



Antimicrobial resistant bacteria

Knowing and fighting the enemy

Fake science

**Turbulent times
for science**

Hemp as a feedstuff

**Getting high
on milk?**

Substance transfer

**Under
the skin**

Dear Readers,

“It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.”

We owe this profound piece of wisdom, which also applies to science, to no lesser a person than master detective Sherlock Holmes. It is the facts that we have to face up to without reservation, so that they can lead us to the truth – or to the bad guy, of course, in the case of the detective. If Sherlock Holmes is the researcher among the detectives, the BfR is the detective agency among the research institutions. This issue of our science magazine BfR2GO provides impressive proof of this, as it deals with dastardly villains, hidden motives and puzzling trails.

Our main topic, antimicrobial resistance, deals with the tricks used by disease-causing bacteria, and how to track them down or even stay one decisive step ahead of them, if possible. We also follow criminal trails with FoodChain-Lab – all along the food chain, as our report reveals. The program helps to trace risky pathogens in the maze of global goods flows.

Fake science, forged science, is an issue of increasing sensitivity which involves far more than catching the crooks. Those who cheat jeopardise the credibility and acceptance of science, as the article in the magazine discloses.

With psychological finesse, researchers of the BfR at the German Centre for the Protection of Laboratory Animals are trying to find out what mice really want. Knowing what motivates the rodents can make animal experiments better to the benefit of both man and mouse, as the BfR2GO report concludes.

As you can see, a flair for detective work is in great demand at the BfR. This applies to aluminium, too! A substance whose trail leads us to the realm of the nano world. The idea that little things can be big things was already put forward by our English chief investigator: “It has long been an axiom of mine that the little things are infinitely the most important.” Well said, Mr. Holmes.

In this spirit, we wish you lots of fun reading our “detective magazine”!

Professor Dr. Reiner Wittkowski
BfR Vice President







The truth in wine

Putting a stop to wine fraudsters is the goal of a chemical-analytical strategy whose foundations are currently being laid by the BfR and the affiliated Senior Expert Office for the Import Control of Wine from third countries in a research project. The chemical fingerprints of many hundreds of wines are being recorded using a nuclear magnetic resonance spectrometer and then examined for characteristic features such as grape variety, cultivation area and vintage. False declaration and unauthorized additives are easier to identify in this way. To achieve this, examination and evaluation methods must first be standardised so that wine fingerprints from different laboratories can be compared and entered into databases.

More information:

www.bfr.bund.de/en > The Institute > Reference laboratories > Senior expert office for the import control of wine

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Last Reserves



Antibiotics help to combat bacterial infections. More and more often, however, the drugs have no effect. Their wide-ranging use stimulates bacteria to build up counter strategies and become increasingly resistant – even to reserve drugs. The development is being carefully monitored at the BfR.

Veterinarian Annemarie Käsbohrer sucks a cloudy, watery liquid from a thin tube with a pipette. She spreads it onto a gelatinous substrate in a plastic dish. Routine in a microbiological laboratory. But it's tricky work nonetheless because the tubes contain foodborne bacteria that antibiotics have no effect on – potentially dangerous pathogens. They originate from regional state laboratories which have sent the microorganisms to the National Reference Laboratory for Antimicrobial Resistance for further testing. Professor Annemarie Käsbohrer and her team examine here how pronounced the resistance is. Her laboratory is an important player in the struggle against a medical scourge of our times – durable pathogens that resist medication.



2,400 deaths every year

Just how dangerous antimicrobially resistant pathogens are can be seen from a glance at the statistics: according to the Robert Koch Institute, every year roughly 54,500 people in Germany become infected with pathogens that are resistant to several antibiotics, i.e. multi-resistant. Almost two thirds of them take ill in hospital. Approximately 2,400 people die every year after becoming infected with multi-resistant bacteria. The topic has also taken root in public awareness in the meantime. According to the BfR Consumer Monitor, 89 percent of respondents have heard of antimicrobial resistance. Two out of three are concerned about it.

Antimicrobial resistant bacteria propagate above all where drugs are frequently administered – to patients in hospitals and to housed livestock. Whereas methicillin-resistant *Staphylococcus-aureus* (MRSA), which are dreaded in hospitals, tend to be insignificant as foodborne bacteria, other antimicrobial resistant pathogens – intestinal bacteria such as Salmonella, *Campylobacter* and *E. coli* – deserve more attention. They are regularly detected on raw turkey breast and chicken legs. Although they are killed off by sufficient boiling, frying and roasting, they can cause illnesses in the digestive

tract or pass on their resistance to other bacteria if they spread to other foods such as salads or bread before cooking. As soon as pathogens of this kind enter the world they become a problem – because several antibiotics have no effect on them.

