at a subsequent operation. In women and such men as desire it the finger may be conserved, but for the subject employed in manual labour better function may be obtained by amputation.

Summary

1. This paper is based on the experience gained in the study of 183 cases of infections of the hand, of which fifty-one cases were pulp-space infections.

2. Aching followed by throbbing and inability to sleep, associated with induration of the pulp, should be the established indications for immediate operation in pulp-space infection.

3. With adequate drainage inflammation in the pulp readily subsides. If resolution is delayed it is urged that the transfixion operation should be carried out.

4. Complications in pulp-space infection can be prevented by providing adequate drainage in the early stages.

5. In a chronic case it is essential to employ radiological examination before proceeding to treatment.

6. In the treatment of sequestrum formation and the prevention of tenosynovitis it is necessary to employ care in operation, and if possible to conserve the base of the distal phalanx.

ACKNOWLEDGEMENTS.—I wish to thank the honorary surgeons of the Queen's Hospital, Birmingham, for their courtesy in permitting me to carry out this work, and Mr. T. S. Donovan for his advice and criticism in the treatment of these cases. I am indebted to the honorary staff of the radiological department for help in the radiological work. In particular I wish to express my gratitude to Sister Arnold and the nursing staff for the kindness, care, and thought exercised in the treatment of these patients, without which it would have been impossible to conduct the post-operative care and follow-up. My thanks are also due to Mr. Coombs, radiographer to the Sheffield Royal Infirmary, for help with the radiographs. Finally, I wish to record my indebtedness to Dr. F. H. Kemp, clinical assistant in radiology at the Sheffield Royal Infirmary and Hospital, without whose help, criticism, and encouragement this paper would never have been published.

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The annual meeting of the British Association will be held at Nottingham from September 1 to 8 inclusive, under the presidency of Sir Edward Poulton. Thirteen Sections have been arranged—namely, mathematics and physical sciences, chemistry, geology, zoology, geography, economics, engineering, anthropology, physiology, psychology, botany, educational science, and agriculture. Presidential addresses of medical interest are as follows: Dr. G. W. C. Kaye, noise and the nation; Dr. F. L. Pyman, chemotherapeutic research; Professor F. A. E. Crew, the sex ratio; Dr. J. H. Hutton, Assam origins in relation to Oceania; Dr. E. P. Poulton, new views on metabolism and nutrition, and growth in man; Dr. Mary Collins, tests in common use for the diagnosis of colour defect; and Mr. H. G. Wells, the informative content of education. Other sectional discussions will relate to the contribution of physiology to the health of the individual and the community, protein chemistry, recent advances in genetics and cytology, motor vehicles and road safety, and the national food supply. Professor H. Hartridge will deliver a public lecture on illusions of colour. Further information about the programme of meetings, excursions, and accommodation in or near Nottingham may be obtained from the secretary, British Association, Burlington House, London, W.1.

ENTERIC FEVER★

BY

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I must begin by emphasizing that I speak only from the standpoint of a practising medical officer of health. In consequence most of what I have to say must appear somewhat elementary—a reiteration of what is already well known. But administration is mainly concerned with the application of established principles in changing circumstances, and the principles governing the prevention of enteric are no longer in doubt. Although many points of detail still await elucidation, our practical problem is the efficient utilization of the knowledge we already possess.

Reduction of Incidence and Mortality

It is not necessary to adduce statistical evidence as to the great diminution in the incidence of enterica in recent years. When a death rate drops, more or less steadily, from 388 per million in 1870 to 4 per million in 1935 there can be no serious doubt that the disease is becoming less common. Nor are statistics necessary to establish what is within the personal knowledge of senior members of the profession. A generation or two ago enteric was familiar to everyone in practice. To-day it is almost a clinical curiosity: there are many practitioners of standing and experience who have never had occasion to diagnose or treat a case.

