Recognizing meningococcal disease: the case for further research in primary care

STEPHEN GRANIER

PENNY OWEN

NIGEL C H STOTT

SUMMARY

Most studies describing the clinical presentation of meningococcal disease use data derived from hospital-based studies. This paper reviews current knowledge on the presentation of meningococcal disease from a primary care perspective. In a small proportion of cases with classical features, making the diagnosis may be relatively simple. In many cases, however, the general practitioner (GP) is faced with the difficulty of discriminating between the rare patient with life-threatening illness and the vast majority who present with similar symptoms secondary to self-limiting viral illness. In the absence of reliable means of excluding the disease, GPs will need to consider the possibility of meningococcal disease in all ill and febrile patients in whom no cause is apparent. Planned follow-up and clearer explanation to patients may increase the chance of identifying earlier those cases that evolve with time. More research is required to identify key clinical and contextual features that help GPs to predict or exclude serious disease, and to describe how this information is used in decision-making. A framework for conceptualizing the problems of researching illness is provided, which takes into account the many factors that influence clinical practice in primary care.

Keywords: acute febrile illness; decision making; meningococcal disease; meningococcal meningitis; meningococcal septicaemia; risk taking.

Introduction

IN 1995, a total of 1827 cases of meningococcal meningitis and septicaemia, and 185 deaths (10%) were notified to the Office of Population Censuses and Surveys in England and Wales.[1] Early recognition of the disease in the community remains the focus of much attention, both in the media and in the medical literature.[2,3] The importance of this is emphasized by evidence of improved prognosis in patients receiving early prehospital treatment and the absence of effective immunization against most serotypes of *Neisseria meningitidis*.[4-7]

In a small proportion of cases with classical features, a diagnosis of meningococcal disease (MCD) may be relatively simple. More often, however, the general practitioner (GP) is faced with the difficulty of discriminating between the rare patient with a life-threatening illness and the vast majority who present with similar symptoms secondary to self-limiting viral illnesses.

S Granier MRCGP, research fellow, Department of General Practice, University of Wales College of Medicine, Llanedeyrn, Cardiff. P Owen, MD, MRCGP, general practitioner, Llanedeyrn, Cardiff. N C H Stott, BSc, FRCPEd, FRCGP, professor, Department of General Practice, University of Wales College of Medicine, Llanedeyrn, Cardiff.

Submitted: 12 February 1997 accepted: 10 September 1997.

Method

This paper reviews current knowledge on the presentation of MCD from a primary care perspective. Computerized literature searches were conducted using MEDLINE and Bath Information and Data Services from 1986 to 1996. All abstracts including the term 'meningococcal disease' and related terms were read to identify those including research on the clinical presentation. Relevant references cited in these papers were reviewed. As most of these studies were descriptive, and because of the relatively small sample sizes, no papers were excluded.

Results

Table 1 shows the symptoms and signs reported in eight studies on the clinical presentation of MCD.[8-15] All except two reported clinical findings from the time of hospital admission, although some also included information from GP referral letters. Palmer *et al*[14] sent questionnaires to Medical Officers of Health, who were asked to include data from GPs, hospital clinicians, and microbiologists. Riordan *et al*[15] interviewed parents on admission about their reasons for seeking medical advice. The only study to use data collected in primary care[16] (not included in Table 1) included all forms of meningitis but a sample of only 10 patients. All except two studies[12,15] were conducted retrospectively.

One review article was included,[17] as were studies of management or outcome that included descriptions of one or more important signs.[6,18] Four studies described the presentation of all types of bacterial meningitis,[19-22] and three studies focused on diagnostic difficulties.[23-25] Studies or case reviews describing a single minor symptom or sign were excluded.