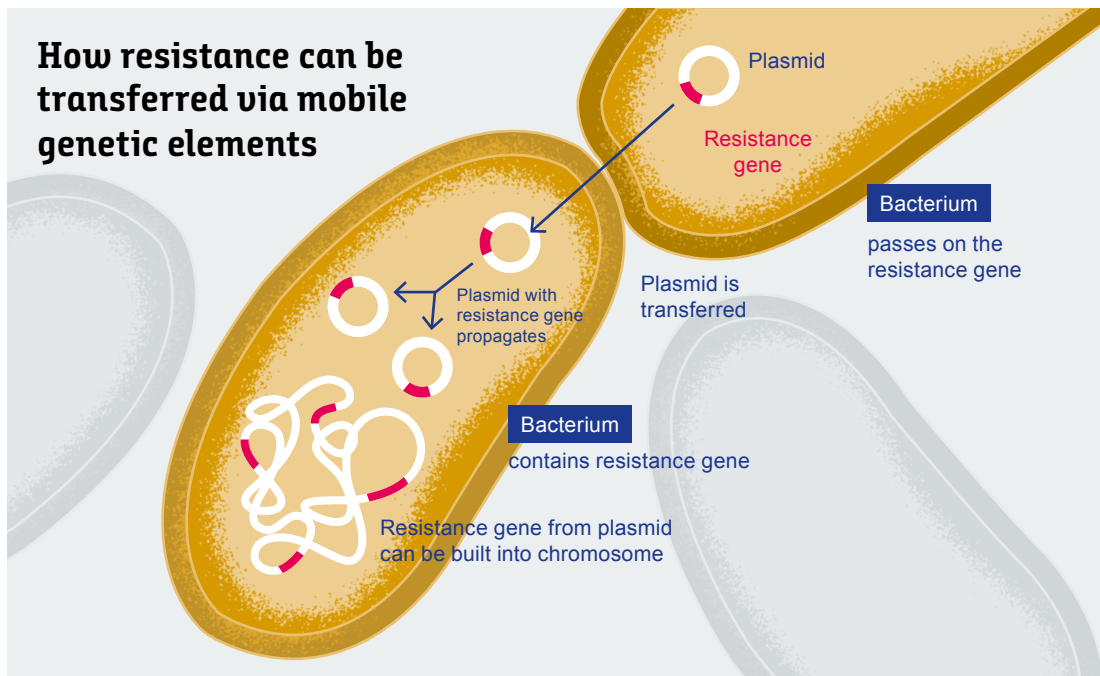
Focus on resistance to reserve drugs

Back to the BfR labs. Special methods are developed here to recognise antimicrobial resistant pathogens. Professor Annemarie Käsbohrer is the head of the reference laboratory for antimicrobial resistance and one of the experts on pathogens that can be transferred via food. She and her laboratory team examine bacteria such as Salmonella and *E. coli*, a basically harmless intestinal inhabitant which can, however, pass on resistance to pathogens. They also test bacteria which form the enzyme ESBL which destroys a range of antibiotics. Certain resistances are of particular interest to Annemarie Käsbohrer and her team: the resistance to colistin and to carbapenems. “Bacteria on which these active substances have no effect are a big problem. Medications with colistin or carbapenems are the last weapon against bacterial infections when other drugs no longer have any effect.” They are the last reserve.



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Bacteria with antimicrobial resistance can survive easily and propagate on turkey and chicken meat.



Ingenious defence

Colistin dissolves the outer cell membrane of certain “gram-negative” bacteria. The microbes succeed in warding off this attack with the help of the resistance gene *mcr*. The “defence gene” contains the assembly instructions for a protein which makes the attachment of colistin to the cell membrane more difficult. The colistin attack is repelled. Research in recent years has shown that the *mcr* gene occurs above all on transferable genetic elements. These plasmids are independent of normal bacterial genetic information. It is thus comparatively easy to transfer resistance to other bacterial species (see chart), including those that occur in humans. The problem here is that the antibiotic is used increasingly for the treatment of infections in humans when no others work anymore. If these resistant bacteria therefore find their way from livestock to humans via food, it is feared that all therapeutic options will be exhausted.

The second problematic resistance Käsbohrer and her team are after is the one to carbapenems, which are also reserve antibiotics in human medicine. “In recent years, we have sporadically been detecting carbapenem-resistant bacteria,” says Käsbohrer. “They are Salmonella and *E. coli* that occur in pig farming.” This is happening even though carbapenems are not used in livestock. The bacteria form a protein which chemically alters the carbapenem, thus inactivating it. This resistance is also easily transferrable between bacteria. New findings indicate that pathogens which have not been monitored up to now, such as *Vibrio*, can also be the carriers and distributors of carbapenem-resistance.

