular surface is complete, the possibility of re-infection remains. It therefore seems imperative that treatment should be maintained long after the signs of infectivity have disappeared.

CONCLUSIONS.

1. The changes occurring in the valves in the acute stage of rheumatic fever are shown to be of such a nature as to afford a suitable site for the implantation of organisms on a purely mechanical basis.
2. The vegetations of subacute bacterial endocarditis may be associated with typical rheumatic verrucæ.

3. Early implantation of organisms on rheumatic verrucæ has been observed.
4. The sites of bacterial vegetations in the subacute type of endocarditis are identical with those upon which the surface endocardial changes are maximal in rheumatic fever.
5. Bacteræmias, originating from focal sepsis, most commonly in the oral region, are not infrequent. They appear to supply the organism responsible for the majority of cases of subacute bacterial endocarditis.
6. Indications relative to the treatment of this disease in the light of these findings are discussed.

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THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS



Plate 1. A.2514 (x30)

Acute rheumatic fever. Valve leaflet showing generalised inflammatory infiltration in both layers of spongiosa. The fibrosa is relatively unaffected.

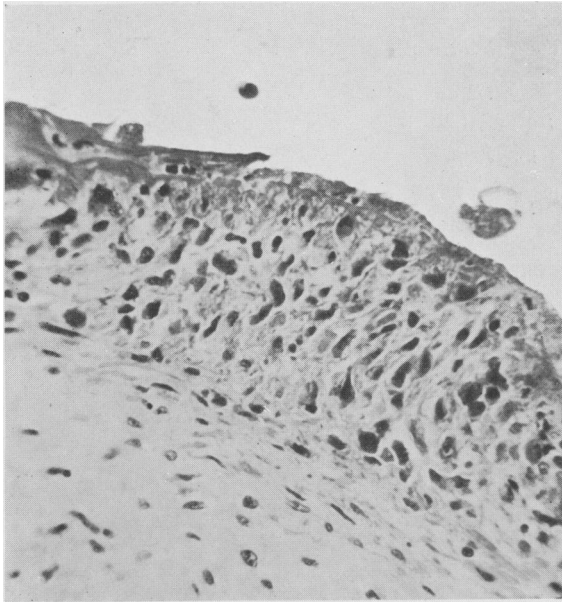


Plate 2. A.4119 (x350)

Rheumatic valvulitis. Palisade arrangement of sub-endocardial cells. The necrosis of collagen extends through the palisade, and is continuous with surface necrosis.

THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS

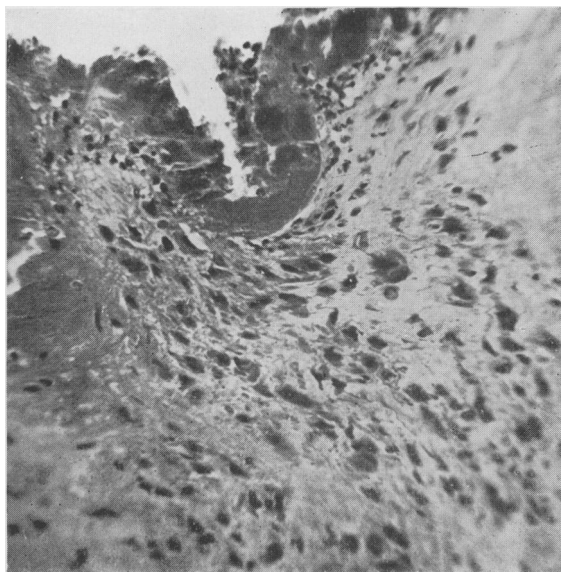


Plate 3. BA.283 (x275)

Rheumatic valvulitis. Marked surface necrosis of collagen. In the deeper layer the specific rheumatic nature of the reaction is shown by the presence of large mononuclears and giant cells.

