

Working Group Report on Bacterial Meningitis and Related Conditions

Meningococcal disease is a serious condition with high morbidity and significant mortality. The Department of Health and Children's Working Group on Bacterial Meningitis and Related Conditions has monitored the epidemiology of Meningococcal disease and in 1997, in its first report, proposed strategies to prevent this infection and its complications. This report has been reviewed and updated and a second report issued in July 1999. This Report describes the epidemiology of Meningococcal disease and includes practical guidance in relation to the management of clusters and chemoprophylaxis. The Report also includes guidelines in relation to the hospital based management of suspected Meningococcal Sepsis/Meningitis and which can be adapted depending on local circumstances.

**WORKING GROUP ON BACTERIAL
MENINGITIS AND RELATED CONDITIONS**

SECOND REPORT

JULY 1999

Department of Health and Children, Hawkins House,
Dublin 2

WORKING GROUP ON BACTERIAL MENINGITIS AND RELATED CONDITIONS

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1. INTRODUCTION

Bacterial meningitis and septicaemia are systemic infections caused by a variety of organisms, the most common being *Neisseria meningitidis*, *Haemophilus influenzae type B*, (*Hib*) and *Streptococcus pneumoniae*.

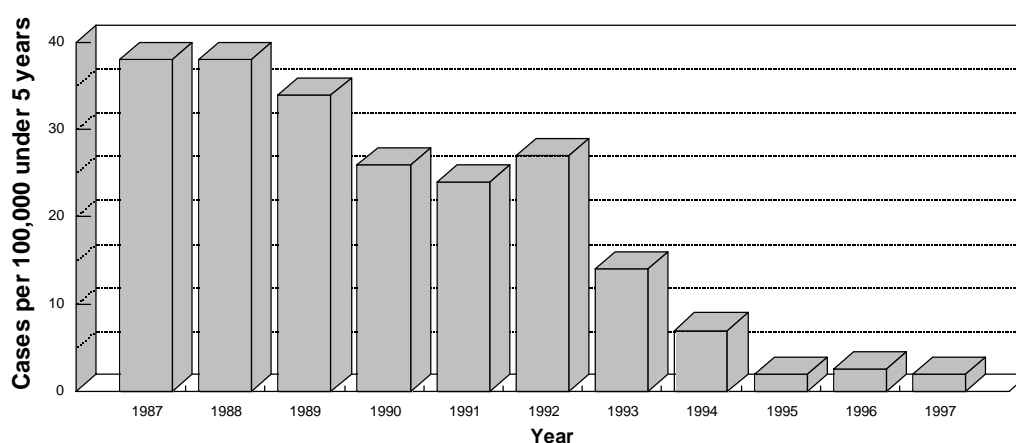
The epidemiology of these conditions in the western world has been well described. This is particularly so in respect of the most commonly occurring of these infections in this country, *meningococcal* disease. This infection is spread by direct contact, can affect any age group but is concentrated mainly in infancy and early childhood. It occurs mainly sporadically but occasionally in epidemic form. Cases are reported throughout the year but the infection peaks during the winter months and carries a case fatality rate of up to 10%.

The most common clinical presentations are meningitis alone, septicaemia alone, and a combination of the two.

Early diagnosis and effective antibiotic treatment of cases are of paramount importance in managing the condition and the effective implementation of chemoprophylactic and immunoprophylactic strategies are required to prevent its further spread.

A vaccine is available against invasive *Hib* disease and its introduction into routine childhood vaccination programmes in recent years has resulted in a significant fall in incidence of this condition to the point of eradication in some countries. In Ireland, subsequent to the introduction of Hib vaccine in 1992, the incidence of the disease has declined tenfold (**Figure 1 below refers**).

**Figure 1: *Haemophilus influenzae* type b disease incidence
Republic of Ireland 1987 - 1997**



Vaccines are also available against meningococcus type A and C and should be given to close contacts of cases caused by these organisms. However, as there is little immunological response in children under 18 months to the group C component and under three months to the group A component, vaccination is not recommended under these ages. There is as yet no readily available effective vaccine against group meningococcal B organisms but intensive research and development work is being carried out world-wide in an effort to develop a safe and effective B vaccine and to further strengthen the effectiveness of the A and C vaccines now available. Significant progress is being reported and it is hoped that new and improved vaccines will be available for use in the next few years. The Working Group on Bacterial Meningitis and Related Conditions continues to monitor these developments.

2. BACKGROUND

During 1994 and 1995, the incidence of bacterial meningitis and related conditions reported formally to the Department of Health by the health boards increased significantly over previous years.

In 1993, 203 such reports had been made, rising to 241 in 1994 and 382 in 1995. In addition, during the winters of 1994/5 and 1995/6 a number of deaths occurring in close temporal relationship to each other raised public anxiety about these conditions. A somewhat similar situation had arisen in the UK where the number of cases and deaths had risen sharply and without apparent explanation during 1995.

As part of its general response to this issue, the Department of Health set up a Working Group with the following terms of reference:

"To examine the incidence of bacterial meningitis and related conditions, and to make such recommendations as may be required to strengthen the surveillance and control of these conditions".

In considering its terms of reference, the Working Group decided that its remit could best be fulfilled by addressing the following issues:

1. Describing the epidemiology of the relevant conditions based on:
 - (a) Official notifications to the Department of Health
 - (b) Published statistics and communication in a variety of regionally located Communicable Diseases newsletters.
 - (c) Independent research carried out and published in peer reviewed literature.
2. Elaborating a set of definitions and criteria for diagnosing these conditions which would be used uniformly around the country in the future for the surveillance of the conditions.

3. Developing a set of guidelines which would assist clinicians and public health physicians in their decisions relating to antibiotic prophylaxis and other preventive measures.
4. Recommending a system of notification and surveillance of the conditions.
5. Identifying areas requiring further research.

The Working Group produced its report in January 1997 and this was circulated to health boards, hospitals and other relevant bodies and agencies. The Working Group has remained in existence to continue to provide advice on the surveillance and control of bacterial meningitis and related conditions. The membership of the Working Group is as follows:

- ◆ Dr John Devlin (Deputy Chief Medical Officer), Department of Health and Children (Chairman)
- ◆ Dr Karina Butler (Consultant in Infectious Diseases), Our Lady's Hospital for Sick Children, Crumlin
- ◆ Dr Mary Cafferkey (Consultant Microbiologist), The Children's Hospital, Temple Street
- ◆ Dr Jeremiah Fogarty (Specialist in Public Health Medicine), Western Health Board
- ◆ Dr Chris McNamara (GP Advisor), Department of Health and Children
- ◆ Dr Martin O'Boyle (Specialist in Public Health Medicine), South-Eastern Health Board
- ◆ Dr Darina O'Flanagan (Director), National Disease Surveillance Centre
- ◆ Dr Fiona Ryan, (Specialist in Public Health Medicine) Southern Health Board
- ◆ Mr Fergal Goodman (Assistant Principal), Department of Health and Children

Review of 1997 Report

Among the recommendations contained in the Report was that the implementation of its recommendations should be evaluated. This evaluation has now been completed with the

publication of the Second Report of the Working Group on Bacterial Meningitis and Related Conditions.

3. EPIDEMIOLOGY OF MENINGOCOCCAL DISEASE

Notifications to Department of Health and Children

For the purposes of notification under the Infectious Diseases Regulations (1981), health boards report the relevant conditions under "Bacterial Meningitis including Meningococcal Septicaemia". The following table indicates the number of notifications received for the years 1992 to 1998:

Table 1

**Cases of Bacterial Meningitis (including Meningococcal Septicaemia)
notified to the Department by Health Boards**

Health Board	1992	1993	1994	1995	1996	1997	1998
Eastern	88	68	79	166	155	199	170
Midland	15	14	15	20	35	27	20
Mid-Western	4	7	9	21	20	36	23
North Eastern	22	25	25	28	55	56	78
North Western	6	7	8	5	21	18	18
South Eastern	17	23	23	30	39	58	54
Southern	51	40	61	96	50	66	81
Western	22	19	21	16	36	46	41
Total	225	203	241	382	410	506	485

Deaths from Bacterial Meningitis

It should be noted that despite the significant increase in the number of cases of bacterial meningitis notified to the Department, there has not been a commensurate increase in mortality, reflecting the improved surveillance, preventive and treatment strategies in recent years (see Table 2 below).

Table 2

Deaths from Bacterial Meningitis (including Meningococcal Septicaemia)

Year	1992	1993	1994	1995	1996	1997	1998
Deaths	32	22	29	28	15	30	23

Other Bacterial Meningitis

The number of cases of "Other Bacterial Meningitis" notified to the Department in 1998 was 40, made up as follows:

<i>Haemophilus influenzae</i>	3
<i>Strep pneumoniae</i>	19
<i>Staphylococcus aureus</i>	0
Group B Streptococcus	3
<i>E coli</i>	1
Tuberculosis	3
Other	11
Total	40

National Meningococcal Reference Laboratory

In 1996 the Department of Health made funding available to the Children's Hospital, Temple Street to establish a national Meningococcal Reference Laboratory (MRL). The twin aims of this laboratory were:

- (i) To provide non-culture diagnosis on Invasive Meningococcal Disease (IMD) using the DNA-based amplification method, polymerase chain reaction (PCR) on blood and/or CSF as a service to all hospitals in the country;
- (ii) To put in place epidemiological serotyping and serosubtyping of isolates of *N. meningitidis* from patients with IMD.

The PCR methodology for specific meningococcal DNA was validated and put in place at the MRL during 1996. A national service for non-culture diagnosis of Invasive Meningococcal Disease by PCR of blood and/or CSF was established in November 1996. A summary of services provided by the laboratory and a protocol for appropriate specimen collection was sent to all hospital laboratories in October 1996. Staff in all laboratories were also encouraged to submit all isolates of *N. meningitidis* for epidemiological typing and detailed antibiotic susceptibility testing.