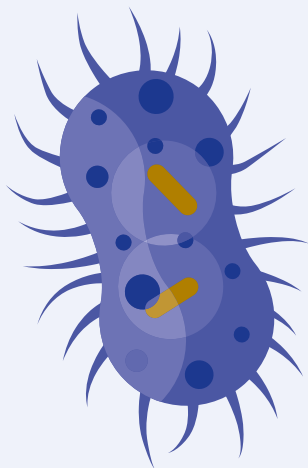
Reserve antibiotics

Antibiotics can be classified into various classes according to their structure and mechanism of action. Active substances from the carbapenem class, for instance, cause bacteria to burst. There are further developments of every class of antibiotics in order to have effective drugs on hand despite the occurrence of resistance. If antibiotics used up to now fail to take effect, the medical profession has reserve antibiotics which are only used when no other antibiotics have any effect on someone with an infection. Resistance to these “last reserves” must be monitored particularly closely.



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Curb antimicrobial resistance

The BfR works in numerous research projects on the goal of reducing the risk of the transfer of antimicrobial resistant bacteria to humans via food. To do so requires more precise detection methods, for example. Here is an overview of several projects:

Europe conducting research on transferrable bacteria

The funding program “One Health EJP” (Promoting One Health in Europe through joint actions on foodborne zoonoses, antimicrobial resistance and emerging microbiological hazards) focuses on pathogens which can be transferred from animals to humans. With this European Joint Programme set to run for five years, the European Commission and involved member states are jointly sponsoring projects from the Horizon 2020 framework research programme. Joint research projects and other integrative projects and training measures deal with foodborne zoonoses, antimicrobial resistance and new infection hazards.

<https://onehealthjep.eu/>

More precise detection in the laboratory

Recording and observing the occurrence and spread of bacteria with antimicrobial resistance in animals and foods is the goal of the IMPART (IMproving Phenotypic Antimicrobial Resistance Testing) research project which is part of the One Health EJP. The methods form the basis for epidemiological monitoring.

<https://onehealthjep.eu/projects/jrp1-impart/>

Expansion of resistance in Europe

In the ARDIG (Antibiotic Resistance Dynamics) research project, a comparative examination of the spread of antimicrobial resistance is made using the example of six European countries. Humans, animals, foods and the environment are observed as part of the One Health EJP. It is recorded what influence the use of antibiotics has on the development of antimicrobial resistant bacteria in addition to climatic influences.

<https://onehealthjep.eu/projects/jrp2-ardig/>

Resistant Staphylococci and food

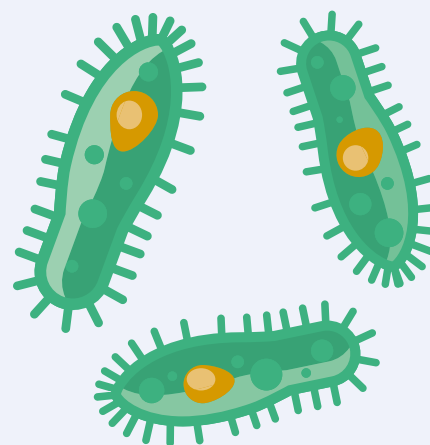
The MedVetStaph research project examined the significance of methicillin-resistant *Staphylococcus aureus* bacteria of animal origin on infections in humans. The Federal Ministry of Education and Research sponsored the interdisciplinary project from 2010 to 2018. The projects carried out at the BfR show that although the transfer of MRSA via food is possible, it is of no great significance.

<http://medvetstaph.net/>

Antibiotics in livestock holdings

The use of antibiotics in food-producing animals is being recorded in selected, representative holdings within the scope of the VetCAB project and placed in connection with information on the treated livestock. The risk assessment of the use of drugs and the derivation of preventive strategies are enabled by this continuous and systematic data collection method. The BfR is sponsoring the project and conducting it jointly with the Institute for Biometry, Epidemiology and Information Processing at the University of Veterinary Medicine Hannover, Foundation (IBEI-TiHo).

<https://ibei.tiho-hannover.de/vetcab/>



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They are everywhere

In his role as an epidemiologist at the BfR, adjunct professor (Privatdozent) Dr. Bernd-Alois Tenhagen has been monitoring for years where resistant bacteria occur in food and how they spread. He compiles the data he receives from the laboratory into trends and reports. “We regularly find bacteria with easily transferrable colistin resistance in poultry samples,” says Tenhagen. “Poultry meat should therefore only be put on the plate once it has been cooked thoroughly.” Tenhagen’s expertise is needed. For example during the annual preparation of the sampling plan for the authorities of the federal states. Based on this plan, they examine specific animals and foods for resistant bacteria. The monitoring programmes are adapted to trends every year. In addition to meat, mussels and plant-based foods like tomatoes and sprouted seeds are also examined, because resistant bacteria are popping up here too. That antimicrobial resistance can also be transferred across bacterial species is a significant finding for epidemiological research. It shows resistance is spreading – and has already spread – in a seemingly unstoppable manner.