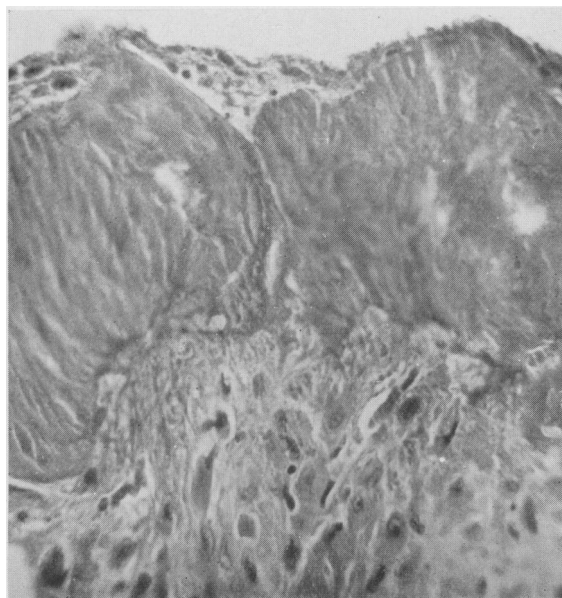


Plate 4. A.3286 (x350)

Typical rheumatic verruca composed entirely of necrotic valvular elements and possibly fibrin, which has entered by seepage. The covering endothelium is still present.

THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS

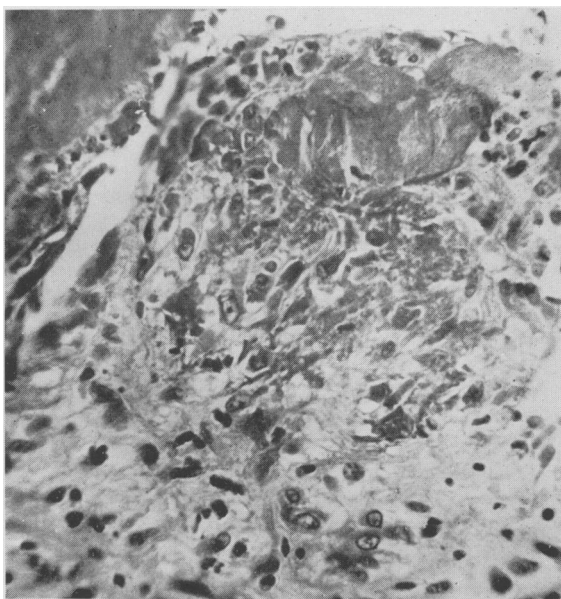


Plate 5. A.4119 (x350)

Rheumatic fever. Superficial necrosis of collagen extending to surface of valve. There has been loss of the covering endothelium.

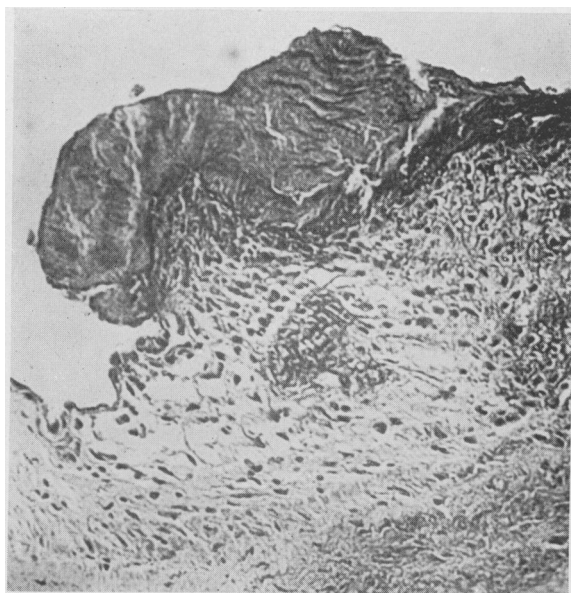


Plate 6. A.4339 (x200)

Rheumatic valvulitis. Verruca projecting from surface of valve and showing superficial deposition of fibrin. There is an underlying rheumatic reaction.

THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS

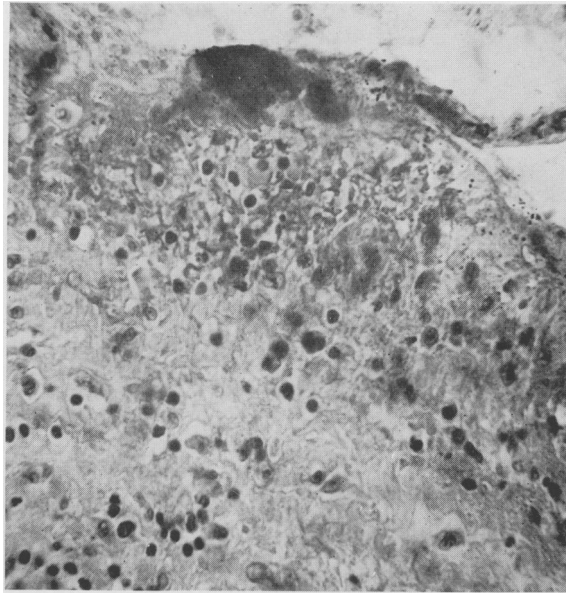


Plate 7. A.2519 (x60)

Early deposition of organisms on surface of active rheumatic lesion.