Since introduction of meningococcal PCR testing at the Meningococcal Reference Laboratory in November 1996 the contribution of PCR diagnosed disease alone to the overall meningococcal disease incidence has been significant. In 1997 and 1998, 1,167 and 1,775 specimens respectively were submitted for PCR. In 1997 23.8% and in 1998 19% of specimens were PCR positive. PCR has had a significant impact on case ascertainment and confirmation of the diagnosis of invasive meningococcal disease nationally. The diagnosis was based on PCR in 43.8% of patients in 1997 and 52.9% in 1998.

Table 3

Work of Meningococcal Reference Laboratory, 1997 & 1998

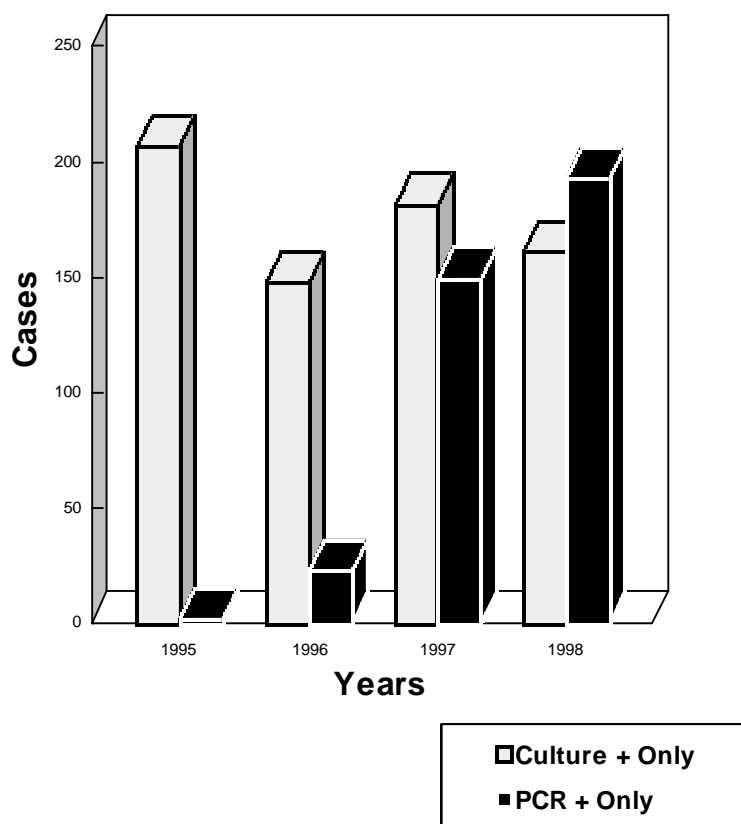
	1997	1998
Number of laboratory-confirmed cases of IMD	343	368
Culture positive	182	161
PCR positive	150	193
Acute and convalescent phase antibody response	11	14

The group was determined by PCR in all but 15 cases (4.4%) in which the diagnosis was based on PCR which facilitated epidemiological intervention.

Data are currently available for a period of four complete years up to the end of 1998. A total of 1,153 cases of laboratory-confirmed meningococcal disease occurred over this four-year period, giving an average annual incidence of 7.95 per 100,000 population for disease diagnosed by culture and/or improved non-culture (PCR or serology) methods.

Figure 2 illustrates graphically the relative contributions of PCR diagnosed only and culture confirmed meningococcal disease over the four-year period 1995 to 1998.

Figure 2 Meningococcal disease, Republic of Ireland, 1995 -1998
(cases confirmed by culture from 'normally sterile sites' and by PCR only)



Meningococcal disease incidence rates in the international context are presented in Table 4 below. (The 1996 data is the latest available.)

Table 4

**Meningococcal disease (laboratory confirmed cases):
International incidence rate data 1996***

Country	Crude incidence rate**
Belgium	2.1
Denmark	4.6
England & Wales	3.0
Netherlands	3.8
Scotland	4.1
Iceland	6.3
Northern Ireland	2.7
USA	1.0
New Zealand	8.3
Australia	1.7
Ireland	5.6

* all 1996 data except USA (1994)

** per 100,000 population

Note: Not all countries have access to PCR. The international figures may therefore underestimate the position.

(**Source:** Connolly M., Noah N., Surveillance of Bacterial Meningitis in Europe 1996. King's European Meningitis Surveillance Unit)

Meningococcal Groups

Neisseria meningitidis is divided into a number of distinct groups based on their antigenic properties, the most common of which world-wide are groups **B, C, A, Y** and **W135**. They can be further subdivided by serotype.

In Ireland serogroup B comprised 54% of all disease for the three-year period 1995-97, serogroup C 44% and other serogroups only 2%. This serogroup distribution has remained constant in the national context over the three-year period. The relative distribution of groups B and C disease by health board is illustrated in the accompanying map (**Figure 3, page 15**).

A total of 251 isolates of *N. meningitidis* were submitted to the Meningitis Reference Laboratory for epidemiological typing in 1997 and 1998. Of these, 56.6% were Group B, 29.4% were Group C and a small number of other serogroups were represented (**W135**, 4 isolates; **X**, 2 isolates; **Y**, 1 isolate and nongroupable, 3 isolates). Detailed serotyping and serosubtyping revealed that 30 individual Group B and 17 individual Group C serotype/serosubtype combinations were isolated from patients with meningococcal infection. One strain, serosubtype p1.4, accounted for 39.4% of group B isolates overall throughout the two-year period.

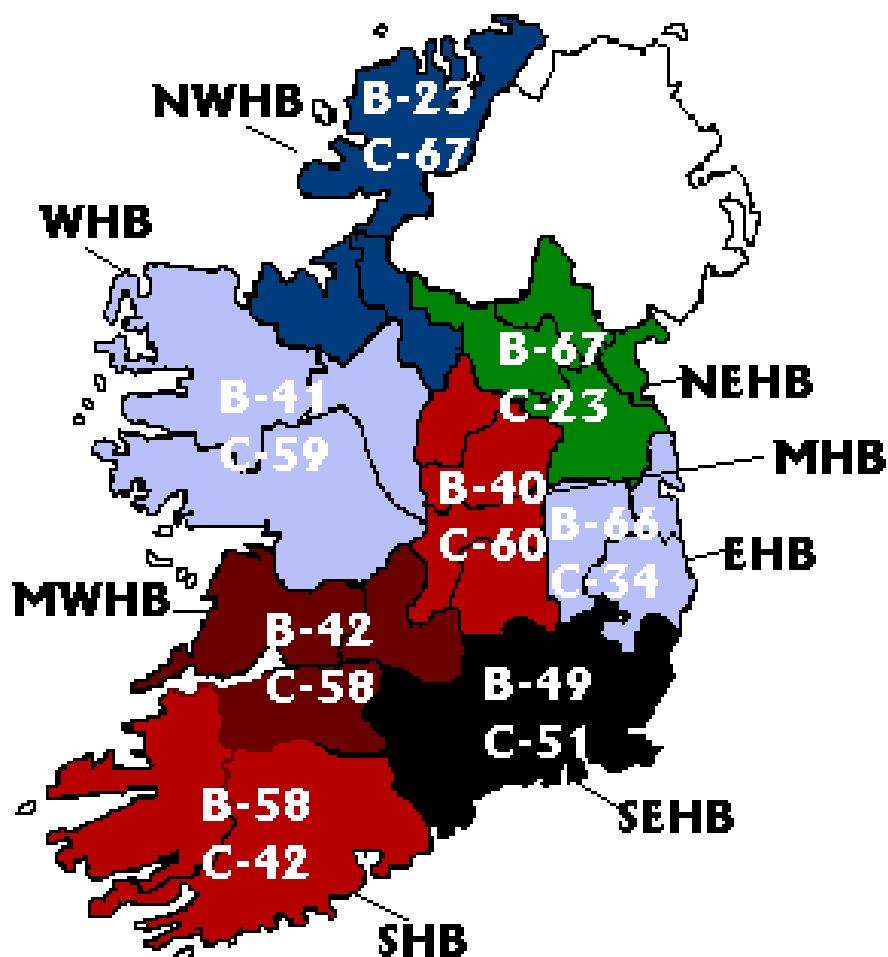


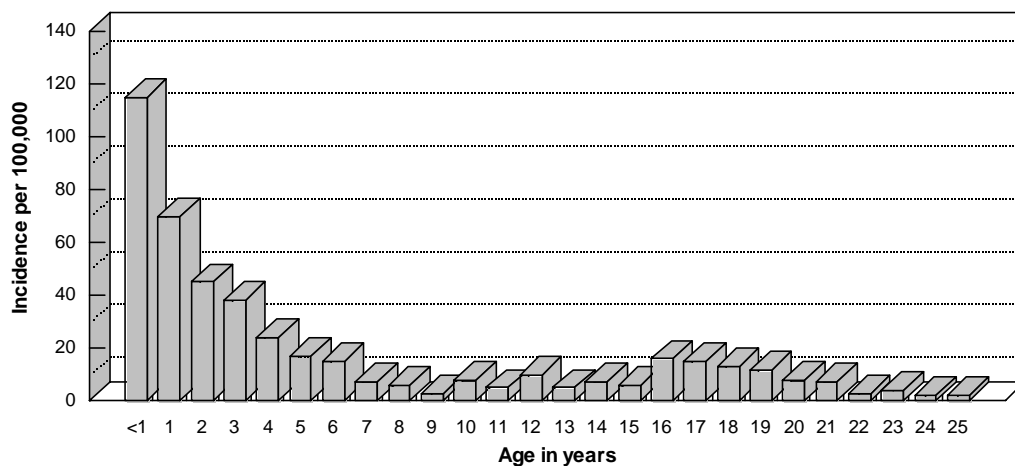
Figure 3
Meningococcal Serogroup % B + C relative proportions by Health Board, 1995-1997

Age-specific infection rates.

The highest incidence of meningococcal disease occurs in childhood, particularly in infancy. Disease rates fall after 2-3 years of age. A slight increase in rate is noted again in the 14-19 year age group (**Figure 4**).

