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# From local to national outbreak of Pseudomonas aeruginosa

PERSPECTIVES

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## Outbreaks affecting several hospitals require good coordination. The Norwegian Institute of Public Health's role in this work should be strengthened, and we need better systems for monitoring outbreaks, rapid access to genetic engineering tools and techniques for microbiological examinations of equipment and the environment.

On 17 November 2021, an outbreak was suspected at the Intensive Care Unit (ICU) of the University Hospital of North Norway in Tromsø (UNN Tromsø) after three patients died of septic shock within a short period of time. *Pseudomonas aeruginosa* was found in the blood cultures of all three patients. The outbreak was confirmed on 19 November, when whole-genome analysis of the three blood culture isolates showed a close relationship between the bacteria.

These were the first confirmed cases in a national outbreak that was subsequently found to have been caused by Oasis Bedbath pre-moistened washcloths contaminated with *P. aeruginosa* (1, 2). During the period between the discovery of the outbreak in the ICU in Tromsø and the declaration of a national outbreak, we gained valuable experience which we would like to share (Figure 1).

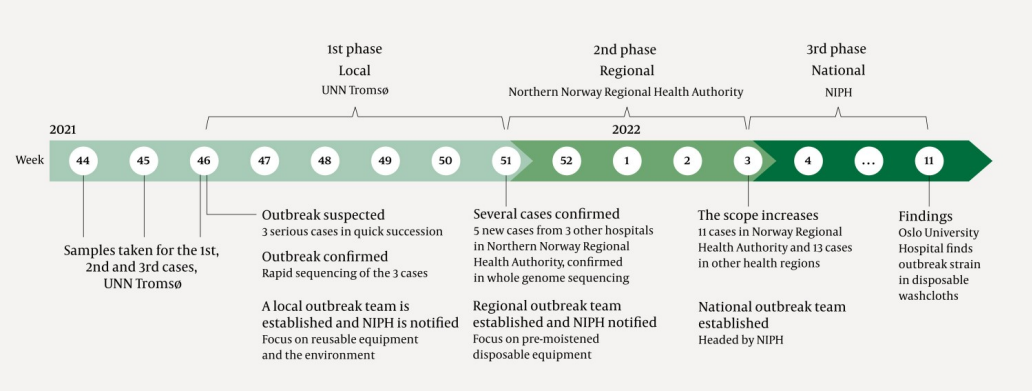


**Figure 1** Timeline for various phases of the investigation of the outbreak of *Pseudomonas aeruginosa* in a hospital in Norway from autumn 2021 to spring 2022.

## The outbreak is discovered in Tromsø

A vigilant infectious disease clinician reacted to three deaths that occurred in quick succession at UNN Tromsø's ICU. The infectious disease clinicians, microbiologists and ICU doctors at Tromsø have a well-established working cooperation, stretching back several years. The microbiologists and infectious disease clinicians meet daily to review the ICU's microbiological samples. The infectious disease clinicians then meet with the doctors in the department. This cooperation aided the rapid response to concerns about an outbreak.

> *«A vigilant infectious disease clinician reacted to three deaths that occurred in quick succession at UNN Tromsø's ICU»*

The National Advisory Unit on Detection of Antimicrobial Resistance at UNN's Department of Microbiology quickly sequenced the blood culture isolates from the three patients who died, and found that the isolates were from the same bacterial strain. This information enabled speedy confirmation of the first cases. After this, there was limited capacity and long waiting times for the sequencing of isolates. The Advisory Unit eventually developed a specific polymerase chain reaction (PCR) test for the strain in the outbreak. This reduced the response time considerably and led to a markedly more effective outbreak investigation in the later phase.

On 19 November 2021, UNN established an outbreak team, led by the head of the ICU. The other participants were an intensive care doctor, a microbiologist, an infectious disease clinician, an infection control senior consultant and an infection control nurse. The Department of Communications, head of division and others participated as needed. On the same day, the outbreak was reported to the Norwegian Institute of Public Health (NIPH).

