Report on the online conference

„Wastewater-based epidemiology – Polio, plague and the pandemic“

An event hosted by Technologieland Hessen on July 15th, 2021

At a glance

Monitoring wastewater for SARS-CoV-2 is a **reliable and cost-effective method** for the **early detection of the spread of infection** and the **emergence of virus variants**. The EU has asked its member states to set up their national wastewater monitoring systems by October 2021 and has made funding available. The goal is to include the results of wastewater analytics in **political decision making and to use it strategically** when introducing or relaxing protective measures. Some countries are already using wastewater analytics in their efforts to cope with the Covid crisis. Furthermore, other pathogens, opioids, and **other parameters relevant for public health can also be detected in wastewater**. For years, wastewater monitoring has been playing an important part in the campaign to eradicate poliovirus.

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1 Summary

A year and a half after the initial outbreak of Covid-19, the pandemic is yet to be overcome. Due to the highly infectious delta variant, numbers of new infections are currently increasing in many countries. With this background in mind, speakers at the second online conference about wastewater-based epidemiology organised by Technologieland Hessen called for a rapid implementation of wastewater monitoring for SARS-CoV-2.

As the title “Wastewater-based epidemiology: Polio, plague and the pandemic” suggests, the conference began with a look into the history of medicine. Historically, the coronavirus pandemic does show similarities with epidemics of times past, and one has to assume that new pathogens with the potential to cause pandemics will also arise in the future. The approach is to detect new germs in wastewater in time and to stop their spread with suitable regional protection measures. Wastewater sampling has already played a decisive role in the global effort to eradicate polio. This was also covered by the conference.

The focus of the session “Fighting the pandemic” was on the call from the European Commission to all member states, to install a national wastewater monitoring for SARS-CoV-2 by October 2021. The EU provides funding for this totalling 20 million euros. The examples from the practice in Germany, Denmark and the USA that were presented afterwards agreed in showing that the amounts of viral RNA measured in the wastewater reflect the spread of infections well, and do so faster and more cost-efficient than testing of individuals. In addition to PCR analyses, genome sequences are increasingly gaining importance in wastewater monitoring, because they facilitate the observation of the spread of viral variants.

The session “Beyond Covid” highlighted that the potential of wastewater monitoring goes far beyond the current pandemic. Rota and noroviruses, cholera bacteria and many other pathogens are present in human excretions and thus can be detected in wastewater, as a talk about the Global Water Pathogens Project (GWPP) made clear. GWPP also produced the initiative Wastewater SPHERE, which collects data on SARS-CoV-2 globally. The presentation from Biobot Analytics showed that wastewater monitoring presents a viable business model. The US company started in 2017 with the detection of opioids in wastewater and has been concentrating on the Covid-19 pandemic since March 2020. The last contribution to the conference addressed a “silent pandemic”. A pilot project from Hessen investigated the spread of antibiotic resistant germs in surface waters. In this area, there is also a need for a wastewater-based monitoring system.

2 Watching the pandemic through wastewater

In February 2021, Technologieland Hessen had welcomed representatives from science, industry and administration to the first online conference “Monitoring of SARS-CoV-2 in the sewage system”. The event made clear that the spread of infection can be monitored with sampling and analytics of wastewater, complementing clinical testing strategies. With the second online conference held now, Technologieland Hessen again wants to call all players to act together. The installation of a wastewater-based monitoring system is urgently required, as the pandemic situation remains serious. Although daily infection figures in Germany and many other countries are still far below the maxima of spring 2021, they are currently increasing again, mainly due to the spread of the more highly contagious delta variant.

Wastewater monitoring relies on infected individuals shedding corona viruses or their fragments, for instance when they use the toilets or brush their teeth. The viral material gets into the sewage system and virus RNA present in wastewater can be detected with the usual PCR tests and genome analyses. According to current scientific knowledge, wastewater does not pose an infection risk. The first event in February had shown that wastewater monitoring is reliable and sufficiently sensitive to detect new waves of the pandemic as well as new variants of the virus at an early stage. In the past few months, the practicality of the method has been proven with further evidence. Sweden, for instance, has established the Swedish Environmental Epidemiology Center, and the Swiss program for wastewater monitoring was expanded with several new sampling stations, such that it now covers around one million residents.