The National Reference Laboratory discovered bacteria with mobile colistin resistance in archived samples that were taken years ago. They were not tested for it at that time because colistin resistance was regarded as non-transferrable.

Joint countermeasures

It has long been clear to experts that the effectiveness of antibiotics can only be maintained for humans and animals through close cooperation in line with the “One Health” concept. This means that the health of humans, animals and the environment is interlinked. Fundamental findings on the spread of antimicrobial resistance and pathogens between humans and animals have been made in recent years in the RESET (see BfR2GO 1/2017) and MedVet-Staph (see BfR2GO 2/2018) research networks in which the BfR was involved. Building on this, the BfR is working in European projects (see Page 10) to improve detection methods, for example. It is being examined how bacteria continue to build resistance to antimicrobial



How to protect?

Bacteria with antimicrobial resistance are also transferred via food. Only one thing helps here: hygiene in the kitchen, i.e. hand washing before and during cooking, using different chopping boards for meat and vegetables and always cooking meat thoroughly.

More information:

BfR brochure “Protection against food infections in private households”
www.bfr.bund.de/en > Publications > Brochures



substances, including reserve antibiotics. Within the German One Health Initiative for instance (see box), the BfR compares resistant bacteria that occur in humans with those from livestock and pets.

A glance at the numbers shows that the use of antibiotics in livestock farming in Germany is on the decline from 1,706 tonnes in 2011 to 733 tonnes in 2017. Bernd-Alois Tenhagen has also determined a slight decrease in resistance in the bacteria tested at the BfR. To continue this trend, he is demanding “further improvements in livestock farming so that fewer animals take ill and fewer antibiotics have to be used to treat them.” Another approach to inhibit bacteria on food, no matter whether resistant or not, is to further improve slaughter hygiene, above all with poultry. Bacteria from the animal gut often spread to the poultry meat in the highly automated slaughter process and still pose a great challenge to many abattoirs. ■

More information:
www.bfr.bund.de/en > A-Z-index> antimicrobial resistance

Together for health: The German One Health Initiative (GOHI)

Several federal institutions joined together in 2017 to come to terms with global challenges such as antimicrobial resistance. In addition to the BfR and Robert Koch Institute, the Friedrich Loeffler-Institute and Paul Ehrlich Institute are funding research projects on One Health, which are being conducted jointly by the institutes. One of the goals is to develop compatible databases to enable direct access to monitoring data on antimicrobial resistance in human and veterinary medicine and the environmental sciences in future.

More information:
www.gohi.online

”

Investigations are carried out in the BfR laboratory to establish which resistant bacteria occur in foods.



“Antibiotics are more valuable than gold for us”

Modern medicine needs antibiotics. Every time they are used, however, there is a risk of resistance – a dilemma. One Health pioneer Professor Lothar H. Wieler on the question of how valuable antibiotics can be sustained in the long term.

Professor Wieler, will there soon be no effective antibiotic for the treatment of infections like pneumonia and meningitis?

There is not so much concern in Germany and Central Europe at the moment, but antimicrobial resistant pathogens must be viewed from a local, regional and global perspective. Healthy people also carry antimicrobial resistant pathogens in their intestines, for example. They can be shed and transported. Pathogens can be carried over long distances thanks to globalisation and widespread travel. It is important to view the situation separately in each region, but to compare the monitoring data with one another. Substance classes that are important for human therapy are not authorised for use with livestock. These include reserve antibiotics for the treatment of MRSA infections in humans.

The One Health strategy processes the occurrence of resistance in both human and veterinary medicine. What have we learnt in the meantime?

That the majority of resistant bacteria – roughly 90 percent – detected in human infections originate from human medical treatment. The quantity of antibiotics used in Germany has remained roughly the same in recent years, but worldwide use is rising continuously. It's not only animals and humans that belong to One Health, by the way, pathogens with antimicrobial resistance are also transferred via the environment, especially water. That's why the waste water from hospitals in particular has to be closely watched, along with areas of intense livestock farming. The interlinked research of all federal institutions, including those from the environmental and pharmaceutical sector, is therefore important.

Where can humans get infected?

The most common source of infection with resistant bacteria is in a hospital, but infection through contaminated food is also common in Germany.

And what can be done to prevent it?

The most important form of protection against infection is hygiene – washing hands thoroughly and disinfecting them too, when necessary. And keeping away from sick, infected persons if possible. Getting vaccinated helps to reduce the use of antibiotics. Above all elderly and immunosuppressed people should get



Professor Dr. Lothar H. Wieler

As President of the Robert Koch Institute, he has an overview of the problems caused by antimicrobial resistance in the field of human medicine. Because Wieler is a veterinarian and a microbiologist, he also knows that pathogens with antimicrobial resistance are a complex phenomenon. For this reason, he helped to launch the German One Health Initiative (GOHI – see Page 12) in order to initiate research projects on the specific use of antibiotics with partners like the BfR.

themselves vaccinated against Pneumococci, for example, to prevent pneumonia. An annual flu vaccination provides protection too, because flu is often followed up by bacterial infections.

