EXERCISE
Orange Circle

SCENARIO

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Background

Approximately 1.8 million foreign pilgrims attend the Hajj, the largest annual pilgrimage in the world, from countries all around the world. In 2009 the main focus of the Hajj will run from 25-29 November.

The Hajj coincides with the dry season across the Northern region of Africa. This part of sub-Saharan Africa from Senegal to Ethiopia is called the meningitis belt due to the relatively high incidence of meningitis. Taking all these factors into account, not surprisingly therefore, the Hajj has long been associated with outbreaks of meningitis, the most recent major outbreak being in 2000, where 330 cases (71 deaths) were reported between 28 February and 26 May in pilgrims or contacts in 12 different countries due to the *Neisseria meningitidis* W_{135} serogroup. Following this, attempts were made to encourage pilgrims to get vaccinated with the quadrivalent (A, C, W135, Y) vaccine, but uptake was not 100% and cases occurred again in 2001. Since then the Saudi authorities have insisted that pilgrims are vaccinated and produce a certificate to confirm this before they are allowed a visa for entry to the country.

As with all vaccines, ACWY Vax (GSK) is not 100% efficient and varies slightly depending on the serotype, with W_{135} exhibiting seroconversion rates in clinical trials of 92.3% in subjects aged 6-30 years. There is also the possibility that the vaccine could be incorrectly administered/stored or the vaccine certificates being presented could be faked (the cost of vaccine for example is $90). One could therefore conclude that, although now less likely following the measures taken by the Saudi authorities, there still could be an outbreak of meningitis at the Hajj. Also, although vaccination reduces risk to the disease, carriage is still possible and widespread transmission of organism at Hajj, could seed the organism into returning pilgrims. The returning pilgrims should be protected against disease themselves but they could expose close household contacts who are unprotected.

Exercise Phase 1

Reports from the Hajj identify a small number of cases of meningitis during the pilgrimage. This is identified as *N. meningitidis* W_{135}.

On return from the Hajj to their country of origin, people from the following member states in the 1 to 60 age group develop symptoms of meningitis :- Slovenia, Romania, Denmark, Poland and Sweden. Approximate number of Muslims in Denmark 108,000, Romania 21,500, Slovenia 48,000, Poland-40,000 and Sweden 280,000. In the 2000 outbreak, about 20000 pilgrims each from France and United Kingdom travelled to Saudi Arabia. Estimates using 0.6% of the total Muslim population means an approximate total of 30000 pilgrims from the above countries went on the Hajj pilgrimage this year.

There is a high profile outbreak in a suburb of Copenhagen, where a trip organised by the local Imam saw over 80 local people attend the event. The cause of the outbreak is rapidly confirmed as *N. meningitidis* $W_{135,}$ it is affecting mainly family members of people who travelled to the Hajj pilgrimage.

ECDC receive reports from various sources about this outbreak that is considered at the Round table discussion. Following this, a small group from ECDC convenes to develop a threat/risk assessment and share and agree this with selected member states.

Exercise Phase 2

Following outbreaks of meningitis in close family contacts of pilgrims recently returned form the hajj in Saudi Arabia, a mass vaccination campaign is undertaken in the local communities affected. Targeting both children and adults in the 2 - 55 year age group is considered desirable due to the occurrence of the disease in all age groups. The previous outbreak in 2000 showed that although 55% of cases occurred in <5y, cases also occurred in other age groups. The tetravalent (A,C,Y,W135) meningococcal

conjugate vaccine is recommended as first choice. Being a conjugate vaccine, it should theoretically minimise carriage compared to ACWY vax which is a tetravalent (A,C,Y,W135) meningococcal polysaccharide vaccine and potentially lead to better and longer term protection in younger children. The vaccine is currently licensed for 2-55y old only. Antibiotic chemoprophylaxis is recommended for close contacts <1y and >55y. In all an approximate total of 150,000 people in Romania, Poland, Slovenia, Sweden and Denmark are vaccinated.

