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Infection epidemiology

Rapporteur's report of the workshop

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Contents

The workshop series on public health

A working group commissioned by the German National Academy of Sciences Leopoldina, the Union of the German Academies of Sciences and Humanities, and acatech – the German Academy of Science and Engineering prepared a statement on public health. Prior to setting up the working group, the three academies explored this diverse field through a series of workshops that started in March 2013 and continued in June 2013 and October 2013. The workshop topics were set by a planning group of Leopoldina's Presidium with participation of the Standing Committee of the National Academy of Sciences Leopoldina. Each workshop covered one of seven topics (see below). The workshops were designed to bring together the latest facts and knowledge on each topic. Each workshop brought together the expertise and views of experts from Germany and abroad.

Topics	Coordinators	Date
History of public health in Germany and abroad	Alfons Labisch (Düsseldorf) Ilona Kickbusch (Geneva)	16 March 2013
Living conditions, social and psychological determinants of health and epidemiology – addressing the challenges of establishing causality and making evidence-based public health recommendations	Axel Börsch-Supan (München) Peter Goldblatt (London)	19 June 2013
Public health genomics	Peter Propping (Bonn) Martina Cornel (Amsterdam)	9 March 2013
Public health workforce – academic and non-academic	Bernt-Peter Robra (Magdeburg) Antoine Flahault (Geneva)	15 March 2013
Health education and prevention	Uwe Koch-Gromus (Hamburg) Hans-Peter Zenner (Tübingen) Jean-Francois Bach (Paris)	21 March 2013
Infection epidemiology	Jörg Hacker (Halle) Jos van der Meer (Nijmegen)	20 June 2013
Public health: national and global strategies	Detlev Ganten (Berlin)	23 October 2013

Summary of results[1]

- The co-operational interface between public health and infectious disease specialists is crucial; this cannot be stressed enough. It is important to develop this interface further, since previously it has only been possible within the limits of the few available experts and limited resources. Experts in infectious diseases welcome more interaction between clinical medicine, medical microbiology, epidemiology and public health.

- The growth of the world population, the ease of travel, the increase in immuno-compromised and frail persons, the poor compliance with vaccinations and the close connections with livestock and other animals have a great impact on the incidence of infectious diseases. This situation becomes worse by poor diagnosis of infection, misuse of antibiotics, antimicrobial drug resistance, a lack of new antimicrobial drugs, non-compliance, unavailability of the right antibiotics, poor nutrition, and interactions with other drugs. Here, again, intensified interaction between clinical medicine and public health is needed.

- Antimicrobial resistance (AMR) is mainly a problem because of the large threat it poses to patient safety. Patients suffering from the effects of AMR have limited options for treatment, increased length of hospital stays, increased morbidity and mortality.

- Outbreak management is in the first place outbreak recognition and control measures. With regard to the latter, it requires knowledge and grip on processes that lead to decisions on measures taken by professionals and on communication and uptake by the population. This implies that outbreak management needs systems to monitor the development of perceptions and social interactions, to be able to provide answers to the public.

- We need to keep in mind the economic costs of outbreaks. For example, the cost of the EHEC is estimated nearly 1.6 billion Euros. Even limited

[1] This report documents the presentation and discussion at the Workshop on 20 June 2013. For the reader to be able to follow the chain of reasoning, it was aimed to stay close with the spoken words and to document also the variety of suggestions that were made, even if they are contradictory.

outbreaks may have enormous economic consequences. Therefore, we need to have proper precautions in place to adequately handle outbreak situations

- We live in a world where tuberculosis (TB) can be eliminated, and hopefully will be so by 2050, because we know a lot about its cause, transmission, treatment and prevention. So far, TB has not been eliminated because we need more understanding of the complex survival strategies of the causative organism, its synergies with other pathogens such as HIV, host factors involved, and the mechanisms of development of resistance to antibiotics.

1 Welcome and introduction

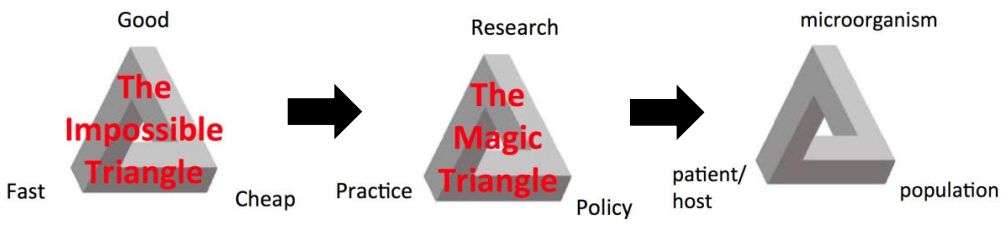
Detlev Ganten / Jörg Hacker / Jos van der Meer

Public health services have a long history in Germany, dating from the Charité and Rudolf Virchow until today, including many ups and downs. We had already several intense, controversial, and engaging debates in the last year during the planning process of this series of workshops, and now hope to continue this dialogue in this workshop. We hope that we can proceed with some recommendations on how to best practice public health in and for the future.

2 The interface between clinical infectious diseases, medical microbiology and public health

Winfried Kern

This presentation looks at the interface between clinical infectious disease, medical microbiology research, and public health from a clinical perspective. For this, it is useful to draw upon an analogy from the business world: the so-called "impossible triangle" which requires a product to be good, cheap and supplied fast. One can transfer this concept of a triangle to the realm of public health in general with the three corners being practice, policy and research. Furthermore, it can be transferred to an infectious disease setting. Then, the corners are with population, patient/host and microorganisms. When public health practitioners try to fulfil all the characteristics of the "magic triangle" (research, practice, policy) the point of view and knowledge of infectious disease practitioners is of importance.



The impossible / magic triangle applied to public health and infectious diseases

This triangle shows the basic conceptual interface required for public health and infectious disease specialists to work together in order to practice health interventions and solve health crises. There are examples in the past of collaborations between public health experts and infectious disease experts working against microbial resistance, including the cooperation during the EHEC crisis and the German Antimicrobial Resistance Strategy DART. Nevertheless, the question remains, whether the right co-operational framework is in place to deal with infection outbreaks and where collaboration between

disciplines is required. How to develop the future? The following three examples will explore this further.

<u>Example 1:</u> The magic triangle for Methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* infections

The magic triangle for Methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* infections includes MRSA research focus, MRSA control policy items and MSSA disease burden & MSSA/MRSA optimised management. In public health policy issues there is more focus in research on methicillin-resistant *Staphylococcus aureus* (MRSA) than on methicillin-sensitive *Staphylococcus aureus* (MSSA). Especially in Europe, great attention is given to the large burden of disease coming from MRSA, but the large burden of disease from MSSA is missed. Thus, research on MSSA and the resulting discussion should be refreshed. As an example we can look at epidemiological studies done on the *Staphylococcus aureus* bactereia (SAB). SAB still remains frequent (ca.20-30/100,000), and causes significant morbidity and mortality (20-30%). It is also often (ca. 80%) nosocomial/healthcare-associated, which includes MSSA. Dealing with SAB requires in-depth clinical investigation and competency in bedside decisions.

Kraker et al. (2011) looked at the clinical impact of anti-microbial resistance in European hospitals, and in particular at the excess mortality (30-day mortality) and the length of hospital stay (LOS) associated with *Staphylococcus aureus* bloodstream infections (MRSA and MSSA). Compared to controls, patients with SAB had a higher 30-day mortality and extra LOS (Table 1). However, comparing the MSSA and the MRSA cohort, a statistically significant effect due to methicillin-resistance could only be found for 30-day mortality, but not for the length of hospital stay.