In March 2021, the European Commission called on all member states to set up national wastewater monitoring systems by October. The event held now provided information about the EU recommendation and then presented practical examples from Germany, Denmark and the USA. Hessen is leading by example. The group of Susanne Lackner at TU Darmstadt is among the pioneers of wastewater monitoring and acts as a reference laboratory working with the Joint Research Centre of the European Commission. Apart from samples from nearby Frankfurt and Wiesbaden, the team has also analysed wastewater from 44 metropolitan areas across Europe in the context of an EU-led campaign. The next task, Lackner said, is to convince health authorities of the relevance of wastewater datasets.

The idea of wastewater monitoring isn’t new, however. Several years ago, the World Health Organisation has included wastewater analyses in its program to eradicate polio. Wastewater monitoring is also suitable for watching out for antibiotics-resistant bacteria and many other pathogens, and also as an early warning system for future pathogens with pandemic potential. Nevertheless, there are still some hurdles to be overcome, which require a close collaboration between science, business, politics and administration.

3 Session 1: Setting the Scene

The online conference began with a presentatoin on the history of infectious disease, as comparisons with earlier epidemics may help us coping with Covid-19. The WHO program to eradicate polio can also serve as an instructive example, as it already involved wastewater epidemiology.

3.1 Looking back, every era has its epidemics

"Plague. Power. Society. A historical perspective on pandemics"
Presentation by Prof. Dr. Karl-Heinz Leven, Department of the History and Ethics of Medicine, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany

To many people, the Covid-19 pandemic may appear an exceptional event, but there were epidemics in every epoch of history, as Karl-Heinz Leven, the director of the Department of the History and Ethics of Medicine at Friedrich-Alexander-Universität Erlangen-Nürnberg, explained in his introductory talk. The task of historians of medicine, according to him, is to recognise patterns and learn from past pandemics. He acknowledged the scientific investigation of infectious diseases as a success story, because due to our understanding of infectious agents and infection mechanisms, vaccines could be developed. However, Leven also remarked that success in the sciences is accompanied by societal problems such as the division of the population in those who are for and those who are against vaccines.

He also explained various, now outdated ideas regarding the spread of pathogens. Water supplies have always been a concern in this context. On the one hand, many pathogens are in fact spread through drinking water. On the other hand, rumours of intentional well poisoning spread, for instance, during the Black Death epidemic of the 14th century, representing a pre-modern form of a conspiracy theory, variations of which are still being spread in the current pandemic. For instance, the idea is circulating that SARS-CoV-2 has been spread intentionally by the pharmaceutical industry. The hypothesis, not yet disproven, that the coronavirus originated from a laboratory also belongs to this context, Leven said, while emphasizing how important it is that the WHO and researchers are investigating the issue. Moreover, he discouraged appeals to morals. Thus, vaccinations should not be referred to as a moral duty, as this would only deepen divisions in society. It is crucial to remain focused on the facts. For this, clear scientific arguments are indispensable.

3.2 Environmental monitoring to eradicate polioviruses

„Environmental surveillance: Use for Polio eradication and beyond“
Presentation by Dr. Ousmane M. Diop, Global Polio Laboratory Network of the World Health Organisation (WHO), Geneva, Switzerland

The WHO has been using wastewater analyses in its program to eradicate the polio pathogen for years, as Ousmane Diop, coordinator of the WHO's Global Polio Laboratory Network explained in his talk. Poliomyelitis, or polio for short, is caused by polioviruses, of which there were originally three wild types. Wild types WPV2 and WPV3 have already been eradicated. WPV1 still occurs, mainly in Pakistan and Afghanistan. Some regions have also had outbreaks of polioviruses that emerged under specific conditions from the oral polio vaccine, which is a live attenuated vaccine.

The fight against polio is difficult, because the cases observed are just the tip of an iceberg, as Diop said. Only one percent of infected individuals suffer from acute paralysis. However, as all infected people shed poliovirus with their stool, wastewater monitoring lends itself as a warning system. Since 2013, the Global Polio Eradication Initiative (GPEI) has been financing such programs in Pakistan, Afghanistan, Nigeria, Kenia and Angola. In India, China, Egypt and Indonesia it provides technical support. Many European countries have set up monitoring systems with their own funds. By now, 50 countries have laboratories that can detect polioviruses in wastewater.

