Correspondence

Letters to the Editor should not exceed 500 words.

Clostridial Sepsis

SIR,—This laboratory receives occasional requests for advice from hospitals in which a case of gas gangrene has followed a "clean" surgical operation. Because little is known about the circumstances in which this disastrous complication occurs we made a request for information about cases of clostridial sepsis to directors of public health laboratories, and to those hospital pathologists who contribute to the weekly return of infectious diseases of the Public Health Laboratory Service.

In nine months we have heard of 20 cases which conformed to our definition of clostridial sepsis following a "clean" surgical operation. Clostridial sepsis included (*a*) gas gangrene and anaerobic cellulitis—e.g., muscle necrosis and gas in the tissues—or acute swelling with crepitus and toxaemia, from which clostridia were isolated, and (*b*) acute localized inflammation in a wound not less than seven days after operation, when a clostridium was the only potential pathogen isolated. A "clean" surgical operation was one which did not involve the gastrointestinal or biliary tract, or the vagina, and was not for the treatment of an open traumatic lesion.

All 20 infections were due to *Clostridium welchii*. Sixteen patients had gas gangrene or anaerobic cellulitis, and 11 of them died while in hospital. Seven died of clostridial toxaemia and two from the complications of reoperation or amputation; the remaining two died partly or wholly from other causes. Three of the five survivors suffered an amputation or re-amputation.

Four patients had a localized septic infection without gas formation or muscle necrosis; all of them recovered without further operation.

Nearly all of the operations (18 of 20) were on the lower limb and involved bone. They were of two sorts: (1) amputations (eleven, of which nine were through the middle or lower third of the thigh and two were below the knee) and (2) operations in which a foreign body was inserted (seven, of which six were in the upper end of the femur). The remaining two operations were a craniotomy and a lumbar sympathectomy.

Nine of the 11 patients in whom clostridial sepsis followed an amputation had gas gangrene or anaerobic cellulitis, and six of them died. All suffered from arterial insufficiency, and six were diabetics.

The operations which involved the insertion of a foreign body were: arthroplasty of hip with insertion of prosthesis 4; pinning of neck of femur 2; osteotomy of tibia 1. Five of the seven patients died; in three cases the diagnosis was first made at necropsy.

The 20 infections occurred in 17 different hospitals, and all appear to have been sporadic. Information was obtained about the conditions under which 19 of the operations were performed. Twelve took place in modern operating-theatres ventilated with filtered air under positive pressure, and seven in older theatres in which ventilation was by extract fans or by natural air-movement. Dressings were in all cases autoclaved, but arrangements for the sterilization of instruments and other hard objects varied. In 11 instances it was stated that everything used at operation had been autoclaved or sterilized by dry heat, and in two instances all the instruments were boiled. The remainder fell into two groups: those in which most objects were boiled, but a few (e.g., the prosthesis, drills, or saws) were sterilized in the autoclave or by hot air; and those in which most objects were autoclaved, but some (e.g., saws, osteotomes, or chisels) were boiled or kept in disinfectant solutions. Preoperative treatment of the skin in 18 of the operations was said to have been with the following: Hibitane (chlorhexidine) in spirit or isopropanol 8, Savlon in spirit 1, Cetavlon (cetrimide) in spirit 1, Savlon 2, Cetavlon 1, Merthiolate in spirit 1, spirit of biniodide 1, iodine in spirit 2, Betadine 1.

Clostridial spores might have reached the wounds in one of several ways: from the air in the poorly ventilated theatres; on instruments where the sterilization methods were inadequate; or from the skin of the operation site. It is clear, however, that clostridial sepsis sometimes follows operations carried out in the most modern operating-theatres with good ventilation and adequate and well supervised arrangements for the sterilization of instruments and dressings.

The site of the operations suggests that the infecting organism may often have come from the bowel of the patient. It is therefore important that the preoperative skin treatment should include the application of an agent which is relatively effective in killing bacterial spores on the skin—e.g., compresses soaked with an iodophor.[1] This appears not to have been the case in at least 15 of the 18 operations about which we have information. In any event, the complete destruction of large numbers of spores on the skin may not be attained, and the physical removal of as much as possible of the "transient" skin flora by repeated washing with a detergent solution is to be recommended as a first step.

Even if the skin is effectively sterilized before operation it is not certain that a wound near the anus can always be kept free from contamination with clostridia during the whole of an extensive surgical operation. This raises the question whether specific measures should be taken to prevent clostridial infection in operations known to carry a risk of this complication. Gas gangrene after amputation through the thigh in patients with arterial insufficiency is a well-recognized hazard, and it is for this reason that penicillin prophylaxis has been recommended for this operation.[2] The fact that operations in which a foreign body is inserted into bone, particularly in the hip region, may also be followed by serious clostridial infection should prompt orthopaedic surgeons to consider giving a short course of penicillin in high dosage to patients who have undergone these operations. None of the patients in this series had received prophylactic penicillin.