Besides the usual and predictable mild adverse reactions in each of the countries undertaking the mass vaccination programme, reports are coming of cases of Guillain-Barré syndrome from some countries via their relevant adverse event following immunisation (AEFIs) scheme. (Some of the more active anti-vaccination websites have also learned there is a potential problem and are reporting the same – news media are therefore aware). Via recognised reporting systems, these countries contact ECDC/MS asking if other countries are experiencing similar levels of adverse events. MS respond reporting the adverse events they are seeing but not the same levels of G-B syndrome.

Questions

Is this scenario credible?

The first one is reasonably credible although the choice of countries may not reflect the likely size of the Muslim populations travelling to Hajj (the UK and France). However, since they are the participating countries in this Exercise we will need to modify the vaccination denominator. Maybe we should vaccinate more people – as for example 20,000 people from France go to Hajj, if you were to offer vaccine to them and their families you would vaccinate at least 100,000 – this would give you a higher denominator and more realistic incidence for the adverse events.

Reference:[A total of 19,749 pilgrims from the UK and 19,100 from France participated in the Hajj 2000. Eight cases of meningococcal disease occurred in the UK and four in France, giving incidence rates in the pilgrim population of 41 and 21/100,000, respectively. No cases occurred in pilgrims from other countries,

although Germany had 18,000 pilgrims and the Netherlands had 4,500 pilgrims. For Finland, Sweden, Belgium, Switzerland, and Norway, no data were available on visas delivered.

Information collected from the only manufacturer of rifampicin in France indicated that the total number of doses distributed to pharmacies represented only half the doses needed to treat the target group (approximately 100,000 persons living in pilgrims' households), indicating that compliance with the recommendations was low.]

The second one is not quite credible – the implication of large numbers of GBS due to a batch is a problem. Batches are huge and if there was an issue it would probably have been picked up with the vaccine being used outside the setting (perhaps before travel to Hajj or in the USA). A more realistic scenario would be say two cases in one country or one in two countries and these would turn out to be unrelated to vaccination – the work involved in showing this would be the same. The overall annual rate of GBS is something like 1-2/100,000. The reported rate of GBS following flu vaccine in the USA (which was a well publicised putative association) was said to be 0.17 / 100,000 in the four weeks following vaccination so by chance one or two cases would raise concerns.

What is the normal reporting route into EMEA of adverse reaction to vaccines?

There probably a reporting system for adverse events (e.g. yellow card in UK) in all member states which goes to the national medicines agency (MHRA in UK). They would then report to EMEA. Reports may also be received by manufacturers who would also report to EMEA.

Are there any additional adverse reactions we can choose? Any better than Guillain-Barré?

Stick with GBS as it is rare and interesting, likely to get spotted and possible associations with other infectious causes (it may be plausible that an infection picked up at Hajj has also lead to GBS events e.g. Influenza).

Do we know what vaccines are used where? There are clearly at least three, one from GSK one from Connaught and one from Aventis which I have come across during my research. Are all 3 still in use?
Most countries would use GSK's vax as this in the polysaccharide vaccine that has been used for Hajj for many years. Aventis's vax is a newer conjugate vaccine designed for use in mass immunisation programmes (e.g. all teenagers in the US) – it may produce better response and may have higher impact on carriage. It might be interesting to use this one in the outbreak (the ECDC group could advise it as it might be better for preventing on-going transmission in the muslim populations). Aventis's vax also has a European license and so would more correctly involve EMEA. It has been associated with GNS reports in the USA.

Connaught vax : No longer used.

What conclusion would be most credible to develop for the reasons behind the adverse reactions – is it a specific batch problem, a brand of vaccine or are these events coincidental and not related to vaccination at all?
Most likely is coincidental. More detailed epidemiology could show an association with flu like illness (acquired at Hajj) or in the community.