Common symptoms occur commonly

Neisseria meningitidis has a range of presentations from a non-specific acute febrile illness through meningitis to fulminant septicaemia with purpuric rash and shock.[17] The most common symptoms are fever (71–100% of cases), vomiting (34–76% of cases), and lethargy (28–89% of cases).[8-11,13-15,17] Non-specific upper respiratory tract symptoms are reported in up to half of patients in the week before admission to hospital.[9,10]

Infants commonly present with non-specific symptoms and signs, with the classical symptoms of neck stiffness, photophobia, and rash occurring less frequently than in older children.[14,18]

These features are common to many illnesses in primary care and are not particularly useful discriminators. In some cases, the presence of symptoms suggesting a definite cause for a patient's febrile illness, such as upper respiratory tract infection, may cause a GP to rule out MCD erroneously.

Rashes occur in up to 90% of patients with MCD.[12] A substantial minority may have macular rashes only; these are poor predictors of meningococcal infection, as many febrile illnesses present with non-blanching rashes. In one study, the presence of a blanching rash caused diagnostic difficulties by leading GPs to rule out meningitis.[19]

Table 1. Comparison of presenting features of meningococcal disease.

Study	Olcen *et al* (1979)[8]	Donald *et al* (1981)[9]	Wong *et al* (1989)[10]	Voss *et al* (1989)[11]	Marzouk *et al* (1991)[12]	Sorensen *et al* (1992)[13]	Palmer *et al* (1992)[14]	Riordan *et al* (1996)[15]
Number of patients	69	298	100	122	69	177	96	126
Source of data	Hospital records	Hospital records	Hospital records	Hospital records	Assessment in hospital by researcher	Hospital records	Medical officers for environmental health	Interview with parents
Non-specific symptoms								
Fever	96%	100%	71%	98%	87%	98%	85%	97%
Nausea/vomiting	61%	48%	34%	69%		63%		76%
Upper respiratory tract infection symptoms		27%	10%					
Any rash	75%		71%		93%		77%	86%
Blanching rash only	4%		22%		13%		11%	
Photophobia				18%				
Headache				34%				34%
Features of serious disease								
Lethargy	87%		21%					89%
Impaired consciousness	91%					65%		
Shock			42%				16%	
Convulsion	4%	21%		16%		19%	11%	
Neck stiffness	76%	77%		79%		71%	39%	11%
Features specific for meningococcal disease								
Petechial/ purpuric rash	71%	48%	49%	61%	80%	66%	66%	
Neck stiffness and rash				26%				

Rare symptoms do not help much of the time

Palmer *et al*[14] studied 119 cases of MCD in Wales. The classical symptoms of headache, neck stiffness, and purpuric rash occurred in only 33%, 39%, and 66% of cases respectively, and together in only 13% of cases. Although the co-occurrence of these symptoms may be specific for the disease, reliance on this combination of symptoms would fail to identify the majority of those infected. Conversely, ruling out the disease in the absence of any of the features of neck stiffness, rash, or photophobia may result in failure to make a correct diagnosis in 10% of patients. In the other studies quoted, the incidence of a non-blanching rash varied from 48% to 71%, but varied with the duration of illness and the age of the patients.[8-15] Marzouk *et al*[12] found that 17 out of 69 children had mixed rashes, and 12 had only a few haemorrhagic spots (fewer than 12) within a predominantly maculopapular rash.

Donald *et al*[9] found that those presenting later in the course of their illness were less likely to develop haemorrhagic rashes, and none of those with illnesses of more than four days' duration developed non-blanching rashes. Haemorrhagic rashes occur in the vast majority (82–97%) of children aged one to four and, in this group, the absence of a rash on assessment in the community may be reassuring.[6,14] Most children between the ages of four and 15 (69–75%), but only a minority of adults, develop petechial or purpuric rashes.[6,14]

There is a considerable variation in the occurrence of neck stiffness in patients with MCD. Although most studies report meningeal irritation in the majority of cases (71–79%),[8,9,11,13] two studies found it in less than 40% of patients.[14,15] Studies including all causes of meningitis generally report a higher incidence of neck stiffness (73–80%)[19-21] than those focusing on MCD. This may be accounted for by cases of MCD presenting with septicaemia in the absence of infected meninges.