Table 1: Outcome for SAB (MSSA and MRSA vs. their respective control groups)

	30-day mortality – odds ratio	Extra LOS – odds ratio
MSSA vs. control	2.4 (1.7-3.3)	8.6 (6.8-10.4)
MRSA vs. control	4.4 (2.8-7.0)	9.2 (5.2-13.5)

Source: Kraker et al. (2011)

Based on the data by Kraker et al. (2011), we made some calculations on the potential effect of certain interventions. For example, we estimated that 14 additional deaths could be prevented if we reduced the MRSA frequency by 60% or 38 death of MSSA rates were reduced by 30%. Admittedly, reducing MRSA with an efficacy of 60% is very ambitious, and many might ask if decreasing mortality at such a rate is realistic. But if we look at second class con-

sistent evidence coming from epidemiological studies, we can see that using certain solutions/interventions, for example the team approach, can lower mortality by nearly 30% or more. Therefore, this deserves consideration.

There is also a study from Freiburg, the "megadatabase study", in which different international centres worked together, looking for the variation in mortality related to modifiable risk factors versus non-modifiable risk factors.

What are then the implications for public health and policy makers when it comes to SAB? It is remarkable that despite of the high mortality due to MSSA, only MRSA is notifiable. How can we solve this from a public health and public policy perspective? Why don't we make all SAB notifiable?

Example 2: HIV/AIDS

These questions become especially poignant when dealing with infections such as HIV/AIDS and the resulting epidemic. In the division of infectious diseases at the University Hospital of Freiburg, there are 500 patients in constant monitoring for HIV infection. Half of the work is in HIV management. Especially in the area of prevention, we have not experienced any success stories, since we have no effective vaccines and a lack of good interventions. Despite the widespread use of condoms, and the attempted development of effective vaginal microbicides and post-exposure and/or pre-exposure anti-retrovirals, we have not been able to decrease the number of new infections. We have therefore not been effective in reducing and controlling the HIV epidemic.

Despite these setbacks, there was recently an impressive study done, which was considered as the breakthrough of the year in HIV/AIDS research (J. Cohen, 2011). Myron Cohen and his team showed that early anti-retroviral treatment (ART) was incredibly effective in reducing the number of new infections. With early ART the transmission of new infections could be reduced by 96% as compared with delayed "standard" therapy (M. S. Cohen et al., 2011).

In a follow-up publication building on the Cohen trial, Tanser et al. (2013) showed that the results by Cohen were also achieved in a real world setting. This study gives a great example of how experts from the realm of infectious diseases can do good science, which can help public health policy issues to be implemented. The study was done with a cohort of 16,667 individuals from South Africa, trying to answer the question whether ART coverage cannot only be effective in reducing infections based on aggregate populations, but also on the basis of individual level monitoring. The results seem to indicate that with early ART therapy we can essentially reduce the acquisition risk at a rate, which would allow controlling future HIV/AIDS epidemics, as long as treatment access and funding is available.

<u>Example 3:</u> The story of the detection of an infectious retrovirus, XMRV

Another interesting study by Lombardi et al. (2009) looked at the detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome (CFS). The study had well defined cohorts monitored over time by notable clinicians in order to answer questions that had been raised about chronic fatigue syndrome throughout the years on the basis of different theories. This led to the discovery of an infectious retrovirus that, according to many publications and their well-defined cohort studies, was found in the blood cells of patients with chronic fatigue syndrome. Regrettably a study released a year later (Erlwein et al., 2010), put a large question mark on these findings since the study could not reproduce the findings that the infectious retrovirus XMRV was causing chronic fatigue syndrome. Based on this and other criticism, the original study was retracted by Lombardi et al. (2009) (van Kuppeveld & van der Meer, 2012). The XMRV story is a good example of how the internet made it possible that different groups immediately clarified the situation. The discovery of a virus may be an important development, with the internet providing a powerful arm and interface to the general public.

At this interface, there are many more examples in the same vein of these breakthroughs/controversies:

- Tuberculosis outcomes changed not only by HIV coinfection, but also by co-morbidity with diabetes
- Infections that are caused by extended spectrum beta-lactamase (ESBL) infection producing enterobacteriaceae and the problem of too many „interpreted“ and insensitive breakpoints for treatment with penicillins and carbapenemae
- „Good“ versus „bad“ antibiotic policies and CDI
- Population-based outcomes of mass azithromycin treatment
- Influenza and pneumococcal vaccine strategies and implementation

In conclusion, going back to the interface of the “magic triangles,” we cannot stress enough how crucial the co-operational interface between public health services and infectious disease specialists is. Additionally, it is important to develop this interface further, since previously it has only been possible within the limits of the few available experts and limited resources. Experts in infectious diseases greatly welcome better microbiology, but our thinking needs to get interfaced with more clinical science and epidemiology.

Discussion

- During infectious disease consultation rounds we see many more MSSA-related problems than MRSA organisms, a lot of which being community acquired and not acquired in the hospital. What are the reasons for this? Is it because of a bias? Or are the conditions that lead to infections with MSSA becoming more prevalent? It is hard to get good data and to set a threshold beyond which clinicians should take action. Often it is not even clear, what are the right steps to take and whom to contact in the public health setting when there is such a problem. We therefore need not only to develop interfaces, but also develop specific monitoring thresholds.

- Clinicians need indicators when to contact the "outside world. This is where we find the interface with public health experts. They are the first who have to be contacted when we have the feeling that a major health crisis is looming which needs a population-based intervention.

- Around 20% of *S. aureus* infections are truly community acquired, i.e., 5 in 100.000 per year. The rest is largely co-morbidity associated. The severity of the disease correlated with the incubation period. Early discharge is one major risk factor for community onset health care associated diseases, a rising issue in our ever increasing economical world. Patients are being discharged with complications after 3-5 days, meaning that they incubate inside the hospitals and then return to their communities with a major disease. This is a major problem in the UK because length of stay is very short and complications are then moved outside the hospital.

- Even though we might like to operate under specific thresholds, we cannot embrace them too willingly because they are not modifiable. We need to rely on the clinician to judge what is normal and what is unusual, which is always a very hard question to answer, since it depends on the critical awareness of the clinician.

- Nowadays, the focus in research is too much on MRSA and too little on transmission of infections in general. It is difficult to disentangle community-acquired infections from hospital-acquired infections.

- There is a strong need for a notification of MSSA in addition to MRSA. Only then it is possible to think about preventive measures based on data.

- Much of the research and surveillance is hospital-based, meaning that we investigate people as they enter the hospital. We look at their hospital his-

tory in the past, which naturally leads to a bias in the studies. There are still too few true population-based studies.

- A modification of the handling of the MRSA bacteria should be considered before thinking about specific prevention measures because MRSA infections can occur inside as well as outside of the hospital and patients have to go to hospital in both cases.

- We need better data on conditions predisposing to infections (e.g. diabetes) in people coming from the community.

- In Germany, doctors have no incentive to take cultures from relevant body sites (e.g, blood). Yet, it is important to create a cohort of physicians who take such cultures.

- In terms of raising awareness, it is important to have whistleblowers and institutions/professionals that hear the whistle. ECDC has created the EPIS discussion platform (Epidemic Intelligence Information System – a discussion platform which allows risk assessment bodies to exchange non-structured and semi-structured information regarding current or emerging public health treats with a potential impact in the EU). This allows the member states to raise questions about specific cases of diseases that we are dealing with.