Figure 4

Average annual age-specific incidence of meningococcal disease, Republic of Ireland, 1995-97



Conclusion

Ireland continues to have a significant burden of morbidity and mortality from meningococcal infection, when compared to a number of our EU partners. However, as has been shown in other countries where this disease has been efficiently reported and closely monitored over many years, the occurrence of Meningococcal infection is cyclical in nature. Increases in incidence may occur periodically without apparent reason, persist for a number of years and then begin to fall again towards previous lower levels. Increasing immunity in the community to infection with particular strains of organism may help partially to explain this phenomenon. The disease will need to continue to be monitored closely in the years ahead.

4. DIAGNOSTIC CRITERIA FOR SURVEILLANCE OF MENINGOCOCCAL INFECTION

For surveillance purposes the diagnosis of meningococcal infection shall be classified as **'Definite'**, **'Presumed'** or **'Possible'**. These diagnostic categories do not necessarily influence the clinical management of a suspected case or the decision to initiate chemoprophylaxis.

A **'Definite'** case of meningococcal infection includes children or adults who have:

- ◆ *Neisseria meningitidis* isolated from blood, CSF or other normally sterile body site (e.g.. blood, synovial fluid, pleural or pericardial fluid) or from a petechial or purpuric lesion.
- ◆ a positive PCR test for meningococcus obtained on blood, CSF or specimen from another sterile site.

A **'Presumed'** case of meningococcal infection includes children or adults who have:

- ◆ Gram negative intracellular diplococcus detected in CSF on microscopy.
- ◆ meningococcus isolated from an eye, throat or nasal swab, together with characteristic purpuric rash*.
- ◆ meningococcus isolated from an eye, throat or nasal swab and who have clinical and laboratory features of bacterial meningitis (CSF pleocytosis) in whom no other cause of meningitis is identified.

* The rash typical or characteristic of meningococcal infection evolves over hours. At disease onset an erythematous macular eruption may be noted. Similarly, fine petechiae may be noted in this early stage. These features alone are not pathognomonic of meningococcal infection and can occur in the course of many viral illnesses. In meningococcal disease progression of these to frank purpura with or without associated haemorrhage into mucous membranes or at i.v. insertion sites is characteristic. Early intervention with antibiotics may abort rash progression. Often the first manifestation noted are 2-3 mm purpuric lesions which can appear without any antecedent eruption.

- ◆ a clinically compatible illness and who have gram negative intracellular diplococci detected in skin scrapings taken from the characteristic haemorrhagic rash.
- ◆ a clinically compatible illness with a serological response which is reported by a reference laboratory as consistent with recent acute infection.

A '**Possible**' case of meningococcal infection includes children or adults who have:

- ◆ Evidence of acute sepsis, with or without meningitis, together with characteristic haemorrhagic purpura.
- ◆ Clinical evidence of sepsis without a purpuric rash, in whom no other cause of sepsis is identified, and in whom meningococcus is isolated from an eye, throat or nasal swab.
- ◆ Received pre-admission antibiotics, have laboratory evidence of bacterial meningitis but are culture negative.

Serological confirmation should be sought in all presumed and possible cases.

Note: All cases of suspected meningococcal infection should be reported.

5. LABORATORY DIAGNOSIS OF INVASIVE MENINGOCOCCAL DISEASE

1.

When invasive meningococcal disease is suspected on clinical grounds, the diagnosis should be confirmed as rapidly as possible. Accurate diagnosis is important for public health and epidemiological purposes. Isolation of *N. meningitidis* from a deep site is the "gold standard". However increasing use of pre-admission penicillin has led to a reduction in the yield from culture. In order to optimise the chances of demonstrating the organism and obtaining an isolate for sensitivity testing and typing additional specimens should be collected on admission. Non-culture methods have been validated at the Meningococcal Reference Laboratory (MRL) at The Children's Hospital, Temple Street, Dublin and should now form part of the routine investigation in culture negative cases.

2. Identification of putative *N. meningitidis* isolates and grouping, typing and subtyping of isolates.

The identification of any putative meningococci isolated from CSF, blood culture, throat swabs or skin aspirates should be confirmed. It is essential for epidemiological strain identification and public health management that isolates are grouped and typed. One relevant isolate from each case should be sent to the MRL for definitive grouping, serotyping and confirmatory antibiotic sensitivity testing.

Appendix 1 contains recommendations outlining the procedures to be adopted in the collection of specimens.

6. CHEMOPROPHYLAXIS

Chemoprophylaxis should be given as soon as possible to close contacts (as defined below) of all cases where the clinical diagnosis of meningococcal meningitis or septicaemia is considered to be likeliest diagnosis by the public health doctor in consultation with the clinician managing the case. In the absence of an alternative diagnosis a feverish, ill patient with a petechial/purpuric rash should be regarded as most likely a case of invasive Meningococcal disease and chemoprophylaxis offered accordingly.

Where the public health doctor, in consultation with the clinician managing the case and the specialist in public health medicine, considers that diagnoses other than meningococcal disease are at least as likely, then chemoprophylaxis is not indicated. This category includes cases treated with antibiotics whose probable diagnosis is viral meningitis. If further evidence emerges to change the diagnosis then appropriate action should be taken.

People who are close contacts of a case of meningococcal disease are at higher risk of developing disease. This risk is highest in the first seven days after a case and falls during the following weeks. The rationale for chemoprophylaxis is that it is given to eliminate carriage of the organism from the network of close contacts of the case and thereby reduce the subsequent spread of the organism to other susceptible persons. It also aims to eliminate carriage from recently colonised susceptibles in the period before invasive disease may develop.

1. Prophylaxis for the index case must be initiated prior to discharge from hospital and ideally may be given as soon as the patient can tolerate oral medication.
2. For the purpose of administering prophylaxis, close contacts are defined as those who in the 7 days prior to the onset of illness of the index case
 - ◆ shared living or sleeping accommodation with the patient; includes babysitters/baby-minders.
 - ◆ had mouth kissing contact with the patient; this does not include cheek kissing

- ♦ gave mouth-to-mouth resuscitation to the patient;
 - ♦ were in the same nursery/creche as the patient; where the nature of nursery/creche contact is similar to that for household contacts; this includes adult carers.
3. Chemoprophylaxis is not indicated for classmates of an index case unless there are two or more cases which are caused or could be caused by the same serogroup during the same term. Two definite cases caused by different serogroups should be regarded as two sporadic cases, whatever the interval between them. However, in all sporadic cases the opportunity should be used to give advice to parents and guardians of all pupils attending the school on the signs and symptoms of the disease as soon as is practically possible.
- ♦ If the cases occur in the same class, all class members and staff should receive prophylaxis.
 - ♦ If the cases occur in different classes, management is more difficult but should be guided by such considerations as:
 - the interval between the cases
 - the size of the contact group
 - the carriage rate in the school
 - whether the cases are due to vaccine preventable strains
 - the degree of public concern particularly if a death has occurred.
 - the incidence of the disease in the wider community

In situations where apparently linked cases occur, management should be discussed with the Specialist in Public Health Medicine with responsibility for Infectious Disease Control, the Infectious Diseases Consultant and the Consultant Microbiologist in the hospital dealing with the case.

Closure of a school when one or more cases occur is **not** indicated as a public health measure. The majority of cases of meningococcal disease occur following

acquisition of the organism from a healthy carrier rather than from a person with the disease.

In situations where the diagnosis is unclear and the child attends an educational institution, it is advisable to discuss the situation with the head of the institution at an early stage. The head will then be in a position to respond to parental concerns. A letter to parents may be required if there is a lot of parental anxiety.

4. It is **not** recommended that prophylaxis be given routinely to passengers on public transport, e.g. bus, train, aeroplane, where an index case has been identified.
5. Special consideration should be given to the attendance of an index case at a house party in the preceding 7 days especially if pre-school children were present. If chemoprophylaxis is appropriate it should be given to all attenders both adult and children.
6. Special consideration should be given to situations in which there is greater than usual interaction between members of the extended family and an index case, particularly where overcrowding or adverse environmental living conditions exist.
7. Ideally, chemoprophylaxis should be given to all contacts as soon as possible after notification of the index case. However, it is appropriate to administer prophylaxis to close contacts, who may not have come to notice initially, up to a month after the identification of the index case as carriage may persist for a long period.

7. MANAGEMENT OF CLUSTERS OF MENINGOCOCCAL GROUP C INFECTION IN THE WIDER COMMUNITY

When an increase in cases of Meningococcal group C occurs in a community, it may be difficult to decide whether and when to intervene. The following advice is consistent with guidelines developed for the management of serogroup C outbreaks in the United Kingdom and the United States.

Recommendations:

Look for links between cases. A social group may be found within which cases are occurring and at whom prophylactic measures can be aimed.

Calculate age-specific attack rate. In calculating this rate, the numerator is the number of confirmed group C cases which have occurred. It is recommended that a minimum of four to six cases should have occurred before considering action. Cases occurring in same household or institution should be counted as one case.

The denominator is the population at risk. This population should be in an identifiable geographical area.

Consider intervention only if the age-specific attack rate in a three-month period is high. The precise threshold for intervention has not been set. However, intervention should be considered when the age-specific instance in a three-month period is in the order of 40 per 100,000.

When considering intervention the following factors should also be taken into consideration:

- (i) the time interval between cases. The more closely together the cases occur, the more likely the requirement for action.

- (ii) the seasonality of the disease. Cases occurring early are more indicative of a significant outbreak than those occurring later in the normal meningococcal season.
- (iii) the virulence of the infection as indicated by the degree of morbidity and level of mortality.
- (iv) whether the outbreak constitutes a recognisable shift towards a particular age group. A shift to an older age group has been noted in previous outbreaks.
- (v) If sub-typing is available, the presence of a single subtype is another factor indicating the need for intervention.