Palmer *et al*[14] reported poor feeding, lethargy, and hypotonia in 64%, 52%, and 20% of infants respectively. Although not specific for MCD, other authors have suggested that these signs are important predictors of serious illness in infants.[25-27] A bulging fontanelle, which occurs in a third of infants with meningitis, may also be a clue to the diagnosis.[17,21]

Other presentations, such as shock or convulsions, although not specific for MCD, would be highly suggestive of serious disease and lead to hospital admission, but occur too infrequently to be useful in most cases.[8-11,13,14]

Most patients with MCD do not present with the classical symptoms and signs. Although thorough examination is recommended for all patients with febrile illnesses of no apparent cause, the absence of the classical features does not necessarily exclude the disease.

Diagnostic difficulties

In up to a half of all cases, the diagnosis may be delayed by more than 24 hours, and by more than 48 hours in a quarter of cases (Table 2).[8,9,22] Reasons could be the delay in requests for medical assessment[23] or difficulties faced by GPs in the early recognition of serious illness. Sorenson *et al*[13] found that over half of

Table 2. Duration of illness before admission.

Duration of illness	Olcen *et al* (1979) (*n* = 69)	Voss *et al* (1989) (*n* = 122)	Donald *et al* (1981) (*n* = 233)	Kilpi *et al* (1991) (*n* = 67)
<24 hours	62.3%		59.2%	46.3%
<48 hours		82%	20.2%	26.9%
>48 hours			18.9%	26.9%

patients with MCD had more than one contact with their GP before admission. Approximately 50% of patients studied by Riordan *et al*[15] had been seen but not admitted by another doctor in the 48 hours before admission.

Many patients admitted to hospital with a suspected diagnosis of MCD do not have it,[7,20] and a third of patients with a final diagnosis of MCD are not recognized as having the disease in the community.[4] Failure to make a correct diagnosis occurs most often in children younger than two and adults over 60 years of age.[24]

Evolution of symptoms

The description of the symptoms and signs of the disease are derived largely from presentation at the time of hospital admission, at which time the disease is at a later stage in its evolution. It is likely that some features may not have been present at the time of assessment in the community. Although some studies also reviewed referral letters, these are unlikely to carry reliable information because of the context in which the letters are written, rapid admission to hospital, and initiation of antibiotic treatment being more urgent than the comprehensive recording of symptoms and signs.

Woodward *et al*[6] found that haemorrhagic rashes detected on admission to hospital had been reported by the referring GP in only half of the cases. This is in agreement with the study by Romer,[19] who found that meningeal signs were detectable on admission to hospital in 50% of meningitis patients whose disease had not been recognized by their GP. Some of this difference could be accounted for by the rapid course of the disease or the possibility that the rash may have been maculopapular in the initial stage of the illness.[28] Inconspicuous petechiae have been described in the centre of some macules if carefully examined.[17] It is also possible that a complete skin examination, with all clothes removed, was not carried out by all GPs, or was carried out in less than ideal lighting conditions.

Oakley and Stanton[29] conducted confidential enquiries into 10 deaths from MCD in children under two years of age. They reported that prodromal symptoms, including irritability, missed feeds, altered cry, and drowsiness, occurred in most cases between three and 28 hours before the onset of the rash.

These findings suggest that follow-up visits or telephone calls in ill, febrile patients with no clear diagnosis are very important. Explaining to patients what physical symptoms to look out for (e.g. a rash caused by meningitis will not blanche when a glass tumbler is pressed against the skin) may assist recognition and reduce anxiety.

A review of the published research on MCD revealed only one study on the recognition of MCD using primary care data. Koorevaar *et al*[16] studied patients with preliminary and hospital discharge diagnoses of meningitis and meningococcal septicaemia, who were identified using data from the Dutch National Survey of Morbidity and Interventions in General Practice. Nine out of 17 (53%) patients whose GP had made a provisional diagnosis of meningitis were found, on admission to hospital, not to have the disease. In most of these patients, no meningeal irritation was found on admission in spite of it having been reported by the GP.