In less developed countries, wastewater monitoring is a challenge, Diop explained. Thus, the number of suitable sampling stations in regions with poor infrastructure may be limited, and the logistics becomes demanding when there is no laboratory nearby. In countries that use oral polio vaccines, the vaccine viruses can cause a background noise in the analysis which can drown out the signal of the pathogen itself. Moreover, it can be difficult to assess the sensitivity of the method, considering the low case numbers. And yet, wastewater monitoring is an important tool in the fight against polio GPEI aims to eradicate WPV1 and thus the last remaining wild type by 2023.

4 Session 2: Fighting the Pandemic

The speakers of the second session focussed on the Covid-19 pandemic. The first contribution in this block dealt with the call from the European Commission to all member states, to install wastewater monitoring systems by October 2021. The examples from Hessen, Denmark and the USA that were presented afterwards, emphasized, the suitability of wastewater monitoring in practical applications.

4.1 Setting up an EU-wide monitoring system for wastewater

„The EU Sewage Sentinel System for SARS-CoC-2 and its variants (EU4S)“
Presentation by Dr. Bernd Manfred Gawlik, Joint Research Centre of the European Commission, Ispra, Italy

In a recommendation released in March 2021, the European Commission asked all member states to set up wastewater monitoring systems for SARS-CoV-2 on a national level by October 2021. The wastewater monitoring is meant to complement rather than replace clinical testing strategies, as Bernd Gawlik from the Joint Research Centre (JCR) of the European Commission emphasized in his talk.

Some countries, such as Finland and the Netherlands, are already incorporating wastewater analyses in their national Covid-19 dashboards. The regional authorities in Catalonia (Spain) have also set up a wastewater-based monitoring system. This now serves as a precedent for a Europe-wide platform.

The European Commission cannot mandate wastewater monitoring for SARS-CoV-2 in member states, but as an incentive, it provides funding up to a total of 20 million euros for the year 2021. The funds are distributed according to the number of residents. Germany can claim 3.6 million euros out of this budget. The EU recommendation makes specific suggestions. Thus, in cities with more than 150,000 residents, sewage works should be sampled at least twice a week. Gawlik advised to involve the relevant health authorities from the beginning. The wastewater data must also be presented in a way that is easy to understand, such as with traffic light symbols, such that health authorities can use them.

The European Commission aims to set up a digital European exchange platform integrating datasets from various sources, including wastewater, weather, clinical and research data. Eastern Europe should become more involved in the future, and the project also aims to zoom into the transportation hubs, Gawlik said. In this context, the metropolitan area of Frankfurt, with Frankfurt Airport is of particular interest. The region is regarded as a ‘super site’, as it combines a metropolitan population centre, tourist destinations, and an international transport hub. As an example outside Europe he mentioned the Olympic village in Tokyo, which has installed a program for wastewater monitoring. The technology is ready to be deployed, Gawlik emphasized, also with regard to the tourism and events sectors. Concerning the lambda and kappa variants of SARS-CoV-2, wastewater monitoring could for the first time influence decisions at a European level.

4.2 Practical example from Hessen: Trends and variants recognised early

„On the trails of SARS-CoV-2 in wastewater - what we can learn from this pandemic“, presentation by Prof. Dr. Susanne Lackner, Chair of Wastewater Engineering, Technical University of Darmstadt, Germany

The group of Susanne Lackner at the Technical University (TU) Darmstadt is among the pioneers in Germany in the field of monitoring wastewater for SARS-CoV-2. During the first workshop in February, Lackner presented a project dealing with coronaviruses in the wastewater from the metropolitan region of Frankfurt. Since then, her team has also analysed wastewater samples from other cities, including the Hessian state capital of Wiesbaden, and from 44 European metropolitan areas in the course of an EU-led measurement campaign. Lackner's group currently works together with the European Commission and the water utilities association Emschergenossenschaft (based around the river Emscher, in the Ruhrgebiet metropolitan area).

From the wastewater data, one can draw two types of information, Lackner explained. Firstly, trends, like rising or falling infection rates, can be spotted a week earlier than with clinical testing strategies. Secondly, the wastewater analysis can yield information about mutated viruses. Thus, the Darmstadt researchers discovered the highly infectious delta variant in wastewater from Wiesbaden as early as mid May. In samples from Frankfurt, this variant was dominating with a representation of 75% by mid June.