- The issue with whistleblowers in early stages of outbreaks is that it is very much microbiology-based. Our Achilles heel in reporting early is the majority of clinical whistleblowers, because they are not trained to blow on the so called proverbial whistle. The key question at the end of the day is how we can train young doctors so that they become whistleblowers, and how do we develop mechanisms where they can put their concerns on the web in order to interact with their colleagues and with public health experts?

3 Outbreak management in The Netherlands

Aura Timen

This presentation focuses on practical outbreak management and the interface to the public in the Netherlands. The Netherlands have a national coordination structure when it comes to outbreak management in crises. First off, we must realise that: Outbreak management is more than outbreak recognition and control measures.

In the Netherlands the municipal councils are responsible for routine communicable disease control. If an outbreak occurs, they will rely on the local and national administrations, which again rely on higher levels of government responsibility depending upon the kind of outbreak.

To show how outbreak management is handled in the Netherlands we will look at a recent measles outbreak. In March 2013, a 13 year-old orthodox protestant girl from a region where people usually abstain from vaccinations for religious reasons was found to have measles. There were 10 children living in the household and all of them were not vaccinated. It is estimated that around 200.000 people in the so-called “bible-belt” abstain from vaccination for religious reasons. The vaccination coverage for MMR (measles, mumps and rubella) is only 50 to 60%, too low to prevent measles outbreaks. This is why the national response team was sent to monitor the progression.

This also was an interesting case because measles are mostly eradicated in the Netherlands, except for a previous outbreak in the orthodox protestant community in 2000 (3292 cases were reported in the whole Netherlands) (Hof, Spaendonck, & Steenbergen, 2002). The connection between cases of measles and low vaccination coverage in the Dutch “bible-belt” could be established for the 2000 measles outbreak (Hof et al., 2002).

After sampling the orthodox protestant population to measure protective serotiters against measles, we saw that even though most of the Dutch population is protected against measles, in particular children below the age of 13 in the orthodox protestant population are very susceptible to acquire measles (Mollema et al., 2014).

Then, in June 2013 there was a new notification of measles by another orthodox protestant family, with 7-8 cases being reported on the same day, which led to completely different results from the March 2013 measles incident. Whereas the first one did not cause an outbreak, the second case led to nearly 130 infections within in a few days (Giesbers, 2014).

This was the moment when the National Outbreak Management Team was called in. The Outbreak Management Team assesses every national crisis or threat that might lead to a public health problem. During an outbreak, it is concerned with the following items:

- monitor progression of the outbreak,
- identify dilemma and anticipate on the expected magnitude of the outbreak,
- structured assessment of the public health risks within the community,
- coordinate control measures with the public health services,
- coordinate (perform) communication with professionals and public.

The National Centre for Public Health and the Environment (RIVM) chairs the team and draws upon a specific list of partners and experts from inside and outside the institution (epidemiologists, virologists, public health doctors, public health nurses, communication specialists) that they work together with. Depending on the disease and the outbreak, team members vary.

For the June 2013 measles outbreak, the team consists of microbiologists, public health doctors, paediatricians and vaccinators. They convened to decide the best measures that need to be taken in order to prevent further transmission from a scientific basis. Advice is then given to policy makers in order to look at the given scientific advice from a policy perspective. The realm of policy must then ask itself what health intervention can be done, can it be afforded and can it be explained to the public? The Minister of Health finally decides upon all of these inputs and specific control measures that are to be implemented.

For a more general approach towards outbreak management in crises we can also look at the crisis definition by the WHO: *"1. A situation that is perceived as difficult. Its greatest value is that it implies the possibility of an insidious process that cannot be defined in time, and that even spatially can recognize different layers/levels of intensity. A crisis may not be evident, and it demands analysis to be recognized. Conceptually, it can cover both preparedness and response ("crisis management"). 2. Time of danger or greater difficulty, decisive turning point" (Oxford Pocket Dictionary, 1992).*[2]

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[2] Cf. http://www.who.int/hac/about/definitions/en/index.html (accessed 27 May 2015).

There are different "layers" during a crisis: there is the reality of the scientists, the administrative reality which does not always overlap with the scientific component, the reality of the professionals who carry out the measures, and the public perceptions of the reality and what they make of it.

There are a few studies that cover the experiences of healthcare professionals on what is needed to make outbreak management work. These studies specifically look at the barriers encountered during the work on outbreaks and what leads to outbreak management failure. It is quite clear that outbreak management fails when there are no concrete targets for performance and crucial instructions are lacking. Timen et al. (2010) found that "*crisis guidelines … have 4 generic barriers to adherence: (1) lack of imperative or precise wording, (2) lack of easily identifiable instructions specific to each profession, (3) lack of concrete performance targets, and (4) lack of timely and adequate guidance on personal protective equipment and other safety measures.*" Also, we have carried out a literature review, focusing on the lessons learned from research and practical experiences in outbreak management, with the following results:

Lessons learned for outbreak management

The crisis advice • Clear, consistent and unambiguous with respect to: case definitions, sources and routes of transmission, appropriate professional performance, use of PPE, diagnosis, treatment, isolation and quarantine. • Allow modifications based on new or evolving scientific insights and practical experiences. • Guidelines from various organisations (CDC, WHO, ECDC, national organisations) should be consistent.
Leadership • Flatten the organisation and put a formal command and control structure in place, making clear who is in charge of the final decisions (even in situations when there is no time for consultation).
Professionals • Set up system-wide safety processes to assign priorities to potentially different interests (whose safety gets priority: patients or caregivers?) and address safety concerns and feelings of vulnerability of health care workers.
Communication between organisations • Create a direct, transparent and accountable system-wide communication network (from the macro to the micro level of the individual healthcare providers) for the control and containment of outbreaks

Source: A. Timen (2010)

For decision making and communications, Nicoll & Sprenger (2011) add the following points.

Lessons learned from the 2009 pandemic

Decision making in the pandemic	There should be more formal if rapid independent reviews of earlier decisions at national and international levels. Opinions given should be transparent with those advising being identified and with public declarations of interest.
Communications	Prepare the population and professionals for a range of possibilities. The opinions, concerns and views of the public and professionals should be monitored at national levels during a pandemic and responded to rapidly. A disconnect between technical epidemiological and virological risk assessments and the politically-driven risk management process was evident and partially fuelled by the media coverage in early days of the 2009 pandemic. Many public health authorities are poorly equipped to deal with the multi-source two-way communication platforms of that the internet and social media allows today.

Source: Nicoll & Sprenger (2011)

Specifically in crisis guidance what is needed are the context, control measures, guidance development and implementation. Timen (2010) gave examples for all four points

Context	Control measures	Guidance development	Implementation
- Assess severity and transmissibility - Assess uncertainties - Assess potential impact - Assess perceptions	- Risk assessment - Risk groups - Consequences of the measures, - Uncertainties of the measures - best case/ worst case scenario	- Criteria for selecting, judging, linking evidence - Models from other countries - Criteria for revision - Dissident minority view points - Include all relevant disciplines in the committee	- Consider most appropriate dissemination - Consider barriers - Address responsibilities - Formulate targets for performance (indicators)

Source: Timen (2010)

Applying parts of this model to the June 2013 measles outbreak, the national outbreak team convened, and after a risk assessment decided to institute the following measures:

- Risk assessment:
  - 1,48% of the population accepting vaccination are at risk

- Control measures
  - Catch-up vaccination in the bible belt (proven not to be accepted)
    - Extra MMR to children below 14 m (>6m)
    - in the NL (200.000);
    - in the affected areas (50.000)
    - in the orthodox protestant (who accept vaccination: 3.000)
- Vaccination and infection control policy in hospitals
- Further research
- Monitoring perceptions and communication

The example of the "new flew" showed how one single episode changed the whole anxiety perception. Hence, a main lesson we took from the process is the important need to monitor perception. Not only after a crisis, but also ongoing during the whole process, monitoring perception and interactions between people, and the importance of social media (Twitter and Facebook) for educational information campaigns.