What can be done to reduce the use of antibiotics?

There are many areas. The hygiene aspect in hospitals should be given more emphasis through more, highly trained and specialised personnel. Committees at the Robert Koch Institute are recording gaps and making suggestions and recommendations. Physicians and the general public can also be given more assistance through research and specific information on how to administer antibiotic drugs as efficiently as possible. That is the essence of the problem that we have to solve: only using antibiotics in specific instances, i.e. when it is absolutely essential to do so. ■

© Moritz Wienert



Turbulent times for science

Science is taking a lot of criticism, be it because of falsified research, “predatory journals” or due to controversial or unpopular results. It is also a target of fake news. How can science assert itself in times of fake news?

No matter whether they relate to climate research or the health assessment of plant protection products, scientifically substantiated arguments come across as mere opinions which you can share or not. Hard facts are being replaced by perceived knowledge. The crisis of trust in science was reason enough for the BfR to discuss these latest developments at a conference with renowned experts.

In theory at least, the problem of fake news is easy to solve. “Truth is the conformity of a statement with whatever it is made about,” quotes Bernhard Kühnle, head of the Food Safety and Animal Health department at the Federal Ministry of Food and Agriculture, from the Duden dictionary at the beginning of the conference. Science is indispensable on the way to finding this truth, in areas such as consumer protection. Its assessments form a solid basis for reliable decisions from consumer protection institutions and food companies in Kühnle’s view, and they should also help the general public to decide in favour of a healthy diet. “Science must be strengthened and protected as a reliable source,” says Kühnle. It helps to defend against fake news.

Many people live in a social media bubble and believe everything they read there, says Alois Gerig (CDU/CSU), chair of the parliamentary (Bundestag) Committee for Nutrition and Agriculture. “They allow themselves to be manipulated.” An example of this, according to Gerig, is the unobjective and occasionally hysterical discussion of plant protection products with

the active substance glyphosate. There were suddenly 80 million experts in Germany who were all driven in one direction by the media. Among them, says Gerig, is a tendency towards “emotionalisation, moralisation and polarisation”. The boundary between facts and opinions gets blurred and there is less reporting on issues with a complex scientific background. “To distinguish between fact and fake has become much more difficult in the age of the internet,” says Gerig.

A forger at Stalin’s court

Are there fakes in science too? Professor Dr. Dr. Andreas Hensel, President of the BfR, knows several facets of a multifarious and essentially not really new topic. In Stalin’s Soviet Union in the 1930s and 40s, Russian biologist Trofim Lyssenko faked experiments which were intended to prove the transformation of species. Fraud is not always as obvious as it is with the manipulation of data and test results. The random utilisation of methods and results until they fit in with the concept (cherry picking) is a popular method, as is the one-sided – often ideologically motivated – interpretation of results.

There are various motives for deception, from career advancement, the struggle for funding, publication pressure (“publish or perish”) or maintaining a good reputation. The consequences of fake science should not be underestimated. The credibility of science among the general public is damaged. Falsified study results also lead into dead ends when assessing health risks, for example, or when attempting to reproduce results.



Risk assessment: Is science failing?

Risk assessment is lagging behind its opportunities, criticises Professor Wilfried Kühling from the University of Halle-Wittenberg and scientific advisory board of the NGO Friends of the Earth Germany (BUND), using the example of the prevention of leukaemia in children near high-voltage cables. According to Kühling, it has been scientifically proven that the risk of leukaemia in children increases significantly from a field strength of roughly 0.2 microtesla. Protection against magnetic fields in the vicinity of power lines must therefore be increased significantly. “Is science failing here,” asks Kühling. Where standards and limit values are concerned, the verdict of science alone is not sufficient. In addition to the scientific experts, social groups have to be included. “The solution lies in a joint assessment process,” says Kühling.

Uncertainty is strength

Although life is full of uncertainty, we manage to get along with it quite well. We only expect complete certainty from science. Those who don't spread absolute certainty here are quickly regarded as dubious. Some areas of climate research are criticised as being fake because science is still forced to juggle with possibilities. This, however, is the strength of science, in the opinion of philosopher and physicist Rafaela Hillerbrand. “Scientific statements are reliable not despite but because of their uncertainty,” says the professor at the Karlsruhe Institute of Technology. “I can't make the same demands on accuracy when predicting climate change as I can with Newton's laws of gravity.” Those who discredit research for this reason are disempowering the scientific method as such, says Hillerbrand – a dangerous move.