A local outbreak control committee should be convened to consider whether intervention is indicated. The Working Group on Bacterial Meningitis is available to act as a national resource to local committees if so required.

CHOICE OF PROPHYLACTIC ANTIBIOTIC

- ♦ Rifampicin is the drug of choice
- ♦ Rifampicin should be given promptly and preferably within 24 hours of diagnosis of the index case.

All close contacts should be advised that infection may occur irrespective of whether prophylaxis was administered, as the contact may have been incubating disease, the antibiotic may fail to work or the contact may recolonise and develop disease. Those who show signs and symptoms of infection should receive prompt medical attention. Persons receiving chemoprophylaxis should be advised that the primary aim is to reduce carriage rate, thereby reducing the likelihood of further cases.

Dose of Rifampicin:

Children 0-12 months: - 5 mg/Kg twice daily for two days

Children, 1-12 years: - 10mg/Kg twice daily for two days

Children over 12 years & Adults: 600 mg twice daily for two days

Side Effects:

Rifampicin recipients should be warned about these. They are:

- ◆ interference with the contraceptive pill
- ◆ interference with anticoagulants
- ◆ red colouration of urine, sweat and tears
- ◆ permanent discolouration of soft contact lenses

Contraindications: severe liver disease

Alternative Prophylaxis: ceftriaxone as a single intramuscular dose (250mg in adults, 125 mg in children under 12 years) - see data sheet. Although not licensed for this purpose, a single dose of Ciprofloxacin 500mg orally for adults has been shown to be effective.

Allergic reactions such as facial swelling accompanied by urticaria and tightness of the throat have been reported in a small proportion of cases after use of Ciprofloxacin. Facilities for the management of such reactions should therefore be available if this drug is used.

Pregnancy:

Where close contacts are known to be pregnant, options following counselling should include giving no prophylaxis, giving ceftriaxone, or taking a throat swab and giving ceftriaxone if meningococcus is cultured. While no drug can be regarded as absolutely safe

in pregnancy, harmful effects on the foetus have not been documented in relation to this agent. The contact's obstetrician should be informed.

Vaccination

If the strain is vaccine-preventable, i.e. **A, C, Y** or **W-135**, vaccination should be offered to these contacts who are given prophylaxis and can be of benefit up to three months after the diagnosis of the index case. Vaccination is not generally recommended for contacts of group **C** disease under 18 months as there is little immunological response in children of this age. Stocks of these vaccines should be kept available. It is not current policy to vaccinate index cases against Group **C** disease.

There is, at present, no readily available safe and effective vaccine against group **B** organisms.

Risk to Third-Level Students

A study was undertaken in the United Kingdom during the summer of 1997 to examine whether students in the age-group 18-25 years were at increased risk of vaccine-preventable meningococcal disease (i.e. Group **C** disease) and to determine whether such students should be offered meningococcal **A + C** vaccine as part of a university immunisation programme. It was found that university students in their first year at university attending certain universities had approximately two-and-a-half times the risk of developing Meningococcal Group **C** disease compared to the corresponding age group of the general population.

Examination of situation in Ireland

In the light of the UK study referred to, the Working Group on Bacterial Meningitis and Related Conditions has examined the incidence of the disease in Ireland and has compared this with the situation in the United Kingdom.

An examination was undertaken of the incidence of Group **C** Meningococcal disease in Ireland by age group in 1995 and 1996. This found that the highest incidence of the disease

occurred in children under four. The next highest incidence was in the 15-19 year-old group. The incidence for 20-24 year-olds was considerably lower.

A comparison was also undertaken of the incidence in Ireland of Group C Meningococcal disease between the 17-24 year-old student population and the 17-24 year-old total population, during the period September 1994 to August 1997. The incidence was found to be higher amongst the student population but to be dispersed across those at different stages of their academic studies.

Recommendation

As the incidence of cases in Ireland is more dispersed across the age-bands than is the case in the United Kingdom and as Group B disease is the more prevalent in Ireland, it is not considered that a general programme of immunisation against Group C Meningococcal disease is appropriate. However it is recommended that, in line with existing practice, immunisation take place where there are outbreaks in establishments such as schools or third-level institutions. The currently available vaccine used in outbreaks works well in some situations but has a short duration of efficacy.

8. TREATMENT OF MENINGOCOCCAL INFECTIONS

1. Primary Care

In view of the high mortality rate from meningococcal infection and the often rapid deterioration of the patient prior to hospital admission, early treatment of suspected cases of the condition with benzylpenicillin may be life-saving and it is recommended that GPs carry supplies of this drug in an emergency bag.

Recommended Dosage of Benzlypenicillin:

Adults and children > 10 years	1200 mgs
Children 1-9 years	600 mgs
Children < 1 year	300 mgs

Penicillin, ideally, should be given intravenously; it can be given by the intramuscular route in shocked patients but is not as effective.

If there is a history of penicillin anaphylaxis (which is extremely rare, of the order of 0.002% of exposed patients), penicillin should not be given and the patient transferred to hospital as soon as possible.

2. Hospital

Each hospital Accident and Emergency Department should have a protocol for the clinical management of acute meningococcal infection displayed in an accessible place to be used by all doctors dealing with such cases. This protocol should also emphasise the necessity of reporting the case.

In 1998, at the request of the Department of Health and Children, an expert group established by the Royal College of Physicians of Ireland prepared a template

guidelines document on the hospital treatment of persons with suspected meningitis, which appears as **Appendix 2** to this Report (page 43).

It has been circulated to health boards, voluntary hospitals and other interested parties. It is intended that the guidelines should serve as a basis for the preparation of a protocol suited to local needs and they may therefore be adapted as considered appropriate.

9. REPORTING & SURVEILLANCE

1. A case of confirmed or suspected meningococcal infection must be reported to the local Health Board by the doctor who diagnoses or suspects it.
2. Cases should be reported to an identified health board medical officer whose name and telephone number are immediately accessible to the reporting doctors.
3. On receiving the notification, the health board should institute immediate appropriate preventive measures.
4. Health boards should continue to notify the Department of Health and Children within 24 hours of a case occurring in addition to the routine weekly returns. Suggested reporting forms for the reporting of cases to the Department of Health and Children are included in **Appendix 3**.

A Bacterial Meningitis Disease Registration form is suggested for use in each health board - see **Appendix 4**. This data should be transferred in electronic format. The frequency of transfer of data will be agreed by the newly-formed National Disease Surveillance Centre and the Departments of Public Health in each region.

It is the intention that the arrangements for the notification of infectious diseases will be changed, probably later in 1999, so that health board notifications will be made to the National Disease Surveillance Centre instead of to the Department of Health and Children.

5. The identification of any putative meningococci isolated from CSF, blood culture, throat swabs or skin aspirates should be confirmed. Non-culture methods have been validated at the Meningococcal Reference Laboratory (MRL) in the Children's Hospital, Temple Street and all isolates and specimens for non-culture diagnosis should be sent there.

6. It is essential from the viewpoint of epidemiology and public health surveillance that isolates are grouped and typed and the results reported to the health board. The development of close working relationships between Public Health Departments, Infectious Disease Consultants and Hospital Microbiologists is a prerequisite for success in this area.
7. On a quarterly basis, the health boards are required to review the notifications received and exclude those notifications which finally prove not to be actual cases of meningococcal disease as defined or those which were reported more than once.
8. There is no formal arrangement regarding the availability of health board medical staff out of normal working hours. While this matter is to be considered as part of the review of the operation of the Departments of Public Health, the Working Group is of the view that the issue should be addressed as a matter of urgency.
9. The Meningococcal Reference Laboratory in the Children's Hospital, Temple Street, Dublin 1 is designated as a National Centre for laboratory investigation of this condition.

10. RESEARCH

The Working Group's first report noted that there were many areas in the clinical, laboratory and epidemiological aspects of this condition which would prove fruitful subjects for research. The following were considered to be of particular importance:

- (i) The identification of particular sub-groups within the population who may be at particular risk of contracting this condition.
- (ii) Clarification as to whether there may be genetic susceptibility to infection with the organisms causing this disease.
- (iii) The early management of the acute condition both at primary care and hospital level.
- (iv) Follow up of surviving children who have been infected to determine the nature and frequency of long term sequelae.
- (v) Audit of general practitioner treatment of the condition.

Since then research has been undertaken on a range of issues identified in that report, including whether particular sub-groups within the population may be at particular risk of contracting meningococcal infection, the question of genetic susceptibility to infection, the early management of the acute condition, and on the follow-up of surviving children.

11. RECOMMENDATIONS MADE IN FIRST REPORT AND ACTIONS TAKEN TO IMPLEMENT THEM

Recommendation

- 1. Public awareness of meningococcal infection should continue to be raised by a combination of public information campaigns by the health services and by support of voluntary bodies engaged in this area.**

Action taken

The health boards, in conjunction with voluntary bodies, have conducted extensive educational campaigns on Meningococcal Disease. There continues to be close liaison between the health boards and the voluntary bodies concerned, principally the Meningitis Research Foundation. The Health Promotion Unit's information leaflet has been updated and in 1998 a video entitled "Meningitis: Prompt Action Saves Lives" was produced by the Office for Health Gain in conjunction with the Foundation. The Irish College of General Practitioners also designate education officers in each health board area who are in a position to assist in the event of an outbreak of meningococcal infection.

Recommendation

- 2. Continuing medical education for General Practitioners, Hospital A & E doctors and Paediatricians should give particular emphasis to the diagnosis and management of this condition. Written protocols should be available in all hospitals and GPs should always carry benzylpenicillin in their emergency bags.**

Action taken

The Working Group has discussed these issues with the Irish College of General Practitioners and the College has indicated that it took a number of actions following the publication of the 1997 Report, in particular in the area of continuing

medical education. It has been agreed that there should be ongoing contact between the Committee and the College, as required.