In conclusion, outbreak management is in the first place outbreak recognition and control measures. It requires having (at least) knowledge (and ideally grip) on processes that lead to decisions on measures and their uptake by the population. In addition to that outbreak management involves systems to monitor development of perceptions and social interactions to be able to provide answers to the public.

Discussion

- ECDC tried implementing more Twitter and Facebook. What was found is that first of all, it is the healthcare professionals themselves that have to adapt. Currently, we still rely on a few educated people within the public health community that are communicators on social media platforms. To reach students and non-professionals it is important to use Facebook. We also need to realise that social media are only effective in countries with broad internet access.

- It is difficult to assure the quality of messages posted on Twitter/Facebook. How can this be controlled? One (incorrect) message can have large effects. We also need to keep in mind that while Twitter and Facebook can play a helpful role it also can lead to widespread panic if erroneous messages get spread.

- The role of social media needs to be considered from the very beginning. At RIVM there is now a team of people that tries to issue correct messages

and re-tweet once they encounter a wrong message. It is also important to convey a consistent content, i.e., to send the same message from different sides (e.g., professional societies, RIVM and others).

- Despite of efforts to correct messages, a main challenge remains how to send out messages that are accepted by experts (and the public).
- Ideally, public opinion during outbreak management should not be done retrospectively, but should be studied in real time.
- Infection epidemiology and outbreak management is not only a challenge for the Western world, but the grand challenge in this regard really is in the developing world. How can we transfer outbreak management to world infectious disease problems?

4 Functional molecular infection epidemiology of *Mycobacterium tuberculosis*

Sayed Hasnain

Global estimates of tuberculosis (TB) show that incidents, prevalence, and mortality are all decreasing. This development can largely be attributed to the global campaign against TB, even though the large uncertainty band should remind us that TB remains a disease which we have to worry about. When we look at TB prevalence per region, it is decreasing as well, but the uncertainty bands remain high.

Globally incidents rates are also falling by about 1% per year. With this incidence rate there should be a complete plateau for new incidents by 2015, with TB being completely eliminated by 2050.

This leads us into the double trouble which is TB-HIV. HIV impacts TB in two primary ways (see Special: Tuberculosis: *Nature Medicine*, March 2007): On the one hand it reactivates latent TB infection, while on the other it increases rate of TB recurrence. If a patient is already being treated for HIV and then develops TB, the decision what to do medically becomes very difficult. WHO regularly publishes key figures on TB[3]: E.g. in 2013 WHO estimated 9 million new TB cases, 1.1 million HIV-negative and 0.36 HIV-positive people died from TB in 2013. WHO estimates that XDR-TB cases, which are resistant to all most potent first-line and second-line, reserve drugs, were about 50,000, the majority of which are lethal. A lot has been achieved in treating TP so far (e.g., cure rates today are greater than 85 %, mortality has been reduced significantly). Despite of these achievements, TB incidence is declining far too slowly and elimination is impossible with current tools. We face a number of challenges:

- Causes: we must better understand the pathogen.
- Transmission: we have to understand the drug-resistant varieties and population specific strains spread and diverge.

[3] Cf. http://apps.who.int/gho/data/node.main.1315?lang=en and http://www.who.int/gho/tb/en/ (accessed 27 May 2015).

- Treatment: we have to solve the problems of diagnosis, lack of new drugs and of the synergies with other pathological conditions (such as HIV infections, diabetes).
- Prevention: we have to develop other vaccines than *M. bovis* BCG.

The main problem we are facing here is that we still only have one drug for fast-track mechanisms and the issue of multi drug resistant strains requires from us a better understanding of the pathogen. We need to know how drug resistance is spreading, when Myxobacteria are mutating, and what the transmission mechanisms are.

This is why a whole genome scan of global isolates was done in order to obtain genotypic evidence for strain divergence (Hasnain, 2003; Hasnain & Ahrned, 2004).

Can this pattern be translated into potential markers for a particular TB strain and for identification of drug resistant isolates?

Our approach is to use functional molecular infection epidemiology. This not only implies descriptive host-pathogen genomic associations or risk analysis, but rather the interplay between pathogen and host genomic variations to functionally demonstrate the role of the genetic variants during infection. Hence, classical molecular epidemiology is augmented to derive functionally relevant markers instead of “neutral” markers.

Using this approach the sequencing of *M. tuberculosis* revealed ‘mysterious’ families of proteins called ‘PE/PPE/PGRS’ proteins.

It turns out that TB strains are diverse. What is the relevance of strain diversity to TB control and management? First of all, different genogroups have geographic predilections, based on ancestral lineages/strains (Gagneux & Small, 2007). India has a large circulating cluster of ancient genotypes (Beijing /W family of strains, Haarlem type of strains, South American-Mediterranean family). But do these strains also contribute to drug resistance? Out of new TB cases, only 2.8% are multi-drug-resistant in India, compared to 13% in Russia. Why is our treatment success reaching a level of around 90% compared to 58% in Russia? Why have there been no institutionalised outbreaks in India, as compared to South Africa. Is the lower burden of drug resistance in India compared to, for example with the Beijing strain in Russia, due to a particular ancestral strain?

We therefore have several issues to ponder:

1. Ancestral lineages are widespread and perhaps do not allow spread of other genogroups

    - Host adaptation?

- Preferential colonisation?
- Genetic resistance?

2. Are ancestral strains really advantageous for a TB control programme?

- Slow disseminating types?
- Are they protective?
- Are they less virulent?
- Are they more 'cooperative'?

3. How long does this advantage sustain?

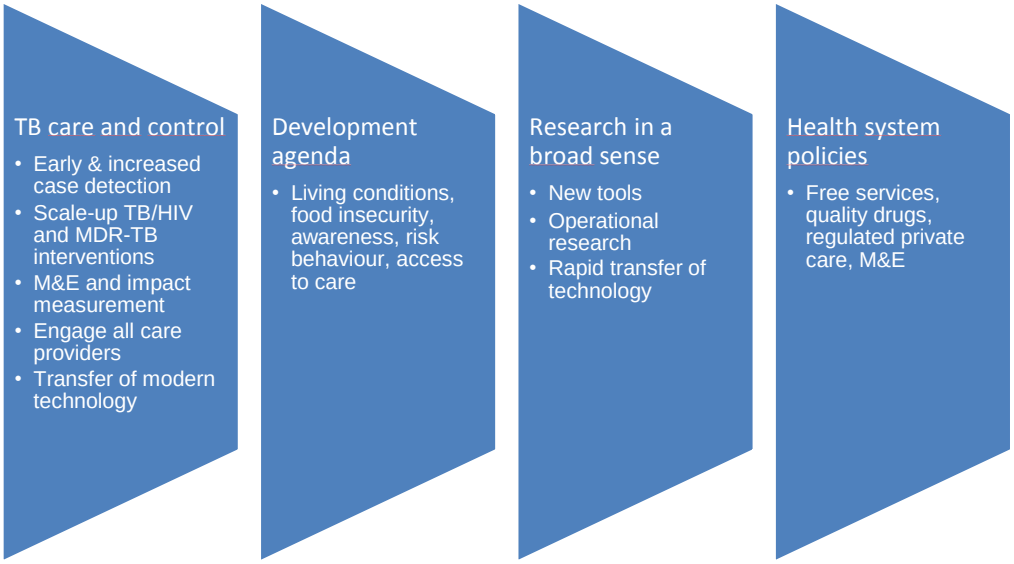
These issues are especially important to ponder when we consider the possibly looming infectious disease catastrophe for developing countries such as India with currently 8 Million TB cases, 5.7 Million cases of HIV-AIDS and 30 Million people suffering from diabetes. Additional pressure is put on the system because of lifestyle changes, rising population density, upcoming diagnostic issues and a rise in the numbers of notifiable diseases. Moreover, new threats such as autoimmunity due to environmental triggers develop. This leads us into the desperate needs and actions required for the future:

Future needs and actions

Therapeutics: new drugs and shorter regimens	• develop public-private partnerships for drug development
	• speed up drug evaluation and approval processes
	  ○ exploit bioinformatics for more flexible designs for studies
	  ○ develop markers for clinical outcomes
	• support basic research in drug development

HIV and TB related issues	• provide access to assisted reproduction techniques (ART) to decrease the susceptible population • provide access to TB therapy at the right time to reduce chances of IRIS
Interrupt transmission	• develop, implement and monitor site appropriate infection control strategies in health care facilities • develop new vaccines • alleviation of social and economic conditions and health disparities that breed both TB and HIV

Innovative action is needed in four specific spheres: TB care and control, development agenda, research in a broad sense, and health system policy.



Action spheres

We live in a world where Tuberculosis can be eliminated, and hopefully will be so by 2050, because we know a lot about its cause, transmission, treatment and prevention. However, TB has not been eliminated so far because we still need to understand the complex survival strategies of the causative organism, synergies with other pathogens such as HIV, host factors involved, the mechanisms of development of resistance to antibiotics or the role of host flora. The impact of an increasing world population, ease of travel, increase in immuno-compromised and frail population, and poor compliance with vaccinations have a great impact on the incidence of infectious diseases. This situation is exacerbated by poor diagnosis, drug abuse, drug resistance, a lack of new drugs, non-compliance, unavailability of medicines, poor nutrition, interactions with other drugs, no effective vaccine, poor awareness, and the fact that it is still a social taboo and stigma.

Discussion

- Are diagnostic facilities really that poor in India? A problem when characterizing antigens is that all are based on antigens characterised from isolates reported from the West, leading to many false-positive results. This is why the government of India banned antibody-based tests. Hence, it is necessary to detect more local pathogens in order to prevent the large number of false-positive results.

- We also need to deal with the problem of extreme drug resistance, especially the problem of the wide availability of antibiotics creating multi drug

resistant strains. We should consider that in countries where antibiotics are sold over the counter, legislation needs to be introduced which makes such practices illegal, or to, at least, make it a social taboo to prescribe or use antibiotics for minor complications.

- During studies in Indonesia Alisjahbana et al. (2006) found that diabetes was a very strong predisposing condition for severe TB. Therefore, from a public health point of view, one of the major measures would be to prevent type 2 diabetes. If we share forces, health interventions in this area could possibly pay off much faster than the development of a new vaccine or novel diagnostics, even if the prevention of type 2 diabetes is a difficult task in a striving economy. In India, a movement is developing and campaigns have been set up to motivate people to eat healthy food.

- Even though erroneous self-medication with antibiotics is a public health problem, we need to realise that antibiotics sold over the counter actually allow people who cannot afford to go to the doctor to get treatment. The question is therefore how to balance between ease of access and preventing abuse.

5 Molecular epidemiology of extra-intestinal *E. coli*

[The summary of the presentation is not documented here.]

Discussion

- We know that the host susceptibility affects the pathogenic potential. We are very good in assessing the virulence of *E. coli* but we are poor in assessing the resistance of the host. If this was known, we would be much better in tackling diseases such as *E. coli* infections in the hospital. There is work on developing a clinical scoring system in which a number is assigned to host susceptibility.

- On communication, there are problems between clinicians and microbiologists. Sepsis is easily and incorrectly described as a disease, but it reflects a state of the immune response. When we require an exact clinical diagnosis to associate pathogenicity, sepsis is not a good entity.

- The EU Commission is increasingly concerned about the link between humans and animals. There are many pieces of a puzzle and different actors with different interests and interpretations. But, a final proof of the link is still missing, so that the commission can take action. Policy makers need these clear causal links in order to convince political decision and policy makers. This is seen differently by many researchers who argue that there are clear and proven linkages, e.g. for livestock associated MRSA. However, it has also been demonstrated by genomics epidemiology that even there the link cannot be quantified. Hence, there is a dichotomy between policy makers and researchers regarding what they require as proof and what science is able to deliver. This kind of problem is paradigmatic for different public health situations.

6 Interaction between microbiological laboratory and epidemiology in major outbreaks

Reinhard Burger

Despite of different interests and research foci, epidemiologists and researchers working in the laboratory need to work together and complement each other. When it comes to major outbreaks, both sides are equally important. One good example for such cooperation is the Norovirus-outbreak in schools and kindergartens with food supply by an external caterer that happened from September to October 2012. This was the largest foodborne Norovirus-outbreak in Germany ever, with a peak of cases between Sept. 25 - 28 in the 5 federal states Brandenburg, Berlin, Saxony-Anhalt, Saxony, and Thuringia. More than 11,000 cases were reported, predominantly children, adolescents and personnel in nurseries and schools. Most affected institutions were supplied with food by one single caterer. An analysis of affected individuals and of facilities in case control studies was done, which yielded an association with the consumption of frozen strawberries from a batch (41,000 Kg) imported from China. To identify the pathogen, nested PCR (Polymerase Chain Reaction) was used.

A genetic sequence analysis of the virus was done from stool samples of affected patients from all 5 affected states in the Robert Koch Institute. A broad spectrum of different Norovirus-genotypes was found, with a high sequence homology in viruses from different states. In more than 10% of the cases, mixtures of different genotypes were detected, with two of the genotypes being detected for the first time in Germany.

Table 2: Genotyping results in stool samples

State	Nr. of seq.	Places	GI.3	GI.4	GI.9	GII.6	GII.7/ II.6	GII.7	GII.8	GII.16 / II.13	others
Berlin	43	8	0	21	3	0	3	5	2	8	1x II.4 2012
Brandenburg	26	11	2	11	2	4	2	1	3	4	
Sachsen	33	12	12	17	2	1	5	2	2	0	
Sachsen-A.	12	7	0	2	0	0	3	2	1	3	2x I.b
Thüringen	12	8	1	2	0	0	2	0	4	3	1xI I.15 1x II.12;II.3
total	127	46	13	53	7	5	15	10	12	18	5

Source: Robert Koch Institute (2012)[4]

After a broad search the Norovirus was detected on several samples of the identified batch of frozen strawberries through the Landesamt für Verbraucherschutz Saxony-Anhalt, and the Bundesinstitut für Risikobewertung (BfR). A molecular analysis at the Robert Koch Institute revealed high homology between the sequence of Norovirus from the strawberry batch and part of the patients. The conclusions we were able to draw from this were that:

- findings from epidemiological analysis and distribution channels overlap,
- preparation of the strawberries affects transmission (heating reduces transmission),
- virus genomes from strawberries and patient samples were identical
- broad spectrum of Norovirus-genotypes with frequent mixed infections in patients indicate fecal contamination of water (used for watering, fertilisation or washing of the fruit)

Another interesting example is the large EHEC (enterohemorrhagic *Escherichia coli*) and HUS (haemolytic-uremic syndrome) outbreak which took place in Germany in the early summer of 2011, with the following epidemic profile:

Epidemic profile of the 2011 EHEC/HUS outbreak

Outbreak case	**N**	**Age (median)**	**% female**	**deaths**
EHEC	2.987	46 years	58%	18 (0.6%)
HUS	855 > 20%	42 years 90% adults!	68% > ♀	35 (4.1%)
Total	**3.842**			**53**
Comparison with previous years EHEC: ~ 1000 illnesses/years median age: 5 years HUS: 65 illnesses/year median age: 2 years				

Source: Robert Koch Institute (2011)

[4] For further information cf. http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2014/Ausgaben/19_14.pdf?__blob=publicationFile (accessed 13 June 2015).