The discussion about fake news is “less about false facts but above all about a lack of trust in expertise”, ascertains science journalist Volker Stollorz (see interview Page 18) of the “Science Media Center”. The lack of trust in experts plays into the hands of powerful people with other interests. These people “have recognised how you can spread the most absurd things on communication platforms if you know how to manipulate others”. This tends to be specific disinformation rather than fake news: “Deliberately distorted information secretly fed into the communication process with the goal of deceiving and manipulating”.

Fake journals don't mean fake science

A certain scepticism towards science doesn't only exist in the general public but also within the scientific community itself, as neuroscientist Professor Ulrich Dirnagl (Charité – Universitätsmedizin Berlin) documents using the example of a survey conducted by “Nature” magazine. According to this survey, 90 percent of researchers hold the view that scientific results can only be believed to a certain extent, perhaps because some results cannot be repeated in other studies. The devastating criticism of influential media concerning “rip-off journals” in line with the motto “Fake science – the lie makers” misses the point, however, says Dirnagl. Just because science is published in a “predatory journal” doesn't mean that it has been faked.

A real problem in Dirnagl's view is the non-publication of data, often because it simply “doesn't fit in with what we're doing”. Depending on the area of specialisation, this applies to 40 to more than 50 percent of studies, the physician estimates. The compulsion for success distorts results too. Using statistical tricks, results are manipulated until the story “fits”, which is where the expression “story telling” comes from.

Science: reliable but uncertain

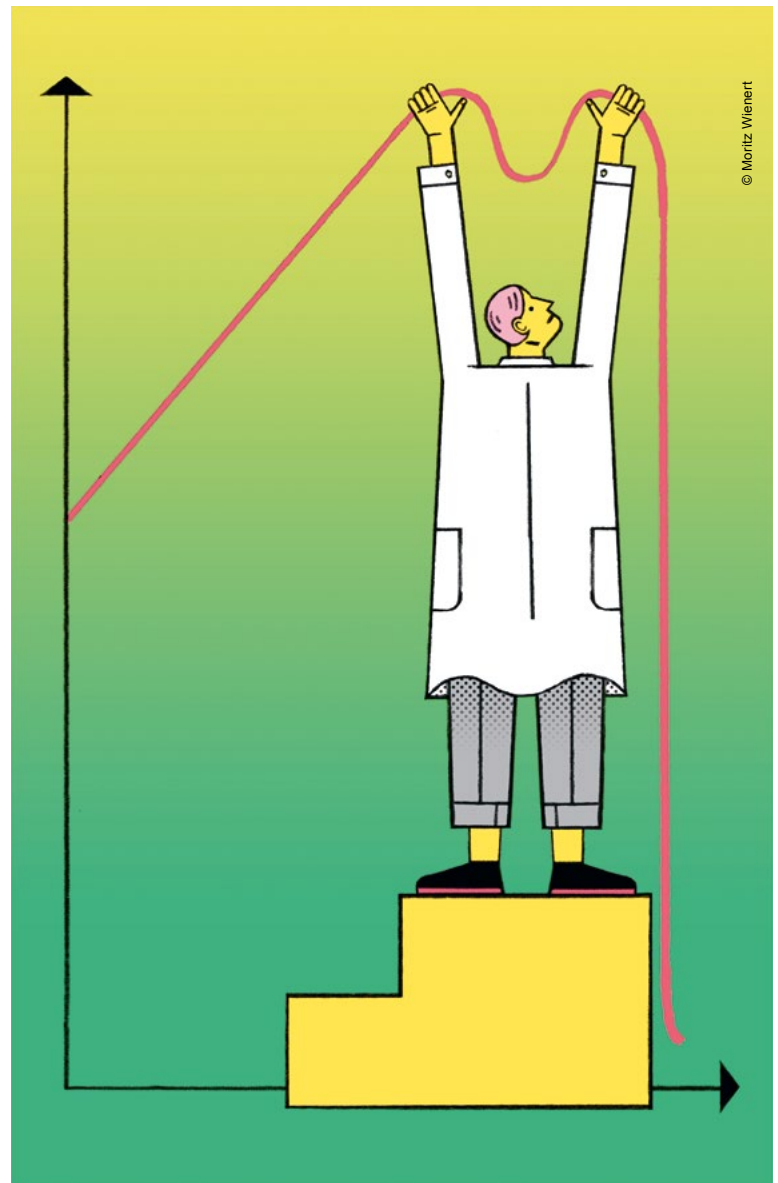
For Dirnagl, the “elephant in the room” is the term “uncertainty”. In science – as similarly stated by the philosopher Rafaela Hillerbrand – it is central to everything, not as a weakness but as a strength, as knowledge of the possibilities and limits of cognition. Dirnagl proposes that this strength be made a topic of public discussion. A differentiated assessment is not possible in a “seven second statement” or a single tweet, however.