## Mapping and reporting the outbreak

In the belief that the source of infection might be external, the outbreak team enquired with both the NIPH and the other hospitals in Northern Norway Regional Health Authority if they had observed similar clinical courses or an increased incidence of *P. aeruginosa* infections. The response was that no one else suspected an outbreak. No formal requests or notifications were sent to any other hospitals. UNN nevertheless issued a press release about the first three cases. This was picked up by some other hospitals who suspected an increased incidence of *P. aeruginosa* infections. These hospitals contacted UNN with a request for isolates to be examined by the National Advisory Unit on Detection of Antimicrobial Resistance.

UNN Tromsø initiated a prospective search for new cases by taking screening samples from the airways of intensive care patients twice a week. The microbiology laboratory also actively searched for new cases in all clinical samples from the ICU, and all *P. aeruginosa* cultures were frozen, regardless of sample material.

## The outbreak includes other hospitals

The outbreak team asked both of Northern Norway Regional Health Authority's microbiology laboratories to actively search previously frozen blood cultures for *P. aeruginosa*. On 21 December 2021, cases were found in these samples at other hospitals in Northern Norway as well as in an environmental sample, as shown in the epi curve below (Figure 2).

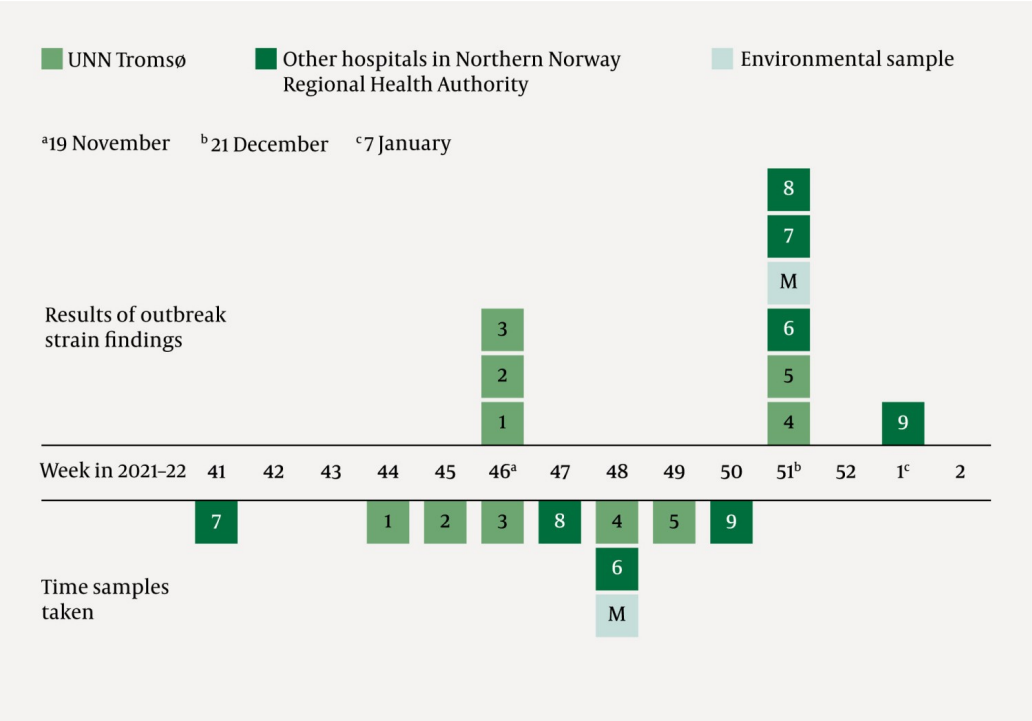


**Figure 2** Epi curve for the period between the outbreak of *Pseudomonas aeruginosa* in Northern Norway Regional Health Authority and declaration of a national outbreak. The illustration shows when samples were taken (lower part) and when the outbreak strain was confirmed via sequencing of microbiological samples (upper part), which in several cases was significantly later than the time of sampling. The numbers in the boxes indicate the order of positive samples – a total of nine patients and one environmental sample.
The Northern Norway Regional Health Authority established a regional outbreak team under the leadership of its Regional Centre for Infection Control, with participation from infection control personnel, microbiologists and ICU staff from the hospital trusts in the region. Prospective searches for related cases were carried out at all adult ICUs in Northern Norway Regional Health Authority. The NIPH was contacted again when the findings outside Tromsø strongly suggested an external source of infection. UNN announced the outbreak strain via news outlets and MikInfo, which is a discussion and news platform for microbiologists in Norway under the auspices of the NIPH. Northern Norway Regional Health Authority's Regional Centre for Infection Control notified other regional infection control centres.

