Surveillance of Antimicrobial Resistant Pathogens

Dr David Aanensen began by recalling what Dr John Snow had done when London was faced with the Thames being overloaded with sewage, causing what was called the 'great stink' and an outbreak of cholera. The general belief was that the cholera resulted from the noxious fumes causing the smell – the Miasmic theory. In 1854 Dr Snow found himself faced with many cases of cholera in the area of his practice – and mapped them. The cases clustered round a pump in Broad Street, so he removed the pump handle; the cholera subsided. This showed that the infection was water born. A popular cartoon followed showing a fanciful microscope view of a water drop – teeming with animacules.

He went on to say how, in 1928, Alexander Flemming had left an agar coated plate out with a fungus on it – on his return after a few days he found the fungus had been killed. This led to the discovery of penicillin, but it was not followed up for a decade, and only mass produced to treat war time casualties in 1943. The first case to show resistance to penicillin came in 1940.

Bacteria have been around since life on Earth began, and can mutate to survive in the face of attack by other organisms. The development of resistance to penicillin was natural; other antibiotics have been developed since, as has resistance to them. Indeed, antibiotics can pass genes conferring resistance from one to another. By 2050 it is estimated that there will be 10 million deaths due to antibiotic resistance. This is exacerbated by: over prescribing; not completing a course of treatment (leaving some of the pathogen still alive); and poor hygiene. There is also widespread use on farm livestock, as preventative medicine, particularly in the USA.

To see which antibiotic might work, the pathogen is put on an agar dish with several patches of different antibiotics on it, and see which kill it.

Bioinformatics - When investigating where a resistant pathogen may have come from, one must determine who has infected whom – perhaps in a school or hospital with multiple cases. The key to this is to record cases by place (as John Snow did) and time, together with the make-up (genome) of the pathogen.

Bacteria have one chromosome comprising 5 million or so base pairs, and there may be several strains. By plotting cases the order in which the strains developed can be found, and one can work back to the origin of an outbreak; and the centres of secondary outbreaks. All this enables remedial action to be taken, and the best way of tackling the pathogen - or its variants.

Dr Aanensen went on to describe how the method was developed (and, modestly, his contribution to it), and how with the rapid advance of the technology it is now done.

Analysing a bacterial genome was a slow and costly business; one of the first large scale investigations between 1977 and 2007 was into MRSA (Methicilin Resistant Staphylocus Aureus). Across Europe EMRSA-15 has been reached.

Plotting the results by hand was wearisome - Dr Aanensen spent two days plotting a few hundred results; the graph showed the history of an outbreak, but he realised that a different graphical presentation would be better understood and came up with a tree (based on an evolutionary tree), with secondary outbreaks shown with a links from the primary outbreak.

However, new developments have brought rapid base-pair analysers not much bigger than a cigarette packet that can be connected to a (G4) smart phone and run off an app. Data from different analyses can then be transferred to a laptop and graphs produced.

The techniques began to be applied within countries, but with worldwide travel they are becoming universal. The lead was taken by the CDC in America and the ECSC in Europe, and the WHO is now involved, giving priority to AMR pathogens.

Not only are the pathogens studied, but the genomes of patients and healthy people. Why have healthy people not succumbed? Knowing the genome of a person can assist in tailoring which treatment will do them most good.