But if enteric in its endemic form is no longer a constant menace, it is still capable of manifesting itself on occasion in formidable epidemics. The greatest water-borne outbreak on record—that which occurred at Barcelona and caused 1,847 deaths—was no further back than 1914. The outbreaks at Pforzheim in 1919, at Hanover and Rostoff-on-Don in 1926, and at Lyons in 1929 were all epidemics of the first magnitude, affecting thousands of people, while so recently as 1927 Montreal experienced a milk-borne epidemic, wherein 5,002 persons were infected and a tenth of them died. We have fortunately escaped tragedies of such dimensions, but sufficient outbreaks have occurred in recent years to remind us that enteric is still to be reckoned with as a serious problem in public health.

There is not much room for doubt as to the conditions which have determined the reduction of its incidence. Of no other infective disease can we say with the same confidence that sanitary activities have completely justified themselves. There is no reason to suppose that, in the absence of those activities, enteric would not be as prevalent to-day as it was in the middle of the last century. There is no evidence to suggest that it is less virulent or less capable of spread in a susceptible community, or that herd immunity to infection is greater than in former times. An almost savage scepticism is essential to the sanitarian, who is constantly tempted to believe that improvements in health are the result of his efforts to bring them about; but in this connexion scepticism appears misplaced.

The diminution of mortality, so far as Great Britain is concerned, came in three stages. From the early seventies it fell fairly steadily till 1885. From that date till about 1900 there was little improvement. At the

* Read in opening a discussion in the Section of Hygiene and Public Health at the Annual Meeting of the British Medical Association, Belfast, 1937.

beginning of the century the fall recommenced, and has continued till the present day.

One is aware of the temptation to over-simplification in discussing such phenomena, but there does appear to be justification for believing that the change in the incidence of the disease reflects the change in our views as to its aetiology. The hypothesis that insanitary conditions were the *cause* of infectious disease has been replaced by the belief that they are responsible for its spread, and the acceptance of the latter view has greatly influenced our attitude towards prevention. The first efforts of sanitary reformers were directed to environmental improvements—provision of better water supplies and substitution of sewers for privies. The success of those efforts was explained in terms of the pythogenic theory, Pettenkofer's ground-water theory, and the belief that enteric might be spread by sewer air—views that were held by observers whose opinions were entitled to all respect, but which, despite their value in promoting reform, are now regarded as ill founded.

Advances in Pathology

Further advance had to wait on the more accurate knowledge of pathology which accumulated during the last years of the century. The bacterial origin of the disease was recognized by the profession, the introduction of Widal's test put diagnosis on a sound basis, and the conviction that the enteric patient was the real source of enteric infection gained ground. Finally, the discovery of the potentialities of the carrier provided a credible explanation of the apparent *de novo* origin of epidemics.

Meantime, sanitary administrative machinery was being improved. More attention was given to the protection of food against gross contamination, and, in particular, the practice of removing enteric patients to hospital was increasing. This, I suggest, was one of the most important causes of the disappearance of endemic enteric, especially in rural areas, where "sanitary" improvement was often non-existent. I know many parishes where the disease, common during the 'nineties, has been practically unknown during the present century. There are still no sewers, the water supplies are still obviously open to pollution, flies still pass unchecked from privy to larder, but the enteric patient is no longer allowed to remain in a country cottage throughout the course of his illness, a constant danger to his immediate associates, a potential menace to the whole district.

Recently the carrier problem has been exhaustively studied, much information on preventive inoculation has been collected, and important advances in bacteriological technique have made it possible in many cases to obtain direct evidence on what in former days could only be inferred. But nothing has happened to modify the orthodox belief that the prevention of epidemic enteric is essentially a matter of protecting drinking-water and food, especially milk, from specific infection.

Now it is obvious that if the incidence of an infectious disease falls, not from natural causes but as a result of human effort, that effort must be maintained if recrudescence is to be avoided, and we must consider from time to time whether accumulation of knowledge justifies, or altered conditions demand, any change of our methods.