Fuller details of the findings in this investigation will be published later. We wish to thank the colleagues who have provided us with information, and to ask those who encounter similar cases in the future to inform us.—I am, etc.,

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1 Lowbury, E. J. L., Lilly, H. A., and Bull, J. P., *Brit. med. J.*, 1964, 2, 531.
2 Taylor, G. W., *Brit. med. Bull.*, 1960, 16, 51.

Ascorbic Acid and Colds

SIR,—I read with considerable interest the article by Dr. Georgina H. Walker and her colleagues (11 March, p. 603), in which they described their studies on the use of ascorbic acid for the treatment of symptoms in the common cold. While they are to be congratulated on a critical examination of this difficult problem, I feel that it is important to question the interpretation of some of their results. Their studies were conducted on a selected group of volunteers, but they did not indicate their sexes or ages. They used an artificial method for infection of their subjects consisting of the intranasal instillation of a saline suspension virus which they claim produces comparable symptoms to those experienced by people exposed to natural infection. Their numbers were small, since only 36 patients developed colds out of the 91 subjects who were inoculated, yet no information was provided about whether the subjects had all received a comparable intake of ascorbic acid prior to the investigation. For three days preceding intranasal instillation of three selected viruses which frequently cause colds, the experimental subjects received 3 g. of ascorbic acid, but the experimental results provided no evidence that ascorbic acid affected the incidence or severity of colds, or the duration or type of symptoms in the subjects under these conditions.

In the general population colds develop in a rather more random fashion, and a variety of factors may influence their incidence and course. Among these factors the consumption of large doses of ascorbic acid in the very early stages of a cold is popularly believed to have a therapeutic effect in suppressing symptoms; Dr. Walker and her colleagues used this type of medication in their studies. The effect of ascorbic acid has been investigated in Dublin in large field surveys during two winter periods of six months each since 1965. In these surveys tablets have been given to the subjects daily, and the ability of ascorbic acid to prevent the occurrence of colds in a population—that is, its prophylactic effect—has been studied. The results of these investigations are not yet

analysed completely. Nevertheless, the initial results in these prophylactic trials do not appear to support the totally negative view which arises from the experimental work on the therapeutic effect of ascorbic acid which has been reported from Salisbury. These results will be described when the analysis has been completed.—I am, etc.,

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Lead Absorption in Children

SIR,—The indiscriminate use of the terms absorption, exposure, intoxication, and poisoning by Dr. Neil Gordon and his colleagues (20 May, p. 480) is misleading. They measured only blood lead concentration and inferred that it reflected absorption.

The blood lead concentration represents an equilibrium in which absorption, excretion, and tissue deposition participate. Recent animal studies in this department have shown that lead can accumulate in the liver following oral administration of lead compounds without significant change in the blood lead. Conversely, while the significance of a raised blood lead is not disputed, it is not necessarily indicative of absorption but could represent release of tissue lead.

Lead poisoning in childhood usually occurs between the ages of 1 and 5 years; death and cerebral damage are well-documented sequelae.[1] It is questionable whether the measurements reported by Gordon and others in older children and adolescents are relevant in any way to the aetiology of mental handicap.—I am, etc.,

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REFERENCE

[1] Byers, R. K., *Pediatrics*, 1959, **23**, 585.

Treatment of Choriocarcinoma

SIR,—Dr. K. D. Bagshawe (15 April, p. 178) appears unduly concerned that our paper (4 March, p. 521) may have weakened the case for the treatment of choriocarcinoma in specialized centres such as his at Fulham Hospital. We wish to assure him that we have the highest regard for his good work, and, although we do not support the view that all cases of choriocarcinoma should be treated in specialized centres, we do agree that difficult problem cases should be channelled without delay to such centres for chemotherapy by experts like himself.

In his eagerness to defend his position Bagshawe has made certain statements which require examination. In the opening paragraph he says: "Before chemotherapy was applied to choriocarcinoma no clinician ever saw more than a few cases." This categorical statement may have been true of clinicians in Britain, but not in Asia. Before chemotherapy was introduced into our hospital we had seen two dozen cases or more, and there must be other clinicians in Hong Kong, Indonesia, the Philippines, and other parts of Asia who have seen many more. Such inaccurate statements do not strengthen the cause which Bagshawe is trying to promote.

Two papers on choriocarcinoma from Singapore have recently appeared.[1,2] Bagshawe compared the figures and concluded: "The virtually simultaneous presentation of totally opposite conclusions, drawn from the same data, must cast doubt on their value." This hasty conclusion ignores the fact that the first paper[1] was on pulmonary choriocarcinoma and the second[2] was on all types of choriocarcinoma. Our second paper also included more recent material than that reported in the first, although the duration of follow-up was up to 1966 in both presentations. There is no contradiction in our conclusions or discrepancy in our figures. Neither was there recourse to "spontaneous resurrection," as Bagshawe terms it. The careful reader will find that Bagshawe's assumption is in error. The deaths in the "hysterectomy-chemotherapy" group were 12 in both papers, with one case under treatment. Bagshawe repeatedly refers to our cases of malignant trophoblastic tumours as "hydatidiform mole." He may disagree with our classification, but there is no need to misrepresent the facts.