While the analysis of trends relies on the classical PCR technology, and thus on the detection of a few characteristic regions in the RNA of SARS-CoV-2, monitoring for mutated viruses depends on sequencing the entire viral genome. Most of the mutations of medical relevance concern the spike protein. Some mutations are found in several variant strains, while some are specific for one variant. The challenge is in correctly identifying the variants based on their mutations, Lackner said. In Germany, 10 to 15% of clinical samples with a positive PCR result are currently sequenced. The detection of variants in wastewater is now to be given a boost.

4.3 Practical examples from Denmark: From pilot project to country-wide monitoring

„From pilot to full scale: Implementing wastewater monitoring of SARS-CoV-2 in Denmark“ Presentation by Dr. Sofie Midgley, Danish WHO National Reference Laboratory for poliovirus, Statens Serum Institut, Copenhagen, Denmark

Denmark's fight against the Covid-19 pandemic is characterised by an intensive testing strategy. More than 80% of the 5.8 million residents have so far been tested at least once. The capacity amounts to 200,000 PCR and 500,000 antigen tests daily, plus 5,000 genome sequences per week.

Despite the high vaccination rate one has to assume that SARS-CoV-2 will continue to circulate among the population at a low level, said Sofie Midgley, head of the Danish WHO National Reference Laboratory for poliovirus at the Statens Serum Institute in Copenhagen. She sees wastewater monitoring as a cost-effective supplement to the clinical testing strategy. Analysing a wastewater sample costs 5,000 to 10,000 Danish kroner (650 to 1,300 euros) and captures around 300,000 individuals, according to Midgley. In comparison, she estimated the cost for 300,000 antigen tests at 30 million kroner (four million euros).

After projects to evaluate the potential of wastewater monitoring in Copenhagen and in the towns of Ishøj and Vordingborg, a one-month pilot project was carried out on the island Bornholm, where seven sewage works were sampled daily. The results were in agreement with the case numbers determined clinically. A second Danish pilot project runs for the entire month of July 2021 and covers 16 sewage works and four pumping stations. Statens Serum Institute publishes the preliminary results online every Thursday (https://covid19.ssi.dk/overvagningsdata/overvaagning-af-sarscov2-i-spildevand). From August 2021 to January 2022, samples will be taken three times a week from 230 water treatment plants and pumping stations. The program will be evaluated after a run time of half a year. Concluding her presentation, Midgley took a broader view and emphasized that many other pathogens as well as antibiotic resistance traits can be detected in wastewater. She also briefly discussed Denmark's participation in the initiative to eradicate polio.

4.4 The pandemic viewed by a US wastewater district

„Milwaukee Metropolitan Sewerage District's pandemic response"
Presentation by Kevin L. Shafer, Milwaukee Metropolitan Sewerage District, Milwaukee, Wisconsin, USA

Kevin Shafer, CEO of the Milwaukee Metropolitan Sewerage District (MMSD) described the challenges of the Covid-19 pandemic from the perspective of a water utility run as a private company. As a regional utilities organisation, the MMSD is reponsible for water treatment and flood protection for more than a million residents in 28 municipalities in the metropolitan area of Milwaukee in the state of Wisconsin.

For the monitoring of wastewater for SARS-CoV-2, the MMSD cooperates with Sandra McLellan from the University of Wisconsin in Milwaukee. She initiated wastewater monitoring projects in three cities and districts in Wisconsin (Racine, Milwaukee, and Green Bay). Overall, 12 water treatment plants were sampled. The amount of SARS-CoV-2 in wastewater samples from the two treatment plants operated by MMSD (South Shore and Jones Island) correlated with the official case numbers, as Shafer has shown for the period from January 2020 to January 2021. He emphasized that wastewater analyses for SARS-CoV-2 are also

carried out elsewhere in the US. The hope is, Shafer said, that the wastewater will provide clues enabling authorities to respond to renewed outbreaks of the pandemic more quickly. He referred to the approach of wastewater-based epidemiology as the canary in the coalmine, the vital warning system that reveals a threat in time. The MMSD also has sound economic reasons to be interested in such an indicator. By mid July, the utility had incurred pandemic-related losses of around three million dollars.