An indication that defensive arrangements are not yet perfect is the fact that water-borne and milk-borne epidemics still occur from time to time. These differ in their genesis. Recent investigations have shown that the life of *B. typhosus* in sewage may be considerably longer than was generally supposed, but the actual occurrence

of water-borne epidemics seems to depend on recent and gross contamination, which disappears fairly rapidly—from an epidemiological if not from a bacteriological point of view—unless pollution be continuous. In any case, whether a sewage-polluted stream, a clean source accidentally fouled by excreta, or a well or leaking main contaminated by a faulty sewer be in question, infection is generally massive and comprises a vast bacterial flora in addition to *B. typhosus*. This appears to be the explanation of the occurrence of the widespread outbreaks of gastritis and enteritis which frequently precede water-borne epidemics. At Hanover about 30,000 and at Rostoff-on-Don about 40,000 cases of those conditions occurred just before the appearance of enteric, and the same thing has been observed on a smaller scale in many other places.

Another phenomenon, apparently due to the same cause, is the occurrence of a certain proportion of cases of paratyphoid fever along with the true Eberthian infection. In the two outbreaks I have mentioned about 6 per cent. and 16 per cent. respectively of the total cases were paratyphoid infections. There is not at present sufficient information on the point to speak with certainty, but it seems probable that this coexistence of typhoid and paratyphoid is specially characteristic of water-borne outbreaks, and indicates original massive contamination.

Infection by shellfish may perhaps be considered as a special form of water-borne disease resulting from gross and continuous pollution. It is interesting to note that in many instances shellfish infection has been associated with preliminary enteritis resembling that occurring before ordinary water-borne epidemics. The enteric-infected oyster still constitutes a serious problem in some places. That its importance for us has diminished is due in no small degree to research on the subject in Belfast.

Infection of milk is another affair. Though dairy hygiene still falls short of perfection, gross excremental pollution from human sources is unlikely. The amount of pathogenic material, whether derived from infected water or from a carrier's hands, is presumably small, but it is introduced into what may be an excellent medium for the growth of *B. typhosus*. It is this circumstance which makes prevention of milk-borne epidemics especially difficult. It is not possible to protect the milk supply against the risk of infection by a carrier or an unrecognized case of enteric. A dairyman, however conscientious, cannot be expected to recognize conditions which an experienced physician may have difficulty in diagnosing.

Protection of Water and Milk Supplies

As water and milk become infected in different ways they must be protected by different methods. Safeguarding of water is largely a question of finance, and there should be little need for discussion so far as large towns are concerned. Sources protected against pollution, adequate storage, efficient filtration, and, when necessary, chemical treatment constitute a succession of lines of defence sufficient to secure immunity. If one of those desiderata be lacking special emphasis must be laid on the others. Large communities, moreover, can provide expert supervision and sufficient staff to maintain efficiency. The experience of London in particular shows that by taking proper precautions the risk of water-borne infection may be reduced to negligible proportions.

The position of small towns, villages, and rural communities is different. Their water supplies are still frequently open to serious criticism, but the confidence re-

sulting from years of immunity and the relatively heavy financial burden entailed by improvements discourage sanitary reform. Such small supplies are often under the charge of an officer who has many other duties and who may have no real knowledge of water problems. Serious defects may exist unrecognized until they are discovered by accident or in the course of an epidemic. In a water-borne outbreak affecting sixty-five people, with which I had to deal some years ago, it was found that infection had occurred at leaking joints in the pipes conveying spring water to the collecting-tank. These might probably have been detected and remedied by a trained water engineer, but not unnaturally escaped the observation of the village factotum.

In such small communities, which may have provided sewers and gravitation water supplies many years ago but have neglected to maintain them in a proper state of efficiency, the risk of pollution increases steadily. Most medical officers of rural areas have probably seen contemporary examples of sanitary defects closely resembling those responsible for the classical water-borne epidemics of fifty years ago. It is totally erroneous to suppose that the improvement in water supply during the last quarter of the nineteenth century affected the whole country. There are still many places where the absence of water-borne disease depends on the lack of a source of infection rather than on safeguards against its spread. This is not likely to be remedied until water supply is recognized as a regional rather than a local problem and assistance given to those places whose own resources are inadequate to its solution.

A special danger in rural areas is the "auxiliary" supply, used to supplement an insufficient source of drinking-water. It is practically certain that it will be drunk occasionally. I have known one instance in which cases of enteric occurred at a farm which drew its drinking-water from a well but had an auxiliary supply from a stream near by. The patients were known to have drunk from the latter source despite warnings. About a mile upstream was a cottage provided with a water-closet draining to a cesspool which discharged into the stream. The tenant of this cottage proved to be a woman who had been shown several years previously to be a typhoid carrier, and we were successful in cultivating *B. typhosus* from the cesspool contents.