Clinical presentation and outcome

Two studies assessed duration and outcome.[8,22] All five of the deaths in the study by Olcen *et al*[8] presented within 24 hours of the onset of symptoms. In children with bacterial meningitis of all types, a shorter duration of symptoms before admission (<24 hours) was associated with significantly poorer outcome.[22] Five of seven children who developed sensorineural hearing loss in another study had symptoms of 48 hours' or longer duration.[11] None of 14 children with maculopapular rashes or no rash, studied by Marzouk *et al*,[12] died compared with six of 55 with haemorrhagic rashes. However, one child who had a maculopapular rash on admission died after the rash evolved to purpura.

Clinical problem solving in general practice

This literature review has identified a lack of data on the presentation, diagnosis, and prehospital treatment of MCD relevant to the primary care context. None of the studies examined the issues to be addressed by GPs when faced with a sick child, nor did they recommended how GPs should conduct such consultations. Researchers require an understanding of how clinicians consult with ill patients in primary care and should incorporate this understanding into the methodology of their research.

The process of doctors trying to find out what is wrong with patients has been described in a variety of ways, for example clinical judgement, problem solving, pattern recognition, and decision-making. Gale and Marsden,[30] in their research on the cognitive processes of clinicians, have described a diagnostic thinking process, two elements of which are of particular interest to this literature review. First, they describe how an individual's perception of a diagnostic problem is dependent on the way that person's knowledge is structured or organized in his or her memory. Secondly, the link between knowledge structures in memory and a given clinical situation is formed by especially significant items of information — forceful features. These 'neon light' items are not a property of the clinical information itself but are derived subjectively by the individual from experience and constitute part of that person's memory structure.

The usefulness of any symptom or sign is also influenced by the disease prevalence in the relevant population, with the predictive value of a positive test result increasing as the disease prevalence increases. By similar reasoning, the predictive value of a negative finding increases as the disease prevalence decreases.

A multilevel representation of the consultation with the acutely ill patient is shown in Figure 1. Many decisions are made with each primary care contact. The first is likely to involve a severity rating at an early stage of the consultation and will influence subsequent management decisions. If the patient is not very ill, the clinical process can focus on the breadth of biological, individual, and contextual factors. Management is often not pure-

ly biomedical, and the wider aspects of the consultation are more likely to be considered. If the patient is very ill, the GP may still attempt to form a working hypothesis, but management will often involve admission to hospital, with or without supportive therapy, and the triage route is most likely.

Management decisions are also influenced by an interaction of clinical and social factors,[31-34] including the characteristics of the GP and his or her tolerance of uncertainty, patients' perceptions and expectations, and structural factors.

Increasingly, doctors are being advised to view consultations as a meeting between experts, stressing the importance of responding seriously to the concerns of the patient.[36] Reassurance may not be possible in the context of high patient anxiety, unwillingness to accept uncertainty, and prior personal experience of serious disease. These considerations may necessitate hospital admission.

Other contextual factors, such as lack of time to negotiate alternatives, the time at which the consultation occurs, distance of the patient's home from the hospital, and the lack of access to a telephone, may influence management decisions.[32,33,35]

Decisions are also likely to be influenced by the individual GP's attitude towards risk taking.[37] General practitioner behaviour in response to uncertainty could be categorized in terms of non-risk taking, careful caring, and risk taking. Non-risk takers may be 'safe' doctors but are likely to admit many patients unnecessarily. Careful carers use follow-up and time to gauge the evolution of symptoms. They will save unnecessary admissions but at a high cost to themselves. Risk takers may make correct decisions most of the time but may occasionally put patients at risk by underestimating the presence of serious illness.

Conclusion and focus for future research

Much research evidence used by GPs to underpin clinical decisions is hospital based. However, hospital populations are preselected and are likely to have a different spectrum of disease from those in primary care, and in hospital populations most clinical features have a higher predictive value for serious disease.[37,38] As a consequence, isolated symptoms and signs, such as fever, vomiting, and neck stiffness, which usually suggest serious disease in a hospital context, may occur too commonly in primary care to be of discriminatory value. Conversely, the absence of the classical triad of headache, neck stiffness, and haemorrhagic rash is unlikely to exclude MCD in many cases.