4.5 Open discussion: Covid-19 as a global wake-up call

Wastewater monitoring for SARS-CoV-2 is ready for application, and yet in many countries the implementation is lagging. Therefore, Felix Kaup from Hessen Trade & Invest started the open discussion after the second session with the question, how the initiative to eradicate polio managed to convince countries of the usefulness of wastewater monitoring. Speaker Ousmane Diop from the WHO emphasized that the global unity in this field has been helpful. He mentioned that the approach has already proven its merits, for instance in 2013, when Israel responded to the detection of poliovirus in wastewater with a preventive diagnostic program and was thus able to contain the spread. Susanne Lackner from TU Darmstadt and Sofie Midgley from Statens Serum Institute put their trust in the persuasive effect of the high quality data and the good cost-benefit ratio.

In her talk, Midgley had already pointed out the relatively low cost of wastewater monitoring. This aspect was discussed more deeply in the open debate. Bernd Gawlik from the EU's Joint Research Centre put the costs of wastewater monitoring in relation to the spending for other measures needed to cope with the pandemic. The development of the German corona warning app alone has cost around 69 million euros, he said. Compared to that, the 20 million euros in EU funding are very little, especially considering that the wastewater monitoring funded is set to cover half a billion people. Diop called the current situation a global wake-up call. One should use the current commitment to wastewater monitoring in order to establish monitoring systems that can in future also warn us of new pathogens.

5 Session 3: Beyond Covid

It's not just coronaviruses that leave their traces in the sewage system. Other pathogens, as well as drugs, and other health relevant parameters can also be detected in wastewater. Wastewater-based epidemiology has potential and enables new business models, among other things.

5.1 Viruses, bacteria etc.: Hundreds of pathogens in excrements and wastewater

„Data and tools for understanding global waterborne pathogens“
Presentation by Dr. Joan B. Rose, Homer Nowlin Chair in Water Research,
Michigan State University, East Lansing, USA

Joan Rose from Michigan State University is a distinguished expert in the field of water microbiology. Hundreds of germs causing a variety of diseases from diarrhoea via heart disease through to neurological problems can be found in faeces and in wastewater, she said in her talk. In addition to viral and bacterial pathogens, she mentioned worm eggs and single cell parasites such as Entamoeba histolytica, which causes amoebiasis (amoebic dysentery). Water analytics is important mainly because many diseases, unlike Covid-19, can be caused by polluted drinking water. Rose mentioned the examples of typhoid fever and cholera. The focus of her presentation was on the Global Water Pathogens Project (GWPP). This initiative aims to ensure the availability wastewater disposal and clean water everywhere in the world.

Out of the GWPP, the project Wastewater SPHERE (SARS Public Health Environmental Response) was launched last year. The database of this project is growing steadily and currently comprises more than 15,000 wastewater samples from 620 sampling stations in 24 countries. An interactive online map displays the results (www.waterpathogens.org/content/w-sphere-map). Rose called on all water utilities, laboratories, and healthcare providers to join the collaboration and submit data or use the global datasets.

5.2 Biobot Analytics: Wastewater data as a business model

„Biobot Analytics – we are building early warning health analytics from data available in our sewers“, Presentation by Dr. Mariana Matus, Biobot Analytics, Cambridge, USA

Biobot Analytics is a spin-off from the Massachusetts Institute of Technology at Cambridge, USA. In her talk, co-founder and CEO Mariana Matus made clear that there is money to be made from wastewater data. After its start in 2017, Biobot was first focused on the detection of opioids in wastewater. Before Covid-19, the epidemic of opioid misuse was the predominant health problem in the US, Matus explained. On the basis of Biobot's measurements and subsequent targeted information campaigns, the town Cary in North Carolina, for instance, could reduce the problems of opioid misuse and overdosing by 40%.

Since March 2020, Biobot has been focussing on the detection of SARS-CoV-2 in wastewater. The start-up co-operates with the US Department of Health as well as with the Department of Defense and now collects wastewater data from all federal states. So far, more than 9,000 samples from 350 sampling stations were analysed for SARS-CoV-2, covering more than 30% of the US population.

A few months ago, Biobot launched its own dashboard (www.biobot.io/data), which informs about SARS-CoV-2 in wastewater across the US and juxtaposes wastewater data with clinical case numbers. The company is also active in Canada, Ecuador and Uruguay.