A guidelines document on the hospital treatment of persons with suspected meningitis has been prepared by a committee established by Royal College of Physicians of Ireland and has been circulated by the Department of Health and Children to health boards, voluntary hospitals and other interested parties. The protocol appears as Appendix 2 to this Report (page 43). It is intended that the guidelines should serve as a basis for the preparation of a protocol suited to local needs and they may therefore be adapted as considered appropriate.

The Department has also written to health boards, advocating that general practitioners each be sent a "meningitis pack" so as to promote carriage of penicillin by GPs. Several of the health boards have arranged to issue such packs.

Recommendation

- 3. The diagnostic criteria for the surveillance of this condition should be used uniformly by all health boards.**

Action taken

The standard diagnostic criteria are being followed by the health boards.

Recommendation

- 4. The chemoprophylaxis guidelines should be used by all health boards and hospitals as the basis for their approach to the prevention of spread of infection**

Action taken

The health boards have indicated that these guidelines are being followed. The advice in this regard has been expanded upon in this revised report.

Recommendation

- 5. The proposals for notification should be implemented.**

Action taken

The notification arrangements are in place and are operating effectively.

Recommendation

- 6. All putative cases of meningococcal infection should have full laboratory investigation and the Meningococcal Reference Laboratory in Temple Street Hospital should be designated as a national centre for non-culture diagnosis.**

Action taken

The Department of Health and Children has funded the establishment of the Meningococcal Reference Laboratory (MRL) at the Children's Hospital, Temple Street. A national service for non-culture diagnosis of Invasive Meningococcal Disease by PCR of blood and/or CSF was established by the MRL in 1996 and there has been a very good uptake of this service. PCR has had a significant impact on case ascertainment and confirmation of the diagnosis of Invasive Meningococcal Disease nationally. In 1998 the diagnosis was based on PCR in 52.9% of patients. The establishment of the MRL has also enabled the putting in place of epidemiological serotyping and serosubtyping of isolates of *N. meningitidis* from patients with Invasive Meningococcal Disease.

Recommendation

- 7. Support should be given to research in the areas identified in this report.**

Action taken

Since the completion of the Working Group's first report, research has been undertaken on a range of issues identified in that report, including whether particular sub-groups within the population may be at particular risk of contracting meningococcal infection, the question of genetic susceptibility to infection, the early management of the acute condition, and on the follow-up of surviving children.

Recommendation

- 8. The implementation of these recommendations should be evaluated in one year with particular reference to such matters as the availability of comprehensive national epidemiological information and the utilisation of standardised protocols.**

Action taken

One of the objectives of the newly-established National Disease Surveillance Centre is to collaborate with health board Specialists in Public Health Medicine on the continued development of the meningococcal register already in operation to enable collation and analysis of data for 1998 and future years.

12. SUMMARY

1. The number of cases of Bacterial Meningitis including Meningococcal Septicaemia reported to the Department of Health has increased, rising from 131 in 1990 to 506 in 1997. The number of cases for 1998 was 485.
2. Good epidemiological data is now available on meningococcal infection in Ireland. Considerable additional analysis has been undertaken by members of this Working Group.
3. The incidence in Ireland in 1996 of 5.6/100,000 compares to a rate of 3/100,000 in England and Wales and 6.3/100,000 in Iceland. With improved methods of non-culture diagnosis the laboratory-confirmed incidence in Ireland was 10.1/100,000 of the population in 1998. There is however variability in incidence as between health board areas.
4. Analysis of other sources of information such as Regional Laboratory Surveillance reports and peer reviewed articles confirms that Ireland has a significant burden of morbidity from meningococcal infection.
5. To provide support and assistance in the ongoing surveillance and management of this condition, this report sets out:
 - (a) The criteria to be used in defining a case of meningococcal infection to be used for surveillance purposes.
 - (b) Procedures to be used in making a laboratory diagnosis.
 - (c) A set of guidelines to assist public health physicians in the decision making process relating to chemoprophylaxis and prevention.

- (d) Suggestions concerning the primary care and hospital treatment of suspected cases.
 - (e) A guidelines document on the hospital treatment of persons with suspected meningitis, to serve as a basis for the preparation of a protocol suited to local needs.
6. Information is also provided concerning the system of notification and surveillance.
 7. The Working Group will continue in existence and will serve as a resource to the Department of Health and Children and the wider health service in relation to the management and prevention of meningococcal disease.

APPENDIX 1

Specimen Collection

The following specimens should be collected routinely on admission. Specimens for non-culture methods of diagnosis [Polymerase Chain Reaction (PCR) and serology] may be stored at 4°C pending results of culture.

1. **Blood for culture**

Blood cultures should always be taken regardless of pre-admission antibiotic administration.

2. **Blood for non-culture diagnosis by PCR**

Blood for PCR must be collected **on admission** as following antibiotic treatment the specimen will rapidly revert to negative. Ideally a 2.5 to 5.0 mls EDTA sample should be obtained (minimum 0.5 ml) This should be stored at 4°C pending the results of culture. If cultures are negative the specimen should be sent to the MRL. Meningococcal DNA is liable to autolyse if left unprocessed for more than 48-72 hours; therefore delays in despatching the specimen should be minimised. Specimens do not require refrigeration during transport to the MRL.

3. **Cerebrospinal Fluid (CSF) for Microscopy and Culture and PCR**

CSF should be collected if a lumbar puncture is performed. CSF microscopy and culture may be positive even when pre-admission penicillin has been given. If cultures are negative, part of the remaining specimen should be submitted to the MRL for PCR examination. This CSF specimen should not have been centrifuged and should be sent to the MRL in a small and well-sealed container such as a screw-capped Eppendorf centrifuge tube.

4. **Throat swab and/or Pernal Nasopharyngeal swab**

In order to optimise the chances of obtaining an isolate for antibiotic sensitivity testing, grouping and typing, a throat swab (a full sweep of the pharyngeal wall and tonsils) should be taken in all patients. If it is not possible to take a sweep swab (for example in an infant or an unco-operative patient), a pernasal swab rotated on the posterior pharyngeal wall is an appropriate alternative. Fluffy charcoal impregnated swabs are preferred and should be placed immediately in transport medium (e.g.. "Transwab") and submitted to the local laboratory without delay for "culture ? *N. meningitidis*". These swabs should be cultured on a selective medium such as blood agar with polymyxin and vancomycin, or modified New York City medium. These swabs must be processed urgently in the laboratory.

Consideration may be given to the taking of throat swabs from family members prior to administration of prophylaxis with a view to identifying the causative organism particularly when the index case is under 5 years old. To prevent any possible feelings of guilt , it should be clearly explained that the intention is simply to identify the strain causing the illness.

NB: *N. meningitidis is frequently carried asymptotically in the nasopharynx and the significance of a positive nasopharyngeal or throat culture must always be assessed in the light of clinical and other laboratory findings.*

5. **Skin Scrapings and Culture of Aspirate from Rash**

Skin Scrapings: In a patient with a petechial or haemorrhagic rash, skin scrapings should be taken using the following method: *Obtain glass microscopic slides with frosted ends and plastic slide holders. Wearing latex gloves, pinch a skin lesion between index finger and thumb in order to exude circulating blood. "Pick" the surface of the lesions using a sterile scalpel. Apply more pressure to express a drop of tissue fluid and blood; this is spotted directly onto a glass slide by pressing the slide against the lesion - several small smears of 3-4mm in diameter are better than one large one. The process should be repeated with a second skin lesion. Label the*

frosted end of the slides in pencil with patient's name. Place the slides in the slide holder and send to the laboratory for staining. In the laboratory the smears should be fixed with methanol and stained. For optimal differentiation of polymorph nuclei, Wright's stain or dilute Giemsa (one part of stock to 50 parts of buffer at pH 7.2) are preferred to the Gram stain. The organisms stain blue and intracellular organisms only should be reported.

Needle Aspiration: Needle aspiration of a skin lesion may be performed as follows: *Aspiration may be performed using a needle and syringe containing 1-2 ml. sterile saline. The needle should be inserted into the centre of a petechial lesion at an angle almost parallel to the skin followed by gentle up and down movement of the bevel of the syringe. The aspirate should be injected aseptically into a blood culture bottle, clearly labelled and submitted for culture.*

6. Viral Culture

In cases where viral infection is suspected, a throat swab in viral transport medium and a faeces sample should be sent to an appropriate laboratory for viral culture. If possible, an aliquot of CSF should also be sent for Viral culture and/or Enteroviral PCR.

7. Blood for Serology

Paired acute and convalescent sera (clotted samples each at least 0.5mls) should be collected where possible in culture negative cases. The acute phase sample should be collected within 48 hours of admission. The convalescent phase sample should ideally be collected 14 to 21 days after presentation. These paired specimens should be sent to the MRL for testing for IgG and IgM antibody against meningococcal outer membrane proteins.

Specimens for non-culture Diagnosis of Invasive Meningococcal Disease

Test	Specimen Required	Comments
Blood for PCR	EDTA Sample, Minimum in infants and young children : 0.5 - 1.3 mls Older children and Adults : 2.5 - 5.0 mls	This specimen must be collected on admission as antibiotic treatment rapidly causes this specimen to revert to negative.
CSF for PCR	A small aliquot of the neat CSF specimen :- minimum 100 µl 8/10 drops.	Store and transport in a small well sealed container, e.g.. an Eppendorf tube
Paired samples for serology	clotted blood samples	<i>Acute phase:</i> collect within 48 hours of admission <i>Convalescent Phase:</i> Ideally collect at day 14-21

APPENDIX 2

Template Guidelines

HOSPITAL-BASED MANAGEMENT OF SUSPECTED MENINGOCOCCAL SEPSIS/MENINGITIS

[Prepared by Drs. Karina Butler, William Casey, Kevin Connolly, Kieran Crowley, Coleman Muldoon & Aengus O'Marcaigh.] (Amended 1st June, 1999)

Acute meningococcal disease is a life threatening infection. It may present as meningitis and/or septicaemia. More rarely other forms of invasive meningococcal disease are encountered. Overall, the mortality for meningococcal infection is approximately 5 - 10%, but can reach as high as 20 - 40% in severe sepsis/meningitis. Meningococcal meningitis is the most common cause of bacterial meningitis presenting to hospitals in Ireland. The *speed* with which meningococcal infections are recognized and treated is critical to achieving a successful outcome and clinical suspicion alone mandates treatment.