Difficulty in dealing with uncertainty is an experience shared by doctors and patients.[37-42] In the absence of reliable means of predicting or excluding disease, GPs will need to remain aware of the possibility of MCD in all ill, febrile patients in whom no reason for the symptons can be found. Planned follow up, clear explanation to patients, and increased patient education may help earlier diagnosis in cases that evolve with time. More research is required to identify key clinical and contextual factors that help GPs to predict or exclude serious disease, and to clarify how this information is used in decision-making and how this relates to patient outcome.[37] A framework for conceptualizing the problems of researching acute illness is provided, which takes into account the many factors that influence clinical practice in primary care. The patient who is clearly ill is not difficult to handle. It is in the earlier stages of MCD that more evidence is needed.

References

1. Department of Health and Social Security. *Meningococcal infection: meningitis and septicaemia.* [CMO(88)2.] London: HMSO, 1988.
2. Disease leaves campus in fear. *The Guardian*, 2 December 1996.
3. Kristiansen B-E, Knapskog A-B. Secondary prevention of meningococcal disease. *BMJ* 1996; **312:** 591-592.
4. Strang JR, Pugh EJ. Menigococcal infections: reducing the case fatality rate by giving penicillin before admission to hospital. *BMJ* 1992; **305:** 141-143.
5. Cartwright K, Reilly S, White D, Stuart J. Early treatment with parenteral penicillin in menigococcal disease. *BMJ* 1992; **305:** 143-147.
6. Woodward CM, Jessop EG, Wale MCJ. Early management of meningococcal disease. *Commun Dis Rep* 1995; **5:** R135-R137.
7. Cartwright K, Strang J, Gossain S, Begg N. Early treatment of meningococcal disease. *BMJ* 1992; **305:** 774.
8. Olcen P, Barr J, Kjellander J. Meningitis and bacteraemia due to *Neisseria meningitidis*: clinical and laboratory findings in 69 cases from Orebo county, 1965 to 1977. *Scand J Infect Dis* 1979; **11:** 111-119.
9. Donald PR, Burger PJ, van Zyl LE. Meningococcal disease at Tygerburg Hospital. *S Afr Med J* 1980; **60:** 271-275.
10. Wong VK, Hitchcock W, Mason WH. Meningococcal infections in children: a review of 100 cases. *Pediatr Infect Dis J* 1989; **8:** 224-227.
11. Voss L, Lennon D, Sinclair J. The clinical features of paediatric meningococcal disease Auckland, 1985–87. *NZ Med J* 1989; **102:** 243-245.
12. Marzouk O, Thomson APJ, Sills JA, *et al.* Features and outcome in meningococcal disease presenting with maculopapular rash. *Arch Dis Child* 1991; **66:** 485-487.
13. Sorensen HT, Moller-Petersen J, Krarup HB, *et al.* Diagnostic problems with meningococcal disease in general practice. *J Clin Epidemiol* 1992; **45:** 1289-1293.
14. Palmer SR, Corson J, Hall R, *et al.* Meningococcal disease in Wales: clinical features, outcome and public health management. *J Infect* 1992; **25:** 321-328.
15. Riordan FA, Thomson APJ, Sills JA, Hart CA. Who spots the spots? Diagnosis of early meningococcal disease in children. *BMJ* 1996; **313:** 1255-1256.
16. Koorevaar R, Bruinzeels MA, van der Wouden C, *et al.* Patients with suspected meningitis: a study in general practice. *Eur J Gen Pract* 1995; **1:** 21-24.
17. Steven N, Wood M. The clinical spectrum of meningococcal disease. In: Cartwright K. (ed.). *Meningococcal disease.* Chichester: John Wiley and Sons, 1995.
18. Cartwright K, Strang J, Reilly S, White D. Mortality in meningococcal disease. *BMJ* 1992; **304:** 116.
19. Romer F. Difficulties in the diagnosis of bacterial meningitis. *Lancet* 1977; **ii:** 345-347.
20. Nielsen B, Sorensen HT, Nielson JO. Children admitted for observation for suspected meningitis. *Scand J Prim Health Care* 1988; **6:** 229-232.
21. Haggarty RJ, Ziai M. Acute bacterial meningitis. *Adv Pediatr* 1963; **13:** 129-181.
22. Kilpi T, Antilla M, Kallio MJT, Peltola H. Severity of childhood bacterial meningitis and duration of illness before diagnosis. *Lancet* 1991; **338:** 406-409.
23. Tonjum T, Nilsson F, Bruun JN, Haneberg B. The early phase of menigococcal disease. *NIPH Ann* 1983; **6:** 175-181.
24. Mathiassen B, Thomsen H, Landsfeldt U. An evaluation of the accuracy of clinical diagnosis at admission in a population with epidemic meningococcal disease. *J Int Med* 1989; **226:** 113-116.
25. Valman B. Preventing infant deaths. *BMJ* 1985; **290:** 339-340.
26. Thornton AJ, Morley CJ, Hewson PH, *et al.* Symptoms in 298 infants under 6 months old, seen at home. *Arch Dis Child* 1990; **65:** 280-285.
27. Morley CJ, Thornton AJ, Cole TJ, *et al.* Baby check: a scoring system to grade the severity of illness in babies under 6 months old. *Arch Dis Child* 1991; **66:** 100-106.
28. Baxter P, Priestly B. Meningococcal rash. *Lancet* 1988; **i:** 1166-1167.
29. Oakley JR, Stanton AN. Meningococcal infections during infancy: confidential inquiries into 10 deaths. *BMJ* 1979; **2:** 468-469.
30. Gale J, Marsden P. Diagnosis: process not product. In: Sheldon M, Brooke J, Rector A (eds). *Decision-making in general practice.* London: Macmillan Press, 1985.
31. Elstein AS, Shulman LS, Sprafha SA. *Medical problem-solving: an analysis of clinical reasoning.* Cambridge: Harvard University Press, 1978.
32. Howie JGR. Clinical judgement and antibiotic use in general practice. *BMJ* 1976; **2:** 1061-1064.
33. Bradley CP. Factors which influence the decision whether or not to prescribe: the dilemma facing general practitioners. *Br J Gen Pract* 1992; **42:** 454-458.
34. Di Caccavo A, Reid F. Decisional conflict in general practice: strategies of patient management. *Soc Sci Med* 1995; **41:** 347-353.