5.3 Antibiotic resistant pathogens in surface waters

„Antimicrobial Resistance - Detection of multi-drug resistant pathogens in surface water“
Presentation by Gudrun Bettge-Weller und Susanne Harpel
Centre for Health Protection at the Hesse Health State Office, Dillenburg, Germany

The last talk of the online conference was dedicated to the detection of antibiotic-resistant bacteria in surface waters. This pilot project of the Hessian public health authority, the HLPUG, was triggered by a near-drowning accident of a 69-year-old man, which happened in Frankfurt in 2017. After his rescue, bacteria of the species Klebsiella pneumoniae were discovered in his respiratory tract. These bacteria were resistant against four groups of antibiotics and produced the enzyme carbapenemase, which inactivates carbapenem antibiotics. Because of this, numerous surface waters in Hessen were investigated for the presence of resistant germs.

In 2018, the HLPUG took samples from 25 bathing lakes, five bathing ponds and the river Lahn. The river was sampled 12 times, at ten-kilometre intervals moving upstream from Limburg, and taking into account the locations of relevant institutions such as the university hospitals of Gießen and Marburg. The sampling of the river Lahn was also repeated the following year. The contamination in lakes and ponds was so low, however, that no follow-up investigation was carried out. The microbiological analyses of the river water samples revealed the majority of resistant bacteria to be Escherichia coli. However, resistant strains of Klebsiella pneumoniae and some other bacterial species were also discovered both in 2018 and in 2019. This is worrying, as these resistant germs can reach the human population, for instance, through the use of river water for agricultural production. Across Europe, around 35,000 people per year are already dying from infections caused by bacteria against which the drugs are powerless. Speaker Gudrun Bettge-Weller therefore called the increasing spread of antibiotic-resistant germs, which isn’t being monitored, as a ‘silent pandemic’.

5.4 Open discussion: All eyes on future threats

The broad spectrum of pathogens begs the question which germs wastewater monitoring should be focussing on. Susanne Harpel of HLPUG recommended paying more attention to multiresistant bacteria. Among other reasons, this is highly important because resistance traits can be passed on to other species. The US microbiologist Joan Rose also called to look out for antibiotic-resistant germs, but mentioned other candidates for wastewater

monitoring as well, such as new variants of noroviruses, which are rampant worldwide and cause violent stomach and intestinal diseases.

Rose suggested setting up adjustable monitoring programs. For germs with low abundance, screening methods would suffice, which only show the occurrence or absence. In the cases of other pathogens, such as SARS-CoV-2, genetic variants and outbreak waves must be recorded. Biobot founder Mariana Matus added that the monitoring systems must also be adaptable to regional requirement. She would like to see a standardised platform which could, for instance, monitor Ebola virus in Africa, poliovirus in Israel, and opioids in the US.

6 Conclusion and outlook

The second online conference about wastewater-based epidemiology held by Technologieland Hessen made clear that monitoring wastewater for SARS-CoV-2 is ready for practical application and should be implemented swiftly. The wastewater analyses are not meant to replace medical diagnostics of Covid-19 but to complement them. The talks also underlined that wastewater monitoring is important beyond the current pandemic, as it can recognise new threats. In the fight against poliovirus, such monitoring programs already play an important role.

Nevertheless, the setup of wastewater-based monitoring programs still has some weaknesses to overcome. Several speakers referred to the cooperation with health authorities as a challenge. Both in preparing wastewater data for the health system and in the data transfer, there is still a need for optimisation. Especially in less developed countries, the logistics, such as the transport and storage of samples, is proving difficult. Furthermore, participants called for a standardisation of procedural steps from sampling through to data storage – as they had done during the first online conference in February.

There have been pandemics in every epoch of history, as the introductory talk offering a glance at the history of medicine has shown, and our time hasn't been spared. On the contrary: climate change, factory farming, and other factors are favouring the spread of dangerous germs. Thanks to rapid progress in genetic analyses, wastewater monitoring now offers a cost-effective and reliable instrument to fight pandemics. Governments around the world should use this chance not only to overcome Covid-19, but also to try and avoid, if possible, getting into such a dramatic situation as the one triggered by SARS-CoV-2 in the future.