Clinical Evaluation for suspected bacterial meningitis or meningococcal septicaemia

History

- Headache/Photophobia
- Neck and back stiffness
- Off feeds/vomiting
- Irritability
- Lethargy/altered consciousness
- Fever
- Rash

Suspect Septicaemia if

- Rapid, low volume pulse
- Slow capillary refill time
- Skin to core temperature difference
- Evolving characteristic rash
- Oliguria
- Hypotension (late sign)

Examination

- Airway** is clear
- Breathing** pattern is satisfactory
- Circulation** pulse rate and volume, BP, Pyrexia
- Characteristic rash
- Meningism
- Bulging Fontanelle
- Decreased Level of Consciousness

Beware:

Bad Prognostic Signs include

- Differential skin/core temp > 3°C (children)
- Systolic BP < 85 mm Hg (adults)
- Low white cell count
- Metabolic acidosis, Base deficit > 8.0
- Coagulopathy
- Rapidly evolving characteristic rash
- Absence of Meningitis
- Glasgow meningococcal prognostic score (GMPS) > 8 (see appendix 16)

These patients constitute a very high risk group and warrant vigilant monitoring and early aggressive therapy

Monitoring in Casualty

- Non invasive blood pressure monitoring
- Oxygen saturation monitoring
- Core and peripheral temperature monitoring

HOSPITAL MANAGEMENT OF MENINGOCOCCAL INFECTION

For additional detail on each point see similarly numbered appendix

1. **ADMINISTER $\geq 40\%$ O₂**
2. **SUMMON HELP** (Ideally >1 doctor should be present to optimize initial management).
3. **ORDER FIRST DOSE ANTIBIOTICS TO BE DRAWN UP**
(while work proceeds)

Antibiotic	Age	0 - 1 month	1 - 3 mos	> 3 mos	Adults
Cefotaxime		50 mg/kg	75 mg/kg	75mg/kg (max 2g)	2g
Ampicillin		75 mg/kg	100 mg/kg		
Gentamicin		2.5 mg/kg	2.5 mg/kg		

In true penicillin allergy (hx.anaphylaxis/urticaria) use **chloramphenicol** 25 mg/kg/dose (max1g)

4. **SITE I.V. CANNULAE** (as large as practical, ideally 2)
5. **DRAW BLOODS** In order of priority: if delayed >5 mins., give antibiotics.

1. Venous blood gas	4. Dextroxtix/glucose	7. Group & hold
2. FBC, diff., meningo PCR	5. Blood culture	8. Serum store
3. INR/PT, APTT	6. U & E	

6. **GIVE ANTIBIOTICS WITHOUT DELAY** (re. dexamethasone see appendix 6).
7. **IV FLUID RESUSCITATION:** bolus 20 mls/kg Hartmann's; repeat if necessary.

If fluid bolus > 40 ml/kg required : **Intubate & ventilate**
 Fluid bolus > 40 – 60 ml/kg : **Intubate & insert central line** (keep CVP 10 – 15mmHg) Insert arterial line
 Unstable after 60 ml/kg bolus : **Commence inotropes**
 Adrenaline 0.1 – 1.0 mcg/kg/min *or*
 Dopamine 1.0 – 20.0 mcg/kg/min

Reassess crystalloid fluid requirements hourly. Monitor **blood glucose** & assess need for dextrose.
[Caution: When meningococcal infection presents as Meningitis alone and the patient is haemodynamically stable, fluid restriction may be required]

8. **INTUBATION** may be required if there is an altered level of consciousness.
9. **SKIN SCRAPINGS** and/or **NEEDLE ASPIRATION**
10. **THROAT SWAB** and/or **PERNASAL SWAB**

11. **FURTHER CONSULTATION:** early phone consultation with relevant specialists is desirable, consider tertiary centre referral (appendix 11).
12. **COAGULATION** (appendix 12).
13. **FURTHER MANAGEMENT** (renal failure *etc*: see appendix 13).
14. **LP:** if meningitis suspected & no contraindications **do when haemodynamically stable** (usually day 2 – 3)
15. **NOTIFY** public health and initiate **CHEMOPROPHYLAXIS** if necessary.

Appendix 1: Oxygen

Remember A B C: if not breathing, clear airway and initiate artificial ventilation.

Hypoxaemia is common and rapidly fatal: better to give too much oxygen than too little. Do not wait to document hypoxaemia before administering oxygen.

Appendix 2: Summon Help

Ideally two physicians (anaesthetic and medical) and nursing support should be available

Appendix 3: Antibiotic therapy (N.B: Doses listed are mg/kg/dose)

Meningococci remain exquisitely sensitive to penicillin and 3rd generation cephalosporins. A 3rd generation cephalosporin is usually chosen for initial empiric therapy as, rarely, other organisms insensitive to penicillin can give rise to an identical clinical picture, thus the empiric therapy for meningococcus will additionally cover other common aetiologic organisms in each age group. While some clinicians favour the use of penicillin in addition to cefotaxime or ceftriaxone, evidence supports the use of these cephalosporins as monotherapy in this situation.

As soon as the susceptibility of the isolated organism is available the choice of antibiotics should be reviewed and appropriate changes made e.g. substitution of penicillin G for cefotaxime.

Usual adult doses:	Cefotaxime ¹	2.0 gm every 4 or 6 hours
	Penicillin	2.4 gm every 4 hours
	Chloramphenicol ²	1.0 gm every 6 hours

Empiric therapy for children is age related:

<u>Age</u>	<u>Drug</u>	<u>mg/kg/dose</u>	<u>frequency</u>
0 - 1 mos ³	Ampicillin	75mg/kg	Q6 Hrs
	Cefotaxime ¹	50 mg/kg	Q8 Hrs
	Gentamicin	2.5mg/kg	Q8 Hrs* (Modify if premature)
1 - 3 mos	Ampicillin	75-100mg/kg	Q6 Hrs
	Cefotaxime ¹	75mg/kg	Q8 Hrs
	Gentamicin	2.5mg/kg	Q8 Hrs* (Modify if premature)
>3 mos	Cefotaxime ¹	75mg/kg	Q8 Hrs (Not to exceed 12g/day)

Additional antibiotic doses that may be indicated for children

Benzyl Penicillin	50mg/kg	Q4 Hrs (Max 2.4g Q 4 Hrs)
Chloramphenicol ²	25mg/kg,	Q6 Hrs (Not to exceed 4g/day)
Vancomycin ³	15mg/kg,	Q6 Hrs (Not to exceed 4g/day)

- (1) Ceftriaxone may be used in place of cefotaxime, and can be administered once or twice daily
- (2) A clear history of penicillin anaphylaxis is a contraindication to use of penicillin or cephalosporin antibiotics. A history of skin rash or G.I.T. upset is **not** a contraindication to penicillin therapy. Chloramphenicol is indicated if there is a history of penicillin anaphylaxis.
- (3) In neonatal meningitis, once the susceptibility of the organism is known *and* the CSF is sterilized, antibiotics may be modified to the most active and least toxic. For GBS this is penicillin G, for Listeria this is ampicillin. With gram negative organisms choice will depend on susceptibility data.
- (4) If initial CSF gram stain results show gram positive cocci, consistent with pneumococcal meningitis, add vancomycin at dose listed above pending confirmation of sensitivity of isolate to **penicillin and cephalosporins**

Duration of IV antibiotic therapy (total course must be given intravenously)

Uncomplicated meningococcal infection	7 days
Uncomplicated <i>Haemophilus</i> infection	7 days
Uncomplicated pneumococcal infection	10 days
Group B streptococcal infection	14-21 days
Listeria Monocytogenes infection	10 -14 days, 21 days in immunocompromised
Gram negative infection	21 days (minimum 14 days post sterilization of c.s.f.)

Appendix 4: Intravenous access

Ideally site two large intravenous cannulae. Remember the intraosseous route can be used in children < 7 years.

Appendix 5: Blood Sampling

This should be carried out at time of cannula insertion and should not be permitted to delay overall management. As colour coding of tubes can be institution specific it is suggested that each institution list local requirement clearly in this appendix.

- 1. Venous blood gas:** 0.3ml in a heparinised syringe
- 2. FBC, differential & meningococcal PCR: EDTA tube**
Blood for PCR **must be collected on admission** as following antibiotic therapy the specimen will rapidly revert to negative. The minimum sample size is 0.5ml collected in EDTA tube. This should be stored frozen at -20C pending results of culture. If cultures are negative the specimen should be sent to the Meningococcal Reference Laboratory at The Children's Hospital, Temple Street. Meningococcal DNA is liable to autolyse if left unprocessed for more than 48 - 72 hours, therefore delays in dispatching the specimen should be minimised. Specimens do not require refrigeration during transport
- 3. INR/ PT, APTT: Coagulation tubes**
Additional parameters of coagulation status, e.g. fibrinogen, d-dimers, and protein C level can be useful adjuncts in the management of patients if available.
- 4. Dextrostix.**
- 5. Blood culture – Aerobic bottles only**
- 6. U &E.** Some may choose to obtain Calcium, and LFT's if readily available
- 7. Blood group and Hold,** serum tube
- 8. Meningococcal serology –** may be convenient to take an admission, but can be obtained any time in first 48 hrs.

Acute and convalescent serum samples

Seroconversion in association with the acute illness will allow the clinical diagnosis to be made in bacteriologically negative cases. The acute serum sample should be obtained within 48 hours of admission and stored. If a bacteriological diagnosis is not made, a second serum sample must be obtained, ideally 14 - 21 days after presentation (but take prior to discharge if there is concern that patient may not return for follow up). These paired specimens will be sent to the Meningococcal Reference Laboratory at The Children's Hospital, Temple Street for testing for IgG and IgM antibody against meningococcal outer membrane proteins. The acute specimen will be stored and not sent until the matched convalescent specimen is available.