Looking at the incidence of HUS (cases/100.000) by likely counties of infection it was clear that there was a connection to northern Germany, especially Schleswig-Holstein and the North and West of Mecklenburg-Vorpommern.

On May 19th 2011 the initial call for support came from a local health department in Hamburg. Immediately the response team went to Hamburg and did a substantial number of cohort and control studies. In less than 3 weeks sprouts were identified as the only risk factor, even though patients denied it. Through good cooperation with other actors, in less than 3 weeks the source was discovered and the agent was identified as well within a few days. This was done mainly through the investigation of 30 cohorts designed to identify the vehicle of infection and further cases, specifically. The following analyses were carried out:

- Cohort studies of travel groups (in cooperation with foreign authorities)
- Cluster analysis of different restaurant-associated outbreaks
- Analysis of billing data of guests at an affected canteen; results published on June 3, 2011 (press release RKI-BfR)

The real breakthrough happened through a “recipe based cohort study” that was carried out independent of what individual patients remembered. For this study, 10 cohorts with a total of 168 patients were identified, all of whom had eaten dinner in the same restaurant between 12 and 16 May 2011. 18 % had suffered from bloody diarrhoea or EHEC/HUS (31) within 14 days. Patients were asked which meals they had ordered. Photographs helped as reminders. This information was cross-checked with booking/billing information and group photos. Finally, the chef of restaurant was interviewed for detailed ingredients of the dish. It turned out that the relative risk of disease was 14.2 times higher (univariate analysis) compared to people not served sprouts – All 31 patients had eaten sprouts.

Eventually it was uncovered that the effected sprouts came from Egyptian fenugreek seeds which led to outbreaks not only in Germany, but also in France. The fenugreek seeds were delivered from Egypt via two intermediaries to a horticultural farm in Lower Saxony from where the sprouts were delivered to various addresses in Germany. The seeds were also delivered to France where they were responsible for an outbreak.

There was a similar outbreak in the USA in 2008, where a *Salmonella* Saintpaul outbreak was caused by contaminated chilli peppers. People were asked if they ate chilli peppers, which was denied by most patients, without taking into consideration that chilli peppers in a finely chopped form are present in a widely used salsa dip. Because of this complication it took nearly 7 weeks from outbreak detection to identification of the source, which shows

that the 3 weeks it took in Germany is an achievement. This leads us to the concept of “stealth food”.

One specific issue in the case of the EHEC outbreak where the laboratory was not successful was the lack of a direct proof of the identification of the harmful bacteria in the seeds/sprouts. Even though the epidemiological evidence was convincing, all attempts to identify it in the seeds/sprouts were unsuccessful, with a single exception, which was a single box of sprouts from the incriminated producer that was opened in a household with EHEC cases.

One issue that we also need to keep in mind in such cases is the large batch size we need to deal with. This may lead to sampling errors. In addition, *E. coli* can survive on dried seeds for years, meaning that infected seeds could still be in the supply chain.

We also need to keep in mind the economic costs that even such limited outbreaks have; the estimation is that nearly 1.6 billion Euros were lost because of the EHEC crisis. Even very limited outbreaks can have enormous economic consequences, which is why we need to have proper precautions in place to adequately handle outbreak situations.

Discussion

- Obstacles encountered during the EHEC outbreak were that responsibilities and duties are distributed between federal institutions and the individual states on the health side and veterinary and food safety authorities. During the past years the number of staff at county level has been dramatically reduced. Information transfer thus takes time. In addition there is a plethora of institutions. At the federal level there are already two different institutions dealing with food safety. In addition, media pressure was enormous. The media demanded information.

- In the EHEC outbreak, it would have helped a lot if more clinicians really called the local health authority. We would have known about the outbreak one week earlier if only a proper diagnosis had been made and notified to the local health authorities. The lag of notification was not between local health authorities and the RKI. It is very important to integrate the clinicians on site and make them aware that they are part of the public health system. Some physicians even did not know that HUS is a notifiable disease.

- It would be good if large distributors of food were obliged to store their information. Smaller lot sizes in food industry would increase safety.

- Another issue is to prevent the large number of human product contacts to reduce contamination. In livestock production, products can now be regularly traced at all stages of the value chain. The same is true for vegetable producers and large companies, who do quality control for their own sake. A close tracing system would be desirable to have in hospitals, too, particularly as the technology is there.

- Tracing is crucial, but the chain gets more complex. To detect microbial contamination, all steps in the chain are crucial.

7 The threat of antimicrobial resistance for Public public Health health

Dominique L. Monnet

ECDC is "an independent agency, named the European Centre for Disease Prevention and Control … to identify, assess and communicate current and emerging health threats to human health from communicable diseases." (ECDC Founding Regulation (851/2004), Article 3)

ECDC's main body of work consists of:

- EU-level disease surveillance and epidemic intelligence
- Scientific opinions and studies
- Early warning system and response
- Technical assistance and training
- Communication to scientific community and the public

What does antimicrobial resistance (AMR) really mean and who is involved:

- Several, inter-related compartments of healthcare, (i.e., patients in primary care, hospitals, nursing homes and long-term care facilities), food animals, food, environment;
- Many types of human infections, i.e. respiratory tract, urinary tract, skin and soft tissue, bloodstream, surgical site, related to medical devices, etc.);
- Many microorganisms;
- Many antimicrobials and mechanisms of resistance.

The bottom line is that it involves dealing with patients with infections due to resistant bacteria. Before we delve into the further details of AMR we should realise that AMR is not just a "human issue". It is a problem that includes the questions of where bacterial pathogens dwell and how they move between hospital patients, the general population and animal livestock.

Antimicrobial resistance is mainly a problem because of the large threat it poses to patient safety. Patients suffering from the effects of AMR have

- limited options for treatment,
- increased length of hospital stays,
- increased morbidity and mortality.