In this phase, the NIPH defined the outbreak as regional and was therefore only able to assume an advisory role, but the Norwegian Directorate of Health and the Ministry of Health and Care Services were notified of the outbreak. Northern Norway Regional Health Authority's Regional Centre for Infection Control did not have a mandate outside the region and could only urge the hospitals outside its own remit to search for cases.

## Hunt for the source of infection

*P. aeruginosa* also caused a national outbreak in 2001–02, involving 231 patients at 24 hospitals in Norway. The source of infection was Norwegian-produced mouth swabs, Dent-O-Sept, which were used in health institutions throughout the country (3). At UNN Tromsø, there was therefore an early suspicion that a contaminated disposable product could be the source. But as no other hospital had reported a suspected increase in *P. aeruginosa*, the focus was on finding a local source of infection.

In the first 'local' phase of the outbreak, infection control nurses and ICU personnel carried out field observations with a view to identifying possible sources and routes of infection in the ICU. They identified some minor areas for improvement in the department's infection control routines, which were immediately followed up by the management, but this did not explain the outbreak.

The outbreak team at UNN reviewed patients' medical records to identify clinical courses and exposure to possible risk factors. Case-control studies are normally used in outbreak investigations to identify risk factors for infection, and this was also done in Tromsø. However, it is difficult to select controls when the outbreak bacterium can be both a coloniser and a pathogen.

Identifying risk factors was also difficult. ICUs use a wide range of different equipment. Disposable equipment consumption is not normally recorded, and it is not often possible to trace what reusable equipment has been used for individual patients. Under complex conditions, such as those in an ICU, case-control studies are of little use in the investigation of outbreaks.

## Samples from the environment and equipment

*P. aeruginosa* outbreaks are associated with humid environments (4). A total of 165 microbiological samples were taken from the environment and reusable equipment at UNN Tromsø: from hand sink drains, water supplies to decontaminators, ice cube machines, non-invasive face mask ventilators, temperature sensors for ventilators, oxygen saturation meters, ultrasound probes, bronchoscopy accessories and equipment for cleaning instruments. *P. aeruginosa* was found in ten hand sink drains, but only one of these isolates belonged to the outbreak strain. This isolate was found in a drain at another ward, which was used as a reference point for the general *Pseudomonas* colonisation of hand sinks in the hospital.

Taking cultures of samples from the environment and reusable equipment is not normally a task for hospital microbiology laboratories. Such methods present a number of challenges, both in terms of low sensitivity and the need for special techniques, such as filtering. There is also uncertainty about the clinical significance of findings. The environmental samples were thus tested using non-validated methods.

> *«When cases were identified at a hospital outside Tromsø, an external source of infection in the form of a contaminated disposable item was considered to be the likely cause»*

When cases were identified at a hospital outside Tromsø, an external source of infection in the form of a contaminated disposable item was considered to be the likely cause. The regional outbreak team mapped the systematic use of disposable pre-moistened wipes in ICUs in Northern Norway Regional Health Authority, and found widespread use of non-sterile pre-moistened washcloths, dental care sets and mouth gel. These products were considered possible sources of infection.

Cultures from disposable items of various materials, with numerous preservatives added, are even more complex than cultures from the environment. Despite hypotheses about possible sources of infection in disposable pre-moistened wipes, no microbiological analyses were performed of these.

### NEED FOR SYSTEMATIC MONITORING

Pseudomonas infection had a fatal outcome for three patients in quick succession. All three were immunosuppressed hospital patients with severe COVID-19. The *P. aeruginosa* bacterium is found in the environment and rarely causes serious infections in people with a normal immune system. If the first cases had been less dramatic, the outbreak could have gone undetected for longer.