Appendix 6: Antibiotic Administration & Role of Dexamethasone

It is critical that antibiotics are given without delay.

There is no evidence to support a benefit for steroids in meningococcal septicaemia, however if the patient remains unresponsive to i.v. fluid and inotropic therapy consider adrenal compromise (Waterhouse Friderickson Syndrome) and administer physiological steroid replacement therapy (hydrocortisone 1 mg/kg 6 hourly).

Early use of corticosteroids, ideally given before administration of antibiotics, has been associated with lower rates of neurological sequelae and deafness following *H. influenza* meningitis in children. There is experimental evidence to support a similar benefit in pneumococcal meningitis, however data regarding meningococcal infection are lacking. Many clinicians use steroids for the possible benefit they might afford in meningococcal meningitis. Originally recommended for 4 days, similar outcome with 2 and 4 day regimens have been demonstrated.

The recommended dose is Dexamethasone 0.15mg/kg (4mg in adults) every 6 hours for 2 days.

Appendix 7: Fluid and inotrope therapy

Fluid resuscitation should start immediately with Hartmann's, normal saline, or colloid (whichever is most readily available). In the presence of septic shock in infants and children colloid fluid therapy in the form of 4.5% albumin may be used in the early resuscitation period. There is no advantage for using albumin in place of crystalloids in adults. Fresh frozen plasma should be reserved for patients with significant coagulopathy or very low fibrinogen. Crystalloid fluid (Hartmann's) administration should be at 100% of maintenance requirements until cardiovascular stability is restored. If there is continued evidence of haemodynamic instability repeat boluses of 20mls/kg at 10 minute intervals. Maintain Hb > 8 g/dl. If unresponsive to adrenaline or dopamine consider adding noradrenaline.

Appendix 8: Intubation

If indicated, tracheal intubation should take place *before* moving the patient e.g. from A&E to ICU. Drowsiness alone should be considered an indication for intubation in these patients. Doses of anaesthetic induction agents will need to be modified in shocked cases. In the unstable child, intubation is a prerequisite for inter-hospital transfer. If considering insertion of a central line, intubate first (regardless of level of consciousness). Mechanical ventilation lessens the risk of severe hypoxaemia precipitating cardiac arrest, reduces oxygen consumption and lessens cardiovascular instability

Appendix 9: Skin Scraping/Needle Aspiration

The characteristic rash of meningococcal infection evolves from an early erythematous maculo-papular eruption to the more characteristic purple lesions, misnamed purpura. These lesions do not represent skin haemorrhage, but rather clotting of small vessels in the skin, resulting in ischaemia, that may progress to skin necrosis. The severest manifestation of this necrosis has been called "*purpura fulminans*". Similar pathology also occurs internally.

Technique for taking skin scrapings

1. Obtain glass microscope slides with frosted glass ends and plastic slide holders.
2. Wearing Latex gloves, pinch a skin lesion between index finger and thumb in order to exclude circulating blood.
3. Pick the surface of the lesion with a sterile scalpel blade.

4. Apply more pressure to obtain a drop of tissue fluid and blood, this is spotted directly onto a glass slide by pressing the slide against the lesion, several small smears are better than one large one.
5. The procedure should be repeated with a second skin lesion.
6. Label the frosted end of the slide in pencil with the patients name. Place in the slide holder and send to the laboratory for staining.
7. The excoriated lesion should also be swabbed with a culture swab.

Procedure for needle aspiration of skin lesions

Aspiration should be performed using a needle and syringe containing 1 - 2 ml sterile saline. Insert the needle into the centre of a lesion at angle almost parallel to the skin, followed by a gentle up and down movement of the bevel of the syringe. The aspirate should be injected aseptically into a blood culture bottle, labelled clearly, and submitted for culture.

Appendix 10: Throat Swab/Pernasal Swab

In order to optimise the chances of obtaining an isolate for antibiotic susceptibility, grouping and typing, throat swab (a full sweep of the pharyngeal wall and tonsils) should be taken in all patients. If this is not possible a pernasal swab rotated on the posterior pharyngeal wall is an appropriate alternative. Consideration may be given to taking throat swabs from family members prior to giving prophylaxis with a view to finding the causative organism, particularly where the index case is < 5 years old. To prevent any possible feelings of guilt, it should be clearly explained the intention is simply to identify the strain causing illness.

Appendix 11: Further Consultation

If there is persisting cardiovascular instability, evolving skin lesions, coagulopathy, limb ischaemia, acute renal failure or ARDS, consider referral to a tertiary centre. **The management of severe meningococcal infection is extremely difficult and complex, even for the most experienced, thus it is advisable to consult readily with intensivists, haematologists, nephrologists, and infectious diseases /clinical microbiology specialists, etc.**

Appendix 12: Coagulation Management

Background

Intravascular coagulation plays a major role in the pathogenesis of meningococcal septic shock, a clinical syndrome associated with severe meningococcal infection. This results in the deposition of fibrin strands in the microvasculature of the skin and viscerae leading to poor tissue perfusion and local ischaemia. This can evolve rapidly to “*purpura fulminans*”, haemodynamic instability, end organ failure, and death in certain patients. A severe depletion of Protein C at presentation has been associated with such a rapid and fulminant course and a poor outcome in meningococcal septic shock. Protein C is a naturally-occurring anticoagulant that, when activated by thrombin, can inactivate coagulation factors V and VIII. Acute depletion of Protein C can potentiate disseminated intravascular coagulation by causing a loss of this negative feedback mechanism.

The pathogenesis of coagulopathy in meningococcal infection is complex. Management needs to be tailored for the individual patient. It is therefore critical that expert guidance from a

haematologist experienced in the management of meningococcal coagulopathy be obtained. The order in which blood products and anticoagulants are optimally used can vary from patient to patient and may significantly affect outcome.

Fresh Frozen Plasma (FFP) and Cryoprecipitate

FFP is the standard coagulation factor product used to correct consumptive coagulopathy in bleeding patients, as it contains a wide selection of coagulant and anticoagulant factors, although poor in protein C.

One unit of cryoprecipitate (10 – 20 mls) is derived from one unit of plasma (c. 250ml). Cryoprecipitate should be substituted for FFP when fluid restriction is crucial or when fibrinogen supplementation in particular is required. Fibrinogen levels should be kept above 1.0 g/l in the absence of bleeding, and above 1.5 g/l where there is active bleeding.

Doses: FFP: 10 – 20 ml/kg; cryoprecipitate: 2 units per 10kg.

Platelet transfusions

Platelet transfusions should be reserved for patients with active bleeding, and for those with a platelet count of less than $20 - 50 \times 10^9/l$ and a severe consumptive coagulopathy on coagulation testing. In meningococcal infection the skin rash indicates micro-infarcts and does not indicate platelet deficiency or dysfunction.

Heparin

Heparin is commonly used to counteract the small vessel thrombosis in severe systemic meningococcal infection. Heparinization is part of CRRT.

Administration: after a loading dose of 30 units/kg, commence an i.v. infusion of 15 units/kg/hour. Heparin is not contraindicated by prolonged coagulation indices unless there is active bleeding or extreme thrombocytopenia ($<20 - 50 \times 10^9/L$). Note that confluent apparent purpura does not signify bleeding and should *strengthen* the argument for anticoagulation.

Protein C

Replacement of protein C with protein C concentrate from pooled multiple blood donations is an experimental therapy which has been used in an attempt to reverse the coagulation disorder in meningococcal infection. Protein C is an unlicensed agent. Randomised controlled trials of its efficacy are awaited. As with other pooled blood products there are concerns about blood transmitted diseases. Protein C is available through the BTSB at Pelican House under an existing release procedure and is also kept at some regional centres. **It should only be used in consultation with a haematologist experienced in its use.**

Protein C therapy is usually reserved for patients with rapidly progressive or extensive skin lesions (purpura fulminans), septic shock, protein C activity < 20% and severe consumptive coagulopathy.

As this is an unlicensed product **informed consent (sample form given at end of appendices) must be obtained from the next of kin.**

Appendix 13: Further Management

- **CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)**

This is now the standard method of managing acute renal failure in critically ill patients and in general will be mandatory within 48 hours of onset of oliguria. CRRT involves low-dose heparinization which may be beneficial in its own right.

These considerations raise the question of transfer to a tertiary centre ICU within hours of diagnosis.

- **PLASMAPHERESIS / PLASMA EXCHANGE /WHOLE BLOOD EXCHANGE**

In some centres these “blood purifying” therapies have been advocated in severe meningococcal sepsis, particularly with extensive skin lesions. Generally they are not used in addition to CRRT which has become routine in the most severe cases.

- **OTHER THERAPIES**

RBPI₂₁ (recombinant bactericidal permeability-increasing protein) has been used in severe meningococcal infection. Thrombolysis with rTPA for ischaemic limbs has been performed but its role is uncertain. Likewise, anti-endotoxin antibody (HA-1A) and antithrombin III supplementation are under consideration but of uncertain benefit.

Appendix 14: Lumbar Puncture

4 samples of CSF (8 - 10 drops per tube); cell count , protein & glucose, micro & c/s, viral c/s & meningo PCR)

Lumbar puncture is contraindicated in the following situations

Signs of raised intracranial pressure

Cardiorespiratory instability

Sepsis in the area in which the lumbar puncture needle will pass.

Appendix 15: N. MENINGITIDIS & H. INFLUENZAE PROPHYLAXIS
To be given to contacts (see below) and must be given to the index case prior to hospital discharge

Rifampicin is the standard chemoprophylactic agent

Recipients of rifampicin should be warned that it may:

- ♦ interfere with the contraceptive pill and with anticoagulants
- ♦ discolour urine, sweat and tears (red discolouration) & permanently discolour soft contact lenses

Rifampicin is contraindicated in pregnancy & in the presence of severe liver disease.