35. Bradley CP. Uncomfortable prescribing decisions: a critical incident study. *BMJ* 1992; **304:** 294-296.
36. Tuckett D, Moulton M, Olson C, Williams A. *Meetings between experts*. London: Tavistock Publications, 1985.
37. Grol R, Whitfield M, De Maeseneer J, Mokkink H. Attitudes to risk taking in medical decision making among British, Dutch and Belgian general practitioners. *Br J Gen Pract* 1990; **40:** 134-136.
38. Knottnerus JA. Medical decision making by general practitioners and specialists. *Fam Pract* 1991; **8:** 305-307.
39. Owen P. Clinical practice and medical research: bridging the divide between the two cultures. *Br J Gen Pract* 1995; **45:** 557-560.
40. Mawardi B. Satisfactions, dissatisfactions and causes of stress in medical practice. *JAMA* 1979; **241:** 1483.
41. Kai J. What worries parents when their preschool children are acutely ill, and why: a qualitative study. *BMJ* 1996; **313:** 983-986.
42. Kai J. Parents' difficulties and information needs in coping with acute illness in preschool children: a qualitative study. *BMJ* 1996; **313:** 987-990.

Acknowledgements

The authors wish to thank Drs C Butler, P Kinnersley, L Jacobson, A Edwards, and Professor D P Davies for their helpful comments on this paper.