We find it difficult to understand the self-contradiction in Bagshawe's thinking on the value of hysterectomy. To quote him: "The reader is led to believe that some workers have claimed that hysterectomy is valueless. . . . Such claims have not, I think, been made. . . ." Here he appears to hold no bias against hysterectomy. Then, in the second last paragraph he describes at length the evils of elective hysterectomy and concludes, "unless the uterus has perforated, hysterectomy is better deferred." Uterine perforation is a rare complication in choriocarcinoma. This means that Bagshawe opposes hysterectomy in the majority of cases. In his paper,[3] which we had referred to, Bagshawe also elaborated on the alleged evils of hysterectomy and concluded: "Hysterectomy is thus not only ineffective but also disadvantageous in some patients." Let his own statements be his judge. In our paper we had advocated that such claims "deserve careful study before hysterectomy is abandoned altogether." Indeed, unless a strong protest were raised these claims (based on flimsy evidence) would mislead gynaecologists into giving up hysterectomy altogether.

In our paper we have not claimed that our "results equal those obtained elsewhere," as Bagshawe asserts. We have reported the results of all 80 consecutive cases of malignant trophoblastic tumours seen, treated, or both, irrespective of the state on admission to hospital. We have included no fewer than 12 deaths in patients who did not have the benefit of chemotherapy. Bagshawe's results were based on 23 treated cases out of 28 seen. The hopeless cases were excluded from his results. Obviously no worthwhile conclusions could have been drawn by trying to compare our results with his.

Bagshawe places great faith in the Joint Project[4] which amassed "806 cases of suspected trophoblastic tumours" from 18 different centres in Asia over the period 1948–52 for study by a panel of pathologists in the U.S.A. The non-representative nature of this pooled material led the authors themselves to conclude that "an accurate ratio of choriocarcinoma to hydatidiform mole cannot be established . . . and there is no way of estimating whether the large number of choriocarcinomas is due in part to a large number of hydatidiform moles." Yet Bagshawe makes the bold statement that the Joint Project "found no evidence that mole was a relatively more frequent antecedent to choriocarcinoma in South-east Asia than in the U.S.A." We are of the opinion that the value of the Joint Project is seriously limited by the absurdly small number of cases studied—806 out of a population of several hundred millions or more. Your readers might be interested to know that for the four-year study period of the Joint Project the Singapore participants contributed 41 cases and that these were rejected from the final analysis because of inadequate data. We have studied over 500 consecutive cases in the past seven years. Our results may be expected to give a more truly representative and accurate picture than the collation of hotch-potch data from 18 different sources.

We find Bagshawe's mathematics perplexing. In calculating the ratio of molar to non-molar pregnancies in the last 25 cases of our series he arrives at the figure of 12.5:1. We are at a loss how this figure was arrived at. He states that the "expected number of fatal cases without treatment" in our series would be "about 24." On what grounds? He also states that our "fatality rate is twice that of a somewhat larger series" from his own hospital. May we suggest that all these unfounded statements and self-contradictions do not strengthen the case for specialized centres and may weaken the faith of Bagshawe's supporters. Finally, may we reassure Bagshawe that we do not oppose the treatment of problem cases in his specialized unit, but we do strongly contest the unfair allegations which he has made against hysterectomy.—We are, etc.,

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REFERENCES

[1] Tow, W. S. H., *Proc. roy. Soc. Med.*, 1967, **60**, 239.
[2] —— and Cheng, W. C., *Brit. med. J.*, 1967, **1**, 521.
[3] Bagshawe, K. D., ibid., 1963, **2**, 1303.
[4] Joint Project for Study of Choriocarcinoma and Hydatidiform Mole in Asia, *Ann. N.Y. Acad. Sci.*, 1959, **80**, 178.

Pressurized Aerosols in Asthma

SIR,—I am grateful for your published disclaimer (27 May, p. 584) that I do not support the views of Dr. R. Munro Ford (6 May, p. 375) or others of your correspondents who condemn the use of aerosol preparations in the treatment of bronchial asthma. Indeed, the agent which I find most useful and use most frequently in the treatment of chronic asthma is 5% ocipreneline delivered from a De Vilbiss No. 40 hand nebulizer. As with other medications, I take pains to explain clearly to the patient the way in which it should be used and its limitations.

I deplore the present "hue and cry" approach to the problem of deaths from asthma, and still more the emotional seizing on one valuable form of therapy. A recent paper by Tai and myself[1] indicates how tenuous is the functional state of many patients with asthma who do not appear clinically very ill. This paper suggests that we should look afresh at our abilities in the field of "expectation," rather than talk too glibly of "unexpected" deaths from asthma.—I am, etc.,

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REFERENCE

[1] Tai, E., and Read, J., *Lancet*, 1967, **1**, 644.

SIR,—I have been following with great interest the correspondence in your columns concerning the excessive use of pressurized aerosols in asthma. Little has so far been written about the older asthmatic child in this context apart from the very instructive case described by Dr. W. Pickvance (25 March, p.