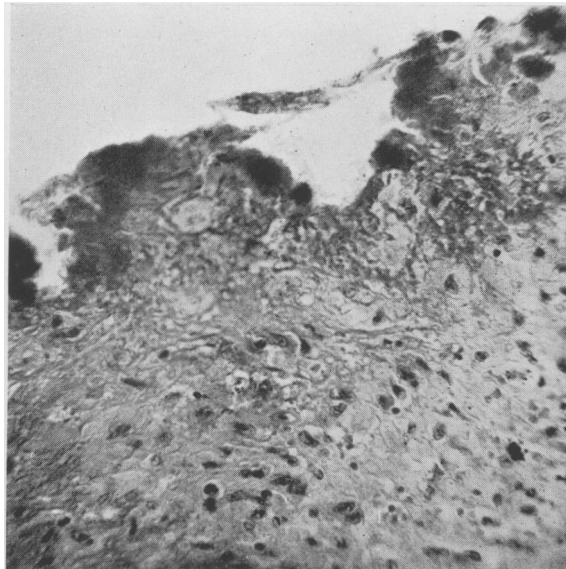


Plate 8. L.4 (x325)

Bacteria implanting on necrotic collagen along surface of mitral valve. The deeper layers show the rheumatic type of reaction.

THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS

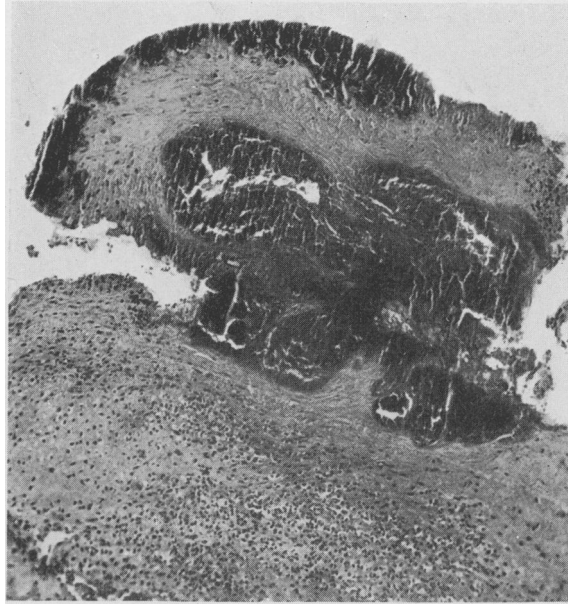


Plate 9. A.2519 (x120)

Later stage in the evolution of the bacterial vegetation. The organisms have multiplied within their protective covering of fibrin. On the outer aspect of the fibrin there is another zone of bacteria.



Plate 10. A.2703 (x20)

Part of large fully-developed bacterial lesion.

THE PATHOGENESIS OF SUBACUTE BACTERIAL ENDOCARDITIS

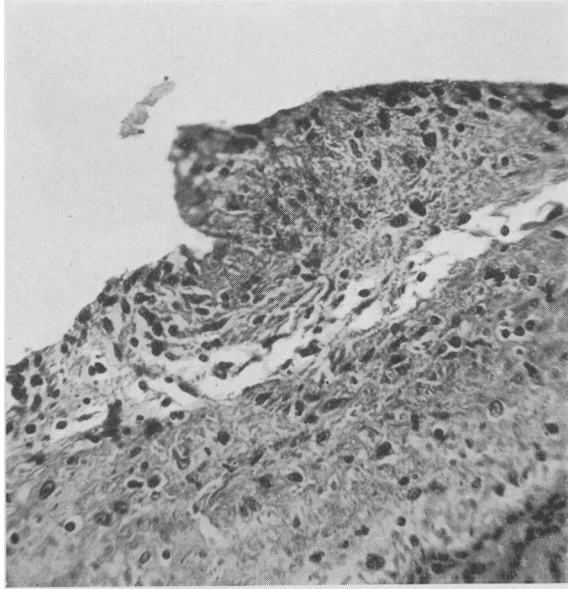


Plate 11. A.2699 (x275)
Rheumatic lesion in left auricular endocardium.



Plate 12. BA.283 (x100)
Intense necrosis of collagen in valve angle in acute rheumatic valvulitis.

REVIEWS

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