8.2.1 Clinical approach 662

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8.2 The patient with suspected infection CONTENTS 8.2.1 Clinical approach 662 Christopher J. Ellis 8.2.2 Fever of unknown origin 664 Steven Vanderschueren 8.2.3 Nosocomial infections 669 Ian C.J.W. Bowler and Matthew Scarborough 8.2.4 Infection in the immunocompromised host 673 Jon Cohen and Elham Khatamzas 8.2.5 Antimicrobial chemotherapy 684 Maha Albur, Alasdair MacGowan, and Roger G. Finch 8.2.1 Clinical approach Christopher J. Ellis ESSENTIALS Infection is most often suspected when patients present with pyrexia and is certainly the most common cause of this presentation, whether in hospitalized patients or those in the community. The other principal causes of fever are primary inflammatory conditions and malignancy, but infections are likely to be most rapidly progressive and acutely life- threatening, and hence must be the physician's first concern. The clinical approach to patients with likely infection begins with a focused history, leading on to a clinical examination which assesses the extent of the physiological derangement and looks for a focus of infection. Standard physiological measures define likely sepsis (see Chapter 8.1.2), which is the commonest reason for their sudden de- rangement in hospitalized patients. Investigations should be phased and must not delay the start of potentially life-saving treatment, the response to which must be carefully followed, especially when treatment has to be started before a complete or certain diagnosis is possible, and compared with the likely speed of response for the putative condition being treated. There is increasing evidence that delays in initiating appropriate therapy, especially antimicrobial medication and circulatory support, increase mortality. Introduction No diagnostic challenge better illustrates the power of traditional clinical methods than the patient with possible infection; clin- icians rarely find themselves in a situation where there is poten- tially so much urgency in establishing a working hypothesis and management plan. It is vital to keep in mind that previously healthy people with life-threatening infections may have few symptoms other than malaise, and little in the way of abnormality on examination other than an altered body temperature and tachycardia. However, at this point only decisive intervention will prevent a rapid decline into circulatory collapse, coagulopathy, and multiple organ failure with a high risk of death. What suggests that the patient's life is in danger? Standard observations (vital signs) are usually valuable pointers to life-threatening situations and have been combined to define sepsis syndromes (Box 8.2.1.1). Observations made routinely on hospitalized patients are now co- dified to produce early warning track and trigger systems, such as the modified early warning score, which highlight developing sepsis. Box 8.2.1.1 Sepsis syndromes Sepsis (systemic inflammatory response syndrome) Defined by two or more of: • Temperature more than 38°C or under 36°C • Pulse rate more than 90/min • Respiratory rate more than 20/min • Leucocyte count more than 12 or under 4 × 109/litre Severe sepsis Sepsis with one or more of: • Hypotension • Confusion • Oliguria • Hypoxia • Acidosis • Disseminated intravascular

coagulation Septic shock • Severe sepsis with hypotension despite fluid resuscitation

8.2.1 Clinical approach 663 In general hospitals, the development of sepsis is currently the most common single reason for patients' scores reaching the trigger point. Although these alarm calls are important, they will not identify all patients in whom urgent treatment is vital. Table 8.2.1.1 lists some conditions that typically present in a bland and nonspecific manner although the patient may be only a day or two from death if not treated appropriately. Infection may be mimicked by life-threatening noninfectious con- ditions. Primary vasculitic conditions commonly present with fever and skin infarcts identical to those seen in patients with endocarditis, while cerebral systemic lupus erythematosus is clinically indistin- guishable from an infective encephalitis. Conditions such as DRESS syndrome (drug reaction eosinophilia and systemic symptoms) may be precipitated by antibiotics, and also mimic severe sepsis. Management before diagnosis Acute medicine has been described as 'the art of making suffi- cient conclusions on insufficient information'. When confronted with a patient who fulfils the criteria for severe sepsis, attention must be paid to oxygenation, circulatory support, and intravenous antimicrobials, even if the clinician is still some way from a de- finitive diagnosis. In these fraught circumstances, organizational confusion can lead to vital actions being omitted or delayed. In particular, the prescriber should ensure the prompt administra- tion of intravenous antimicrobials and deliver a fluid challenge to patients with hypovolaemia, bearing in mind that up to 40% of effective circulating volume can be lost, usually through vasodila- tation, before vital signs register more than tachycardia. One litre of saline given over 30 min, and repeated if the pulse rate does not fall, is an appropriate prescription for an adult in this situation. The history of the illness Once immediate life-saving measures are in hand, if they are indi- cated, a thorough, focused history must include several questions that are not routinely asked (Table 8.2.1.2). Clinical examination and chest radiograph Examination of a patient with suspected infection can be both rapid and comprehensive. Having noted the vital signs, the clinician can proceed from head to toe. Temporal arteries should be examined in patients over the age of 50 years with fever and headaches; the mouth should be examined for poor dentition and oral candidiasis (a pointer to possible HIV infection), and the heart for murmur(s). Chest examination might reveal signs of consolidation or an effusion. Examination of the abdomen should pay particular attention to liver enlargement and/or tenderness and include several firm blows over Table 8.2.1.1 Conditions presenting in a nonspecific manner Condition Key clue Malaria Travel history Early meningococcaemia Early purpura Bacteraemia Rigor (i.e. visible shivering for at least 10 s) Fasciitis Tenderness to pressure beyond apparent bounds of cellulitis Toxic shock syndrome The patient has fainted on standing (because of incipient shock); erythematous rash Table 8.2.1.2 Questions that must be asked concerning the history of the illness Open question Possible significance Have you travelled? All cases of falciparum malaria imported into nonendemic areas are in people who have visited malarial areas in the preceding 3 months; most are within 1 month. In the UK, 90% of these infections will have been acquired in sub-Saharan Africa Approximately one-half of the cases of legionnaires' disease in the UK are in patients who have returned from Europe or Turkey in the preceding 2 weeks Have you been sexually active? Unprotected sex with a new partner (or a promiscuous regular partner) in the previous 2 months increases the probability of primary HIV and secondary syphilis Have you been exposed to crowds of new social contacts (e.g. university freshers week, new military recruits, or large military deployments)? Increased probability of meningococcal or pneumococcal infection Have you been hospitalized or have you received medical attention recently? Fever following the start of medication raises the possibility of drug fever (typically when a course of penicillin is extended beyond 1 week) Recent administration of antibacterial drugs predisposes to Clostridium difficile colitis Acquisition of a resistant strain of

bacteria (e.g. extended-spectrum β-lactamase-producing or carbapenemase-producing bacteria) Dental work predisposes to endocarditis Previous splenectomy predisposes to fulminating pneumococcal septicaemia Infection of surgical wounds, retained surgical material, or prostheses Partial treatment of an abscess, most commonly intra-abdominal or retroperitoneal, including psoas abscess Is the illness remittent? Characteristically remittent conditions, including vivax malaria, systemic Still’s disease, lymphoma Temporary improvement with antibacterial drugs suggests a possible ‘collection’, a concealed abscess

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