Media scientist Professor Thomas Hestermann of Macromedia University (Berlin and Hamburg) argues that people expect reliability and not uncertainty from science. Journalist Volker Stollorz also sees science as a “mental sewage plant” which provides knowledge as the basis for political decision-making. Affirmation of uncertainty, on the other hand, would be instrumentalised by politics. The motto “Everything is uncertain” would be used to justify doing nothing in issues such as climate change.

If you research the internet, you will find many “truths”. “A whole world exists there which has absolutely no interest in facts,” says BfR President Andreas Hensel. Everyone has to ask themselves how trustworthy the information on their own smartphone is. Will knowledge ultimately become a question of belief again? ■

This text is an abridged version of the report on the 7th BfR stakeholder conference, which took place on 15 November 2018 in the auditorium of the Kaiserin Friedrich Foundation in Berlin-Mitte.

More information:
BfR Communication No. 041/2018 of 13 December 2018



“It is not always easy for amateurs to filter the right things out of the internet”

Biologist Volker Stollorz is a science journalist who heads the Science Media Center Germany, an independent source of scientific information. His organisation offers specialised knowledge and estimations to journalists whenever science hits the headlines.

Volker Stollorz, how has the internet changed the way amateurs and journalists access scientific information in your view?

The acquisition of knowledge has been democratised. Scientific knowledge is more freely accessible nowadays. When I started work as a science journalist in 1992, there was virtually no internet. We needed the “Oeckl” for our research, an address directory of important public institutions. You called up and if you were lucky, you got an expert on the line who could help you. The search for experts has become much easier for journalists and for amateurs too.

The BfR is involved with the risks of consumer products, food and chemicals. How has public perception changed?

What’s new is that the BfR as a scientific institution can communicate directly with the public through the internet, whereas journalists used to be required to open doors. With some scientific institutes, I get the impression today that they believe simply putting their content into the web and twittering is effective scientific communication which the general public will access. That is of course only very rarely the case. Reaching the general public is an art generally to be found in journalism.

The internet has facilitated access to knowledge – does this have disadvantages too?

In their dealings with science, amateurs and often professional journalists too are easily susceptible to the illusion that they believe to have understood something without this actually being the case. They are not aware of their own incompetence in the assessment of knowledge. Filtering out what is correct, important and helpful in the decision-making process from the flood of information that circulates in the internet is not easy for the layman. It can work, but it can also fail spectacularly.

What can be done about this?

What is needed above all is trustworthy institutions through which correct and important information is made available and which provide credible evidence. You still have to find them then, however, in the “jungle” of the internet, because a lot of interest groups with plenty of resources are in there too. They don’t care about correct, important and useful information, all they are concerned with is advertising and in the worst cases, disinformation. Journalism as the gatekeeper used to simply filter out a lot of the “information rubbish”. People who look on the crisis in the journalistic media today with schadenfreude should remember this.

Apropos fake news: where is the border between freedom of expression and the intentional spreading of fallacy?

I’m not a fan of that expression, I prefer to talk about disinformation along the lines of “science doesn’t know exactly either, so we should just do nothing to begin with”. The tobacco industry was tremendously effective here when dealing with the health risks of passive smoking. Of course we have to distinguish between opinion and information. There is no law that prevents people from believing complete scientific nonsense, but deliberately spreading false information to a massive extent doesn’t come under the freedom to express an opinion in my view. There are limits here. A pharmaceuticals manufacturer isn’t allowed to claim either that his drug can cure cancer if this is not the case.

Is fake news not a bit outdated? People have always concealed, twisted or falsified the facts when it suited them.

Without a doubt, there has always been propaganda. Today, however, it is possible to approach certain population groups online without the rest of the world finding



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What is needed is trustworthy institutions that provide correct and important information.

out about it. Everyone in social media lives in their own little bubble where they are fed with special “information” and are no longer directly involved with the opinions of others. I think this will be extremely dangerous for democracy if we don’t learn to do something about it.

The media is being criticised too; they are being accused of partiality and manipulation. Should that not be a cause for reflection?

The struggle for clicks puts serious journalism under pressure. It is not possible to procure scientifically sound information within a short space of time – we’re talking about seconds here sometimes – or to get credible experts in front of a microphone. As two institutions obliged to search for the truth, journalism and science are basically in a similar position here.

In what way?

Science may not simplify complex information either to the extent that it is ultimately wrong. It also has to communicate uncertainty, because science also has to contend with a loss of trust. It is often accused of being “bought”. If it is not about the search for reliable knowledge, however, and the only discussion is about the struggle of interests, then democratic communication is no longer possible. ■

More information:
www.sciencemediacenter.de

Hygiene professionals in the kitchen?

In a current survey, the BfR takes a closer look at the cooking and hygiene behaviour of the German population.