There are estimates that each year in the EU AMR causes ca. 2.5 Million attributable extra hospital days and ca. 25,000 attributable deaths. These figures are an underestimation since they only include 5 multi drug resistant bacteria and 4 types of infections. So what exactly do we know about AMR in Europe? In order to see the development over the last decades we can take a look at a paper from the 90s that examined the percentage of Methicillin-resistant Staphylococcus (MRSA) in Europe in 1990-1991:

Proportion of *Staphylococcus aureus* strains resistant to methicillin in 1990/1991

Country	Percent MRSA
Denmark	0.1
Sweden	0.3
Netherlands	1.5
Switzerland	1.8
Germany	5.5
Austria	21.6
Belgium	25.1
Spain	30.3
France	33.6
Italy	34.4

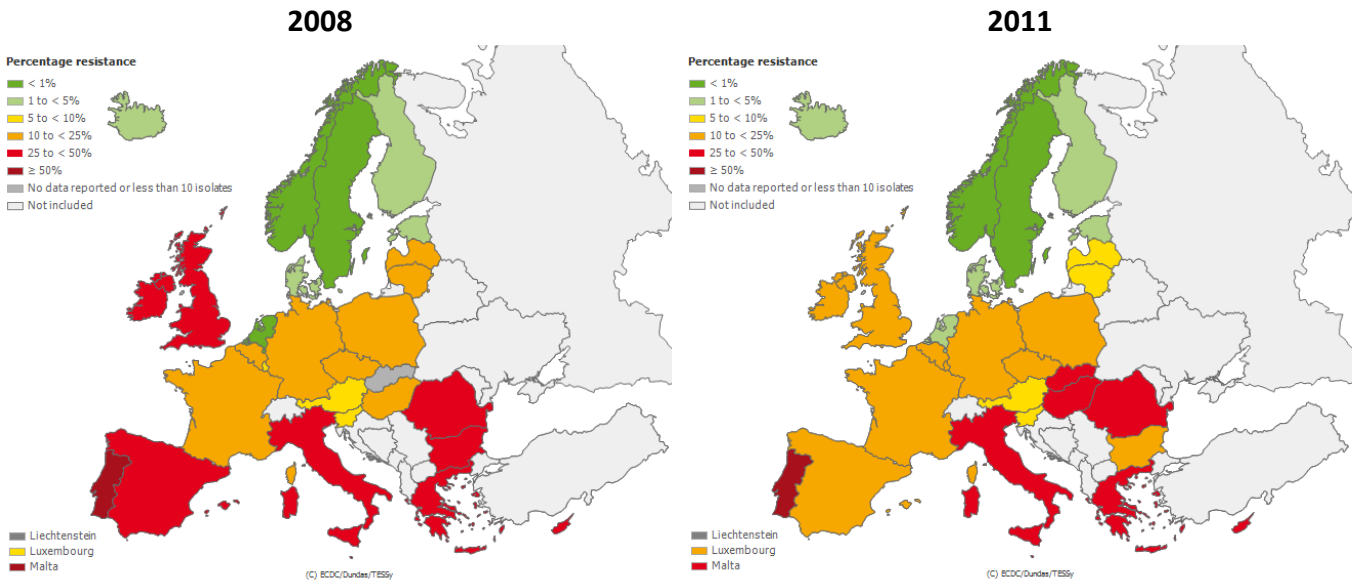
Source: Voss, Milatovic, Wallrauch-Schwarz, Rosdahl, & Braveny (1994)

Also of interest is a paper that examined MRSA in one hospital in Paris (all isolates) and one in Denmark (blood isolates) from 1960 to 1995. Whereas in France[5], starting in 1975 MRSA rates resurged after an initial decline, rates remained low in Denmark. Despite being the “European champion” in MRSA for a while, near-eradication of MRSA in Denmark was achieved through two simple measures:

- Increased awareness about hospital hygiene
- More rational use of broad-spectrum antibiotics

When we look at the development of the percentage of invasive isolates resistant to methicillin in Europe from 2008 to 2011 we can see that many countries have reduced MRSA rates in recent years, especially Great Britain.

[5] Cf. Leclercq (1995)



Note: This report has been generated from data submitted to TESSy, The European Surveillance System on 2015-05-28. Page: 1 of 1. The report reflects the state of submissions in TESSy as of 2015-05-28 at 17:30 - See more at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx#sthash.sJTse4Dh.dpuf

Staphylococcus aureus: percentage of invasive isolates resistant to meticillin (MRSA); EU/EEA, 2008 and 2011

Even though MRSA seems to be at a down-swing in Europe, there are other resistances which show a troubling development, such as *E. coli* resistant to third generation antibiotics such as cephalosporines or fluoroquinolones.

One of the crucial interlinks when it comes to the development of AMR is the interplay between AMR in livestock and food and the effect it has on human beings. In order to investigate this link Overdevest et al. (2011) did a study on patients in four Dutch hospitals using rectal swabs and blood cultures. Chicken meat packages from the major chains of groceries in the region of the 4 hospitals were randomly chosen and investigated. A high prevalence (80%) of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL) was found in the chicken meat. This was then compared to the results from the patients, where identical predominant ESBL genes were found in the chicken meat and in the rectal swabs, with same genes frequently found in blood cultures. Therefore there was a high degree of similarity between the *Escherichia coli* strains found in the meat and the patients surveyed.

Another worrying trend can be seen when we look at country self-assessment of stages for spread of carbapenemase-producing Enterobacteriacea (all isolates) from 2010 and 2013, which only seems to be the tip of the

iceberg. In Italy and Greece the situation has an endemic character and in the middle and Southwest of Europe (Spain, France, Germany, Great Britain, Poland and Belgium) regional spreads have been documented. The situation in the northern countries (Sweden, Norway, Finland, Denmark) looks slightly better because only sporadic hospital outbreaks have been reported (Grundmann et al. 2010; Glasner et al. 2013).

On the basis of the reported data figures the ECDC made a risk-assessment on the spread of carbapenemase-producing Enterobacteriaceae in order to list the risk factors for patient infection or colonisation:

- Prior use of antimicrobials
  - Any antimicrobial
  - Carbapenems (associated with a high risk estimate)
  - Other antimicrobials (fluoroquinolones, cephalosporins, anti-pseudomonal penicillins, metronidazole)
- Cross-border transfer of patients: Strong evidence that it is associated with risk for transmission when:
  - Patients are transferred from countries with high rates of CPE to healthcare facilities in other countries
  - Patients had received medical care abroad in areas with high rates of CPE
- Transfer of patients within units of same hospital
- Immunosuppression, severity of illness, invasive procedures

Also of importance is the relationship between antibiotic use and resistance in Europe that are saliently interrelated. Simplified one can say that the higher the consumption of antibiotics is, the higher the resistance of specific bacteria. Antimicrobial resistance is therefore a part of a continuum of risks and actions throughout life, existing in different settings where we can intervene.

As of 2009 there were 15 novel, systematically administered antibacterial agents that we have in the pipeline, although this is promising there are 13 agents against gram-positive bacteria and only 6 again gram-negative bacteria (ECDC & EMEA, 2009).

So what are some of the main actions that we can take to prevent and control AMR?

- The creation of new antimicrobial agents, with a novel mechanism of action, research and development.

- Improved infection prevention and control (hand hygiene, screening, isolation)
- Prudent use of existing antimicrobial agents (only when needed, correct dose, correct dose intervals, correct duration)

Discussion

- From the presentation one gets the impression that the hospital is a somewhat „hopeless place" outside the rest of the world. We think a lot about the antibiotics that come into the body, but we do not think about the antibiotics that come out of the body, and where they go after that. For example, the sewage system includes many antibiotics and resistant bacteria. The same is true for livestock farms. However, as long as there is no clear evidence of the risk for humans, policy makers cannot act. This should be put in the hands of the European Environment Agency. Antibiotics can be found even on the leaves of cabbage due to the application of slurry.
- Other risk factors are traveling (e.g. cabin crews), or gastritic acid blocking drugs which open up the gut for harmonisation with exogenous microorganisms.
- There is evidence that even subinhibitory concentrations of antibiotics contribute to the selection of resistant bacteria.
- We also need to focus on the issue of reducing the use of antibiotics in livestock production. More research needs to be done that shows the effects of antibiotics on animals, and the results it has on human beings down the line when they consume the animals as food.