An adequately protected water supply is of importance in the prevention of milk-borne epidemics. It is of course possible that an outbreak originally due to polluted water may be continued by milk through someone connected with the dairy trade having been a victim of the water-borne infection. This was well exemplified at Santa Ana (Ca.) in 1924, when an epidemic due to sewage-polluted water and affecting some 370 persons was followed by a milk-borne outbreak of 200 cases in a neighbouring town, which had a separate water supply but derived much of its milk from a dairy at Santa Ana. The risk of such occurrences is very grave, and should enteric be prevalent in a dairying country it is essential that everyone connected with the milk business be kept under close supervision and all milk pasteurized till the danger of infection is past.

Again, milk may be infected through polluted water being used to wash utensils. Theoretically this should never happen, but until all dairies are fully equipped in accordance with modern ideas this risk cannot be ignored. There are cases in which milk has been infected during the cooling process, either by a leaking cooler allowing water to gain access to the milk, or, in the absence of a

sufficient water supply, by the milk-cans having been set to cool in a stream which proved to be sewage-polluted. This appears to have caused the St. Catherine (Ontario) epidemic of paratyphoid fever in 1931. In this case 475 cases were traced to milk from two farms where milk-cans were cooled in a small creek that was contaminated by drainage from a district in which paratyphoid fever had been prevalent in the previous year. Such incidents show the need for securing that all water supplies, whether for drinking or for use in the production of milk or other foods, shall be protected against the risk of contamination. Neglect of this may have far-reaching consequences. A single case of enteric fever in a rural area may mean a big milk-borne epidemic in a distant city. Dr. Russell, then medical officer of health for Glasgow, said many years ago: "The status of enteric fever in Glasgow mainly depends upon rural sanitary administration." The experience of many large cities, both in Europe and in America, has proved that the truth of the observation is of general application.

The Carrier as a Cause of Infection

The main cause of milk-borne outbreaks is of course infection by a carrier, missed case, or contact who handles milk. Unfortunately his existence is generally unsuspected until the outbreak occurs, and even then it may be difficult to confirm. Proof of the carrier state entails detection of the causative bacillus in urine or faeces, and the intermittency of bacillary excretion by carriers may prevent this proof being obtained. Moreover, as I have learned by experience, samples submitted by a suspected carrier may have been borrowed for the occasion! Even after the carrier has been recognized the period during which he can be certified and put under restrictions is too short, and recertification may present difficulties. It should be recognized that after a year the carrier condition is permanent, and recertification should not be required.

Serological examination of suspects may help in detecting the carrier. The ordinary Widal test, however, does not give a sufficiently certain indication. I am not competent to discuss this point, but it seems possible that research on antigenic structure may eventually provide a reliable means of identification. Such a test would be of great value in practical administration.

It is a question whether anything short of universal pasteurization can protect against the risk of milk-borne enteric. The objection that this might lead to neglect of cleanliness in dairying could be met by fixing a sufficiently stringent prepasteurization standard, though the practical enforcement of such a standard would not be easy. Again, pasteurization is not an absolute safeguard, as the experience of Montreal and other places has shown. It would still be necessary to ensure that nobody capable of spreading infection was allowed to handle the pasteurized milk. A recognized carrier should of course be absolutely precluded from taking any part in the milk trade; indeed, in any business entailing handling food. But the control of carriers is so large a question, and raises so many issues, that I can only mention it here.

Conclusion

There are many other aspects of the subject which I should like to discuss did space permit, but there are two in particular which I emphasize in conclusion.

First, enteric fever should whenever possible be treated in hospital. The risk of infection is too great and too prolonged to justify home isolation, except in special cases, and it is in the patient's interest that he should receive

the expert nursing which is more important in this than in almost any other infectious disease.