Author for correspondence

Dr S Granier, Whiteladies Health Centre, Whatley Road, Bristol BS8 2PU. Email wmgdoc@globalnet.co.uk

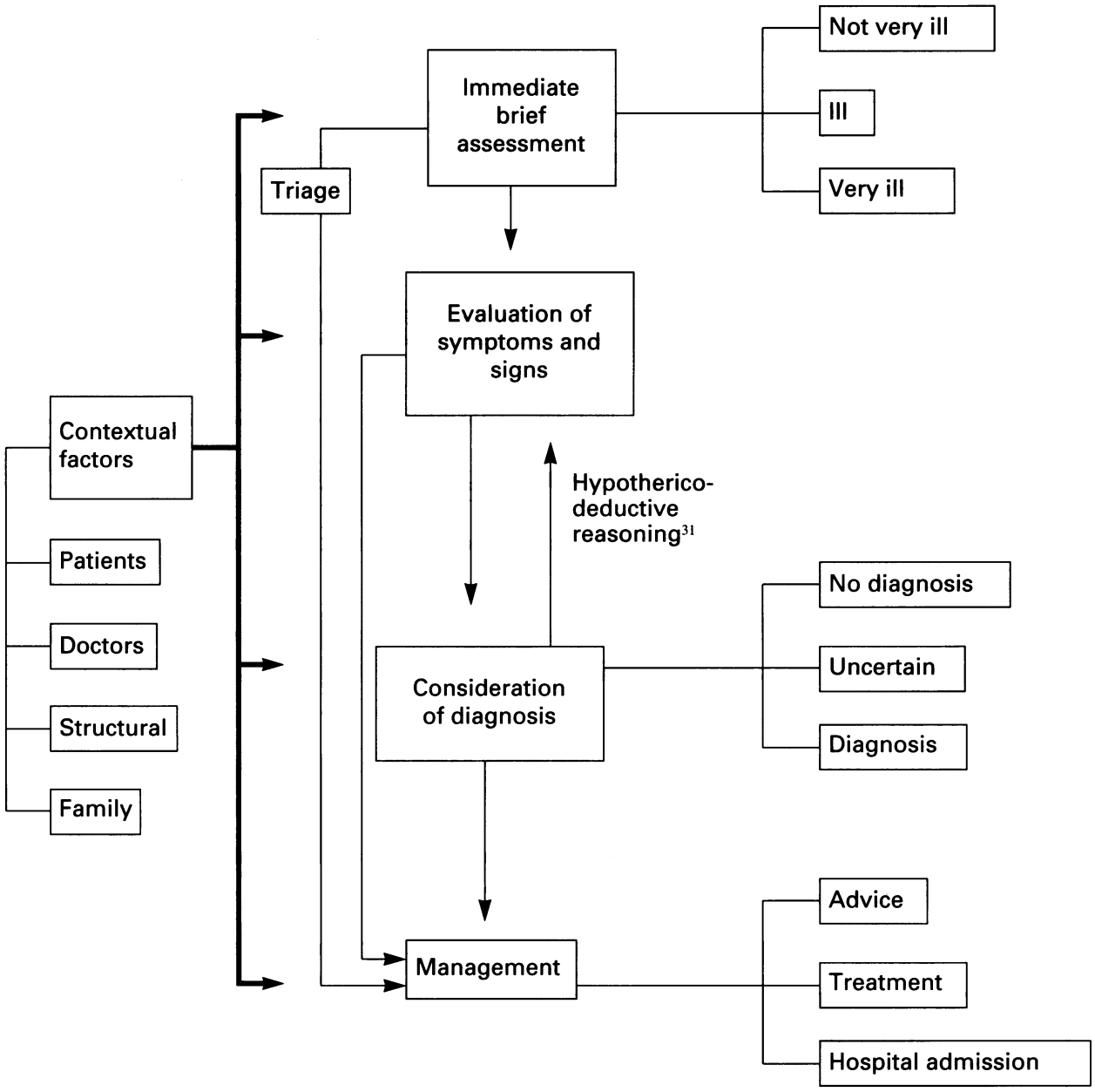

Figure 1. A multilevel representation of the consultation with the acutely ill patient.