Measles

HUMAN NORMAL IMMUNOGLOBULIN (HNIG):

- INTRAVENOUS preparations (indicated for immunosuppressed individuals only) - available from hospital pharmacies

- SUBCUTANEOUS OR INTRAMUSCULAR preparations – available from hospital pharmacies or HPA stockholders.
HPA currently supply SUBGAM (BPL®) dispensed in vials of 750mg (approximately 5ml)

Indications

1. To prevent or attenuate an attack in immunocompromised contacts (see Appendix 1)
2. To prevent or attenuate an attack in pregnant women (see Appendix 2)
3. To prevent or attenuate an attack in infants under the age of 9 months (see Appendix 3)

MMR vaccine may be given where HNIG is not indicated (see below)

Dose

Susceptible immunosuppressed individuals (see Appendix 1)
0.15 g/kg of intravenous normal immunoglobulin
OR 0.6 ml/kg of subcutaneous normal immunoglobulin

The products should be administered by infusion according to manufacturer's instructions.

Susceptible pregnant women (see Appendix 2)
2250 mg of subcutaneous normal immunoglobulin (3 vials)

The product should be administered by sub-cutaneous infusion or by intra-muscular injection, ideally in divided doses at different sites.

Susceptible immunocompetent infants under 9 months (see Appendix 3)
0.6 ml/kg of subcutaneous normal immunoglobulin up to maximum of 1 vial

The product should be administered by sub-cutaneous infusion or by intra-muscular injection, ideally in divided doses at different sites.

Healthy children over 9 months of age and adults may be given MMR (see notes 2 and 3)

Timing of administration

HNIG is most effective if given **within 72 hours** of exposure, but may still be effective if given within 6 days

For immunosuppressed individuals, administration should not be delayed (e.g. whilst awaiting test results) beyond 3 days of exposure. For this group, IVIG may still be considered beyond six days.

Where a second exposure occurs more than three weeks after a first dose of HNIG, a further dose should be given

Definition of significant exposure

Patients with measles are considered infectious from four days before to four days after rash onset, and anyone exposed to the patient during this period should be considered for prophylaxis. For patients with continued exposure, for example in the household setting, exposure is likely to occur during the prodromal period, but for practical purposes, the limit for administering prophylaxis should be timed from the onset of rash in the index case.

Measles is extremely contagious; less than 15 minutes exposure to a case can lead to disease in a susceptible person and transmission has even been reported from indirect exposure.

- Immunocompromised people: prophylaxis should be considered where direct exposure occurs for a very short time (minutes) and may even be considered where exposure is indirect (such as entering a room within a short period after a measles case has left).
- Immunocompetent people (particularly pregnant women or infants): should be followed up and prophylaxis considered if there has been face-to-face contact (irrespective of the time exposed) or exposure for 15 minutes or longer in the same room.

Notes

1. More detailed information and rationale for this guidance can be found in the document "Post Exposure Prophylaxis for Measles: Revised Guidance April 2009" available at http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587

2. Immunocompetent adults and children from age 9 months, who have received no measles containing vaccines, can be given MMR vaccine, ideally within 3 days of contact with measles for post-exposure prophylaxis. However, where exposure is likely to be on-going (for example following a single case in a nursery or during a community outbreak), MMR offered beyond three days may provide protection from subsequent exposures. Individuals who have received only one previous dose of MMR may be given a second dose provided there is an interval of at least one month from the first dose.

3. Infants receiving MMR vaccine before 12 months of age should continue to receive their routine dose of MMR vaccine at 13 months and pre-school as per the national immunisation schedule. For children under eighteen months who received a second dose of MMR at an interval of less than three months from the first, then the routine pre-school dose (a third dose) should be given in order to ensure full protection.

Appendix 1: Management of immunosuppressed individuals exposed to measles

Individuals with compromised immunity (as defined in Green Book Chapter 6: http://www.dh.gov.uk/GreenBook) should be considered for HNIG as soon as possible after exposure.

For individuals with severe defects of cell mediated immunity, HNIG should be considered even in the presence of measurable antibody. **For persons already receiving immunoglobulin intravenous replacement therapy, receipt of a replacement dose within 3 weeks before measles exposure should be sufficient to prevent measles infection**.

All other individuals with immunosuppression who are not already on IVIG replacement therapy should be assessed at the time of an exposure. Since the ability to develop and maintain antibody depends on condition and/or treatment, immunosuppressed individuals should be classified according to Table 1 and then managed as per Table 2.