Secondly, every outbreak should be fully studied by an expert bacteriologist. It seems that sometimes no more is done than the minimum necessary for diagnosis. This is not enough. The bacteriological history of each patient should be recorded as fully as the clinical. Investigation of the channels of spread should be checked by repeated examinations of sewage, water, milk, etc., and this may now be attempted with a reasonable hope of success. If it were done regularly our knowledge of and control over enteric fever would be materially increased.

THE SEX GLANDS THEIR ANATOMY, PHYSIOLOGY, AND BIOCHEMISTRY*

BY

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Since subsequent speakers will discuss in detail the administration of various sex hormone products, I shall perhaps be able to fulfil my function as the opener by giving a brief summary of the present position with regard to therapeutic substances. The object of those who organize discussions such as this is to provide a practical survey of the subject, and I therefore propose to deal only with those substances which are of practical value and which can be obtained in an active stabilized form in the ordinary commercial market.

In the physiology of the sex glands it is necessary to consider two separate stages: first, the activation of the secondary sex glands by hormones of the anterior lobe of the pituitary; and, secondly, the hormones secreted by the sex glands after activation. The relation between the anterior lobe of the pituitary, the ovaries and testes, and the mammary glands can be seen in the following diagram, which is self-explanatory.

Hormones of the Anterior Lobe of the Pituitary

It is a well-known fact that the injection of extracts from the anterior lobe of the pituitary into immature animals will produce the precocious appearance of puberty

associated with ovulation and the formation of corpora lutea in the case of the female; and in the case of the male descent of the testis and spermatogenesis will occur. Conversely, in the hypophysectomized adult animal all sexual activity ceases; and this again can be restored by the injection of a suitable extract. Up to the present, however, there is no such extract of the anterior lobe available for clinical trial.

It was discovered that in certain species the urine of pregnancy contains a substance capable of stimulating the ovaries of the immature animal. The test for the presence of this gonadotropic substance forms the basis for the well-known Aschheim-Zondek reaction; the substance was given the name of prolactin by the original German investigators. The problem then arose as to whether this was a single substance or whether, according to the German view, it was composed of two parts—prolactin A stimulating the ripening of the follicle, and prolactin B being responsible for the luteinization of the follicle. The material which is at present on the market is agreed by nearly all workers to be almost entirely the luteinizing fraction. Therefore when we speak in subsequent discussions of the urinary gonadotropic hormone it must be borne in mind that we are dealing almost entirely with the luteinizing fraction.

It has recently been shown that the serum of the pregnant mare during certain stages of gestation contains a very active ovary-stimulating factor. This has been separated, and is available for clinical trial under the name of "antex." Most workers have agreed that antex is mainly follicle-stimulating, as opposed to the luteinizing fraction.

With these two substances—namely, urinary prolactin and antex—it would appear that the clinician is provided with all the factors necessary for the control of ovarian secretion; but the clinical applications of these will be discussed by subsequent speakers. With regard to the chemical constitution of these substances little is known, but they are available in a stable and standardized form.

Hormones of the Ovary

Reference to the accompanying diagram will show that there are three substances—namely, oestrone, oestradiol, and progesterone. There are other oestrogenic compounds in addition to these, but since they are not available for clinical trial they will not be discussed here. Both oestrone and oestradiol, when injected into ovariectomized animals, will produce all the changes associated with the sexual cycle in the rodent. They will also cause the onset of premature puberty, and they only differ one from the other in their relative potency; oestradiol is by far the more potent of the two substances. Both oestrone and oestradiol are available clinically in the form of benzoates. These esters are used because their absorption is slower, and therefore with a single injection it is possible to get an effect very nearly approaching that of the normal function.

If either of these substances be administered to the monkey it is found that the menstrual cycle cannot be reproduced. Experiments on the ovariectomized rabbit have shown that a second factor is necessary for the complete reproduction of the cycle, and that this may be obtained from the corpus luteum. This material, called progesterone, has been isolated from alcoholic extracts of the corpus luteum, and has been characterized chemically. It is produced commercially in two ways—from the corpora lutea and also by the complex degradation of stigmasterol. If oestrone or oestradiol be in-

* Read in opening a discussion in the Section of Anatomy, Physiology, and Biochemistry at the Annual Meeting of the British Medical Association, Belfast, 1937.