Dose Schedule for Rifampicin: Note: Max single dose 600mg

Age	<i>H. influenzae</i>	<i>N.meningitidis</i>
0 – 12 month	20 mg/kg once daily for 4 days (for infants <1month 10mg/kg/day)	5mg/kg twice daily. for 2 days
1 – 12 years	20mg/kg once daily for 4 days	10mg/kg twice daily. for 2 days.
Children >12 & Adults	600mg once daily for 4 days	600mg twice daily. for 2 days

TREATMENT OF INDEX CASES

In cases of meningococcal or *Haemophilus influenzae* infection initiate oral rifampicin **as soon as the patient can tolerate oral antibiotics. Should be initiated prior to discharge.**

TREATMENT OF CONTACTS: Meningococcal infection

When to give? Within 24 hours if possible, & up to 30 days post identification of index case.

Who should receive prophylaxis:

- (1) Close contacts: i.e., those who in the 7 days preceding the hospital admission
 - shared living/sleeping accommodation
 - were baby-sitters/baby minders of the index case
 - were mouth kissing contacts (not cheek kissing contacts)
 - were in the same nursery/crèche (includes adult carers)
 - gave mouth to mouth resuscitation to the index case.
- (2) Chemoprophylaxis is **not** necessary for classmates of an index case unless there are two or more cases of the same strain in the school during the same term.
 - If the cases occur in the same class, all class members and staff should receive prophylaxis
 - If the cases occur in different classes discuss management with the ID/Public Health service
- (3) Special consideration should be given to situations where there is greater than the usual interaction between members of the extended family or adverse living conditions exist e.g.
 - may wish to give prophylaxis to all travellers on a given site
- (4) Prophylaxis is **not** recommended for co-passengers on public transport.

TREATMENT OF CONTACTS: Haemophilus Influenza infection

When to give; Within 24 hours if possible

Who should receive prophylaxis? All household contacts, irrespective of age or immunisation status, in those households with at least one contact < 48 months who has not been fully immunised. Prophylaxis is not recommended for households where all contacts are > 48 months or where all < 48 months of age are fully immunised.

ALTERNATIVE CHEMOPROPHYLACTIC AGENTS

In cases of meningococcal infection if **rifampicin is contraindicated** alternative agents include:
Ceftriaxone one dose i.v./i.m.: Children <12yrs give 125 mg , Adults give 250mg.
Ciprofloxacin, 500 mg PO is also effective, but is not licensed for this purpose

PREGNANCY:

For close contacts who are pregnant, options following counseling include giving no prophylaxis, giving ceftriaxone, or taking a throat swab and giving prophylaxis if meningococcus is cultured. Harmful effects on the foetus have not been demonstrated with ceftriaxone.

VACCINATION:

For vaccine preventable strains; A, C, Y, W-135, vaccination will be offered by the public health service..

Notification of infectious disease

Under the Infectious Diseases Regulations 1981, all suspected cases of bacterial meningitis or meningococcal septicaemia must be notified immediately to the relevant Medical Officer of Health. Telephone notification should be used initially and this is the responsibility of the admitting team. All telephone notifications should be followed by written notification.

Appendix 16. Glasgow Meningococcal Prognostic Score (GMPS)

	Arrival	1 hour
1. Systolic BP¹: if < 75mmHg ,4yrs or < 85mmHG > 4yrs - Score 3 points		
2. If skin/core temperature² difference > 3 degrees.- Score 3 points		
3. Modified Coma Scale³: If initial score < 8, or deterioration of ≥ 3 points at any time - Score 3 points		
4. Deterioration in last hour: Ask parents or nurse and if yes – Score 2 points		
5. Absence of neck stiffness – Score 2 points		
6. Extent of purpura: Widespread ecchymosis, or extending lesions on review.- Score 1 point.		
7. If base deficit > -8 – Score 1 point		

¹ Use Doppler sphygmomanometer with cuff not less than 2/3 the upper arm length.

² Apply skin temperature probe to toe and to axilla or rectum for two minutes.

³ Modified coma scale

(1) Eyes open:	Spontaneously	4
	To speech	3
	To pain	2
	None	1
(2) Best verbal response	Oriented	6
	Words	4
	Vocal sounds	3
	Cries	2
	None	1
(3) Best motor response	Obeys commands	6
	Localises pain	4
	Moves to pain	1
	None	0

Total = (1) + (2) + (3)

Sample: INFORMED CONSENT FOR PROTEIN C ADMINISTRATION

Protein C is a protein normally found in human blood that prevents the formation of clots in the circulation. A reduction or absence of this protein results in blood clots that can block small vessels in different parts of the body and cause severe damage in various organs. It can lead to skin lesions that may require skin grafting or amputation.

As your doctor has explained to you, your child/spouse/relative has a disorder resulting from a severe bacterial infection that causes the protein C in his/her body to be used up. In addition to the well-established methods for treating the severe infection, this condition may also benefit by replacing protein C in the patient's plasma. A Company named Baxter Healthcare Ltd., has developed a highly purified concentrated form of protein C from human plasma called Protein C Concentrate (Human). This contains large amounts of protein C in a small volume of fluid and this enables your doctor to replace the Protein C and obtain the desired levels without the risk of overloading the patient with excess fluid. Furthermore, this product is highly purified and should contain no other proteins from the plasma (e.g., clotting factors). Preliminary results of treatment with Protein C concentrate (Human) have been encouraging. **However, this product has not been approved for use in severe infections in Ireland. Therefore, its use in treating patients with such severe bacterial infections must be considered investigational.** Although the preliminary studies have shown promising results in the treatment of other illnesses with Protein C deficiency, there is no guarantee the Protein C Concentrate (Human) will be successful in the treatment of your child/spouse/relative's condition.

Protein C Concentrate (Human) is prepared from whole human plasma. When medicinal products such as this (i.e. prepared from human blood or plasma) are administered, disease due to the possible transmission of infectious agents cannot be totally excluded. To reduce the risk of transmission of such infectious agents, stringent controls are applied to the selection of blood donors and donations, and in addition, certain virus removal and/or inactivation procedures are included in the production process. However, the risk of transmission of viral infections from this product cannot be totally eliminated.

As with all infused plasma derived medicines, there is a possibility that our child/spouse/relative will experience an allergic reaction. Minor allergic reactions include fever, rashes, nausea, upset stomach and dizziness. Anaphylactic shock (resulting in shortness of breath, cough, chest pain, fever) although very rare, cannot be ruled out. Your child/spouse/relative will be kept under strict supervision and if any of these reactions should occur, he/she will receive prompt appropriate treatment. In addition, if he/she receives a Protein C concentrate, blood samples will need to be taken frequently to monitor Protein C levels. The drawing of blood is sometimes associated with, but need not include, pain and bruising at the site where the blood is drawn. Occasional light-headedness and rarely fainting may occur during the drawing of blood.

If you do not wish your child/spouse/relative to receive Protein C Concentrate (Human) it will in no way affect subsequent treatment at this institution.

I have read the above and fully understand the potential risks and benefits associated with my child/spouse/relative receiving Protein C. I feel that I have had enough time to consider the decision to allow my child/spouse/relative to receive Protein C. I have been given an opportunity to ask questions that I may have, and all my questions have been answered to my satisfaction.

I give permission forto receive Protein C. I am aware that Dr. or his/her associates will be available to answer any questions regarding treatment that I may have during the course of treatment.

Patient Name

Next of Kin's Signature

Signature of the Physician

Date

APPENDIX 3

Department of Health and Children Reporting Forms

Confidential fax to:

Office of the Chief Medical Officer, Department of Health and Children. Fax number (01) 6710148 and to Director of Public Health and Specialist in Public Health Medicine of Health Board.

(i) Notification to the Department of Health and Children of suspected or confirmed case of bacterial meningitis (including meningococcal septicaemia)

Part 1: To be completed on the day of notification

Name

first name

surname

DOB / /

Age: _____

Sex: M

F

Address _____

Health Board _____ Comm. Care Area _____

Initial diagnosis _____

Admission date _____ Hospital _____

Clinical condition _____

Comments _____

Signature _____

Date _____

Title _____

Part 2: to be completed as soon as information is available or within 2 weeks

Outcome _____

Final diagnosis _____

If meningococcal disease: definite presumed possible
(tick appropriate box)

Group:

Signature _____

Title _____

Date: _____

Department of Health and Children

(ii) Quarterly Report on Bacterial Meningitis (including Meningococcal Septicaemia) from Department of Public Health

Health Board: _____ **Time Period:** _____

Total notifications of bacterial meningitis (including meningococcal septicaemia). This number should exclude cases initially notified as bacterial meningitis which were subsequently found to have another diagnosis.

Section A Meningococcal Disease (Meningitis and Septicaemia)

<i>Meningococcal disease, total number of cases</i>		<i>Number of deaths</i>	
Meningococcal disease definite cases		Number of deaths	
Meningococcal disease presumed cases		Number of deaths	
Meningococcal disease possible cases		Number of deaths	

Number of cases for which information on the group is available

Group B Group C Group A Other Group

Section B Other Bacterial Meningitis

<i>Other bacterial meningitis, total no. of cases</i>		<i>Number of deaths</i>	
Haemophilus influenzae, number of cases		Number of deaths	
Strep pneumoniae, number of cases		Number of deaths	
Staphylococcus aureus, number of cases		Number of deaths	
Group B strep, number of cases		Number of deaths	
E.coli, number of cases		Number of deaths	
Tuberculosis, number of cases		Number of deaths	
Other, specify		Number of deaths	

Signature: _____ **Date:** _____

Title: _____

This form should be completed and returned to the Office of the Chief Medical Officer, Department of Health and Children at the end of each quarter. A copy should also be sent to Community Health Division, Room 9.31, Department of Health and Children, Hawkins House, Dublin 2.

APPENDIX 4 National Recording Form