Table 1: Classification of immunosuppressed individuals

GROUP A	GROUP B
All patients with malignant disease, other than those in group B, until at least six months after completion of immunosuppressive chemotherapy or radiotherapy	Patients on treatment for Acute Lymphoblastic Leukaemia (ALL) within and until at least six months after completion of immunosuppressive chemotherapy
Patients who have received a solid organ transplant and are currently on immunosuppressive treatment	Patients who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer where the patient has developed graft-versus-host disease
Patients receiving systemic high-dose steroids until at least three months after treatment has stopped. This would include children who receive prednisolone, orally or rectally, at a daily dose (or its equivalent) of 2mg/kg/day for at least one week, or 1mg/kg/day for one month. For adults, an equivalent dose is harder to define but immunosuppression should be considered in those who receive at least 40mg of prednisolone per day for more than one week.	Patients with severe primary immunodeficiency (who would not be expected to have made a good initial response to vaccine or disease in childhood)
Patients with immunosuppression due to human immunodeficiency virus (HIV) infection who do not have a diagnosis of AIDS	Patients with a diagnosis of Acquired Immunodeficiency Syndrome (AIDS)
Patients receiving other types of immunosuppressive drugs (e.g. azathioprine, cyclosporin, methotrexate, cyclophosphamide, leflunomide, anti-TNF alpha and the newer cytokine inhibitors) alone or in combination with steroids, until at least six months after terminating such treatment.	

Table 2: Algorithm for assessing susceptibility in immunosuppressed contacts of measles[1]

Age group	History	Immunosuppressed Group A	Immunosuppressed Group B*
Born before 1970	**Of measles infection**	Assume immune	Regardless of history and even if known to be measles antibody positive previously, test[2] again at time of exposure. Issue immunoglobulin if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin. *excluding patients who are already on IVIG replacement therapy for either primary immunodeficiency or severe defects of cell mediated immunity
	No measles infection	Test[2] and issue only if measles antibody negative or equivocal.	
Born between 1970 and 1990	**Of measles infection**	Test[2] and issue only if measles antibody negative or equivocal.	
	No measles infection	Test[2] and issue if measles antibody negative or equivocal. If not possible to test within six days of exposure, offer immunoglobulin.	
Born after 1990	**One measles vaccine**	Test[2] and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin.	
	Two measles vaccines	Test[2] and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin.	
	Unvaccinated	Offer immunoglobulin, ideally within three days.	

1. This table **may not apply** to **immunosuppressed patients born and raised abroad.** For this reason, an individual risk assessment, ideally with rapid IgG antibody testing is recommended. See detailed guidance at http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587

2. Measles IgG antibody testing using commercial assays is now available in all HPA Regional Laboratories and in several NHS laboratories. Although not all offer an out of hours or weekend service, antibody testing should be possible within one working day of receiving the serum sample.

Appendix 2: Management of pregnant women exposed to measles

Pregnant women should be offered HNIG if they have been in contact with a confirmed or epidemiologically linked case and are likely to be susceptible. Assessing susceptibility should be based on a combination of age, history and/or antibody screening (see Table 3).HNIG may attenuate the infection in the mother and, although there is no direct evidence, an attenuated maternal infection is likely to have a reduced risk of foetal loss.

Table 3: Algorithm for assessing measles susceptibility in pregnant women[1]

Age group	History	Management of pregnant woman
Born before 1970	Of measles infection	Assume immune
	No measles infection	Assume immune
Born between 1970 and 1990	Of measles infection	Assume immune
	No measles infection	Test[2] and issue within six days only if measles antibody negative.
Born after 1990	One measles vaccine	Test[2] and issue within six days only if measles antibody negative.
	Two measles vaccines	Assume immune.
	Unvaccinated	Test[2] and issue if measles antibody negative. If not possible to test within six days of exposure, offer immunoglobulin.

1. This table **may not apply** to **pregnant women born and raised abroad.** For this reason, an individual risk assessment, ideally with rapid IgG antibody testing is recommended. See detailed guidance at http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587

2. Measles IgG antibody testing using commercial assays is now available in all HPA Regional Laboratories and in several NHS laboratories. Although not all offer an out of hours or weekend service, antibody testing should be possible within one working day of receiving the serum sample.

Appendix 3: Management of Infants under 9 months of age exposed to measles

Infants aged less than 6 months who are contacts of a confirmed or epidemiologically linked case should be given HNIG as soon as possible after exposure if indicated according to criteria in Table 4.

Infants aged 6 to 8 months -a clinical decision to use either HNIG or MMR is required (Table 4). HNIG is preferred where there may be particular reasons to avoid measles (such as underlying lung disease or recent severe illness) or those who are exposed in the household setting when disease may be more severe. Outside of the household, when ongoing exposure from further waves of infection are likely, MMR may be preferred as it should also provide longer lasting protection against subsequent exposures.

Table 4: Algorithm for post exposure prophylaxis in infants of UK born mothers[1]

Relevant infant history	**Age of exposed infant (completed months)**		
	0-2 months	**3-5 months**	**6-8 months**
Mother is the index case	HNIG	HNIG	MMR vaccine
Mother is known antibody negative or equivocal	HNIG	HNIG	MMR vaccine
Mother born before 1970	Nothing	HNIG	MMR vaccine or HNIG
Mother born between 1970 and 1984 and has had natural measles	Nothing	HNIG	MMR vaccine or HNIG
Mother born between 1970 and 1984 and is unsure of status	HNIG	HNIG	MMR vaccine or HNIG
Mother has had measles vaccine or born after 1984	HNIG	HNIG	MMR vaccine
Infant born before 32 weeks gestation	HNIG	HNIG	MMR vaccine

1. This guidance **may not apply** to **infants of non-UK born mothers**. For this reason, an individual risk assessment is recommended. See detailed guidance at http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587