8 Recommendations

… to funding organisations

- Further research needs
  - to develop more vaccines and to implement vaccination-strategies as a public health measure;
  - to clarify the interconnection between the transmission of AMR from humans to animals, and vice-versa;
  - to assess the role of the microbiome, its inner processes and how the microbes influence resistance. We should also add the host as an entire entity, along with its microbiome.
  - to study the transfer of resistance in order to uncover any missing links between clones.
- We should work together with environmentalists to figure out the effects of climate change on the spread of infectious diseases.
- We need to strengthen existing public health capacities by designing a global research agenda to public health of infectious diseases, now and in the future.
- When it comes to the spread of infections we need more cohort studies to analyze and discover critical control points. It is important to establish a cost-effective screening strategy.

… to research

- Studies, research and ideas must be communicated in a more understandable way. It is important that the right source provides the right information to the right target group. Information content and complexity should be adjusted to target groups. To improve acceptance amongst the general public, medical professionals and scientists need to think like “normal” people when giving recommendations in order to improve acceptance amongst the general public.
- We need a more quantitative approach to quality. We also need more capacity to rapidly draft and communicating press releases and guidance documents during health interventions.

- There should be more collaboration between European and non-European groups, especially on pathogens. We increasingly live in a world with fewer borders, making the spread of pathogens an international issue that can no longer remain local.
- ExPEC is a nice example of how epidemiology, infectious disease and virulence are really linked; the more complex the bacteria genome, the harder it gets to predict pathogenicity.
- We need to match data on virulence with host susceptibility; genome sequencing offers a lot here.
- We need new strategies on how to develop antimicrobial drugs that are not so prone to resistance, for example by targeting virulence factors. To take away pathogenicity without eliminating the microbe.
- We need to improve typing using modern techniques to find high-resolution type bacteria and viruses. Such results may help to predict risks.
- On communication, there are problems between clinicians and microbiologists. For example, sepsis is easily and incorrectly described as a disease, but it reflects a state of the immune response. When we require an exact clinical diagnosis to associate pathogenicity, sepsis is not a good entity.

… to medical professionals

- Professionals and processes should be prepared to detect outbreaks early on. Whistleblowers and institutions/professionals that hear the whistle are needed. The Achilles heel in reporting early is in particular the clinical whistleblowers, because they are not trained to blow on the so called proverbial whistle.
- The key question at the end of the day is how we can train young doctors so that they become whistleblowers, and how do we develop mechanisms where they can put their concerns on the web in order to interact with their colleagues and with public health experts?
- Clinicians need clear guidance indicators when to contact public health authorities. For example, in the EHEC outbreak, it would have helped a lot if more clinicians had called the local health authority. We would have known about the outbreak one week earlier if only a proper diagnosis had been made and notified to the local health authorities.
- Regarding management of severe infections better training and research are a priority.
- Training public health practitioners is a high priority. Such public health experts will need knowledge ranging from biomolecular to epidemiological issues, in combination with policy and research training.

- Infectious diseases are a great challenge and we need to raise the attractiveness to work in the sector of public health, especially through better salaries.

… to governments and health authorities

Data infrastructure

- We need better data on conditions of predispositions to infections (e.g. diabetes) in people coming from the community.
- We need bio-banks for bacteria, preferably on a European scale.
- We all have to match our data on virulence and host susceptibility and improve the development of individualised medicine under the one-health principle.

Communication

- We must have a broad and rapidly available platform of expertise in order to be prepared for unexpected events that require health interventions. Especially the development of an outbreak management team, like in the Netherlands, could help countries in their immediate health interventions. We need a system of experts that can be called in at any time. Of course it is impossible to be prepared for everything, but we need a reliable platform of expertise that can help us to adapt to acute challenges.

- The role of social media needs to be considered from the very beginning of an outbreak. For example, at RIVM there is now a team of people that tries to issue correct messages and re-tweet once they encounter a wrong message. It is also important to convey a consistent content, i.e., to send the same message from different sides (e.g., professional societies, RIVM and others).

Outbreak management

- Increased and improved cooperation between organisations for better over-all performance is needed. We should attempt to break the federal structure for outbreak management in Germany, and try to install an organisation that has national power in order to deal with the magnitude of problems which we could possibly be facing.

- With regard to outbreaks our current typing methods may be inadequate. If there are new unknown clones we cannot trace outbreaks to their fullest extent. We should therefore enforce and implement genomics, with next generation sequencing in the public health setting.

- Another issue is to prevent the large number of human product contacts to reduce contamination. In livestock production, products can now be regularly traced at all stages of the value chain. The same is true for vegetable producers and large companies, who do quality control for their own sake. A close tracing system in hospitals would be desirable, too, particularly as the technology is there.

Awareness

- We need to keep the discussion on antibiotic resistant infections alive but at the same time not forget about the “usual” infections.

- The focus in research is too much on MRSA and too little on transmission of infections in general. It is difficult to disentangle community-acquired infections from hospital-acquired infections. There is a strong need for a notification of MSSA in addition to MRSA. Only then it is possible to think about preventive measures based on data.

- We should focus more on activities to raise public awareness on the severity of antibiotics misuse, e.g. by pushing the idea of an “Antibiotics misuse day” in addition to ECDC’s Antibiotics awareness day).

Stakeholders

We also need to include patients in the equation, since patients can be responsible for their own health through simple measures, such as the regular washing of hands, and not demanding unnecessary antibiotics.

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10 Appendix

10.1 Workshop Programme

Date: June 20, 2013, 11:00 a.m. - 05:00 p.m.

Location: Langenbeck-Virchow House, Room „August Bier“, Luisenstr. 58/59 in 10117 Berlin

11:00-11:30: Welcome and introduction

Detlev Ganten, Coordinator of the Planning Group “Public Health”
Jörg Hacker, Coordinator of the Workshop
Jos van der Meer, Coordinator of the Workshop

11:15-12:15: First Session

The interface between clinical infectious disease, medical microbiology and Public Health
Winfried Kern, Infektiologie UniversitätsklinikumFreiburg
Outbreak management
Aura Timen, RIVM, Bilthoven, The Netherlands

12:15-13:15 Second Session

Functional Molecular Infection Epidemiology of Mycobacterium tuberculosis
Sayed Hasnain, Indian Institute of Technology
Molecular epidemiology of extra-intestinal E. coli
Ulrich Dobrindt, Universitätsklinik Münster

14:15-15:45 Third Session

Interaction between microbiological laboratory and epidemiology in major out-breaks
Reinhard Burger, RKI, Berlin
The threat of antimicrobial laboratory resistence for Public Health
Dominique Monnet, ECDC

15:45-17:00 General discussion

10.2 Workshop Participants

Speakers

- Aura Timen, National Institute for Public Health and the Environment (RIVM)
- Reinhard Burger, Robert-Koch-Institut
- Seyed Hasnain, Indian Institute of Technology, Neu Delhi
- Winfried Kern, Infektiologie, Universitätsklinikum Freiburg
- Dominique Monnet, ECDC
- Ulrich Dobrindt, Universitätsklinikum Münster, Institut für Hygiene

Discussants

- Petra Gastmeier, Charite
- Helge Karch, Universitätklinikum Münster
- Rainer Sauerborn, Heidelberg
- Wolfgang Witte, RKI
- Christian Bogdan, Erlangen
- Gerard Krause, HZI Braunschweig

Member of the planning group and coordinators of other workshops

- Detlev Ganten, Stiftung Charité, Berlin
- Jörg Hacker, Leopoldina, Halle/Berlin
- Jos van der Meer, Radboud Universiteit Nijmegen

Leopoldina Secretariat

- Kathrin Happe, Leopoldina, Halle
- Barbara Döhla, Leopoldina, Halle

Rapporteur

- Julian Kickbusch, Berlin