Following the large national *P. aeruginosa* outbreak some 20 years ago (3), Walberg et al. called for continuous monitoring of the variation in the incidence of infections with selected risk microbes, with a view to identifying outbreaks sooner (5). This has not been established at hospitals in Northern Norway Regional Health Authority, nor, to our knowledge, at any other hospitals in Norway. Automated monitoring methods should be introduced in order to identify outbreaks at an early stage, reduce the vulnerability of manual monitoring and limit the scope and consequences of the outbreak.

### MORE ROBUST NATIONAL OUTBREAK MANAGEMENT

At UNN and in Northern Norway Regional Health Authority, we initially experienced a lag in the national communication about the outbreak to other regions and hospitals. The NIPH provided good support to the local outbreak team, but did not actively communicate with other hospitals. When cases were discovered outside Tromsø, the NIPH defined the outbreak as 'regional'. Local outbreaks of *P. aeruginosa* are plausible, but a 'regional' outbreak with cases more than 500 km apart makes little sense. MikInfo and regional infection control centres were used as communication channels, but these are not formal arenas with the authority to order health institutions to assist in an outbreak investigation.

The outbreak guide for contamination from water, food and animals (6) provides a clear description of the division of responsibilities, roles and reporting duties. A national outbreak is defined in the guide as a situation where several municipalities have an active source of infection. It makes little mention of outbreaks among hospital patients, and we found that the division of roles is not sufficiently clarified for such outbreaks. The NIPH functions well in its role as advisor to the specialist health service, but we found that clarification was needed on how extensive an outbreak in the specialist health service needs to be before the NIPH assumes a national coordinating role. We believe that a national outbreak guide is needed for outbreaks in hospitals, where roles are clearly defined for managing outbreaks that include more than one geographic location.

> *«Clarification was needed on how extensive an outbreak in the specialist health service needs to be before the NIPH assumes a national coordinating role»*

Fortunately, Oslo University Hospital reacted quickly to the notification from Northern Norway Regional Health Authority and was the first to confirm the outbreak strain outside our region. A national outbreak was then declared, and the NIPH took over the coordination of the outbreak investigation. Seventeen weeks after the outbreak was discovered at UNN Tromsø, Oslo University Hospital confirmed the outbreak strain in Oasis Bedbath disposable pre-moistened washcloths (1, 2).

### THE NEED FOR MICROBIOLOGICAL TECHNIQUES

In outbreaks involving a specific microbial clone, rapid access to genetic engineering tools is necessary to identify cases. This is also relevant in outbreaks of, for instance, resistant microbes. The wait for analysis results delays and impairs the outbreak investigation. The

longer the wait, the more difficult it is to identify the risk factors. Time is also a risk factor in terms of further infection in an outbreak and the outbreak strain establishing itself as an environmental bacterium. All regions should have at least one microbiology laboratory with genetic engineering techniques that can be used in outbreak investigations. The PCR test developed to identify clone-specific gene sequences is a very useful tool, and should be used in outbreak investigations (1, 2). When such highly specific techniques are shared nationwide, all regions can quickly equip themselves for participation in an outbreak investigation.

The microbiology laboratories in Norwegian hospitals have a high level of competence in the examination of human samples, but have no experience in examining samples from the environment or equipment. This *P. aeruginosa* outbreak shows that Norway does not have sufficient resources or standardised methods for microbiological examinations of the environment and equipment in hospitals. The NIPH has raised the issue with the Ministry of Health and Care Services.

## PATIENTS BEAR THE GREATEST BURDEN

It is patients who bear the greatest burden during outbreaks, with the risk of illness and death. This outbreak also had implications for the treatment of patients who were not infected, as meropenem temporarily became the first-line treatment for severe sepsis at UNN's ICU. Outbreaks require isolation, and affected departments may need to halt admissions, which reduces the treatment capacity. Effective systems for rapid investigation of outbreaks will improve our robustness and patient safety.

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