98%



People do their own cooking with fresh ingredients in 98 % of all households – on average five times a week. People even cook every day in one third (34 %) of households.

9%

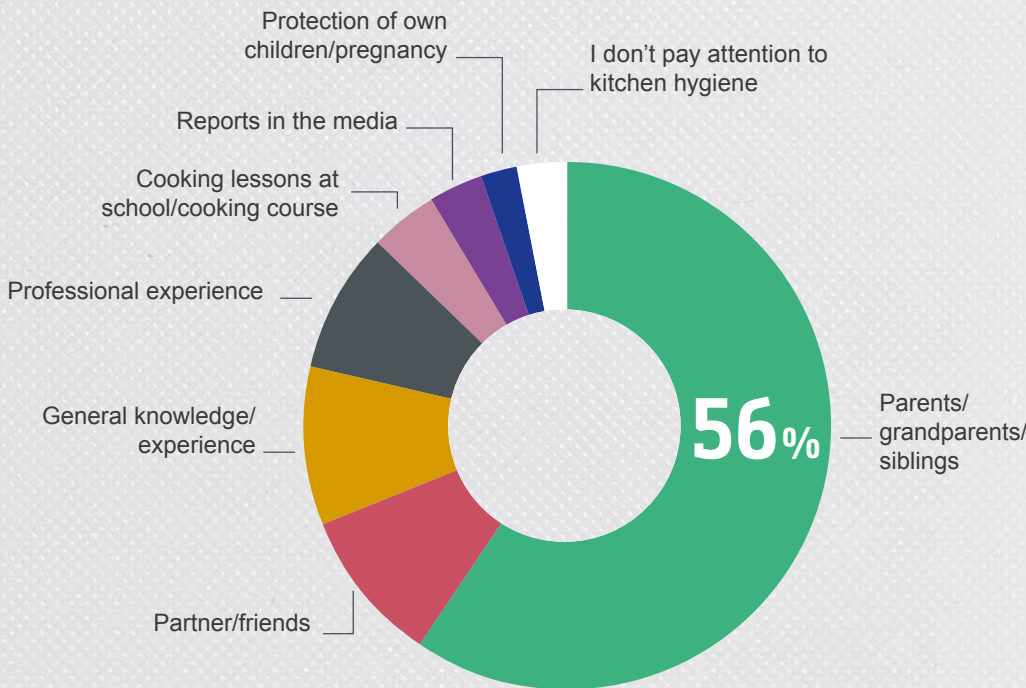
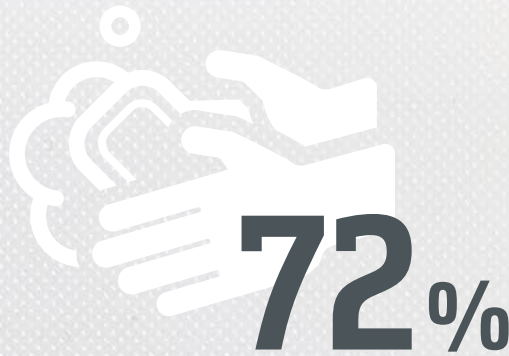


Nine percent of respondents have suffered a food infection at least once. The vast majority suspect an external location, such as a restaurant or canteen, as the source of the infection, whereas 3 % believe that they contracted it at home.

Study details:

Representative telephone survey of 1,003 persons in Germany in the period from January to February 2018

As per self-report, almost three quarters (72%) of all respondents pay strict or very strict attention to hygiene when cooking. Hand washing is regarded as a particularly important measure, especially before beginning preparations.



Social role models, above all in the family, appear to play an important role in hygiene behaviour. When asked who or what had had the greatest influence on hygiene behaviour in the kitchen, more than half of all respondents named family members, followed by other persons from their close social circle.



The joint in the milk glass

Industrial hemp is experiencing a renaissance at the moment. As a traditional feedstuff, it could be an alternative to feed resources that are becoming ever scarcer. If industrial hemp is fed to dairy cows, pharmacologically active substances could find their way into the milk.

Ten dairy cows are standing in the shed. Five of them are ruminating peacefully and there is nothing conspicuous about their behaviour. The others seem to be dazed, sleepy, uncoordinated and have stopped ruminating. Scientists at the BfR observe the animals during a feeding experiment. They regularly measure the animals' heart and respiratory rate and take milk samples. The cows are fed over several days with industrial hemp silage containing different levels of THC. THC stands for tetrahydrocannabinol, a substance which affects the central nervous system so that body functions and behaviours change. It is obvious that the cows whose feed contains higher THC doses are "stoned". Their milk also has higher THC levels than that of cows that were fed low-THC feed.

What is THC?

THC influences the psyche. It is also referred to as a psychoactive substance. Up to 90 percent of the THC is available initially in a preliminary stage as tetrahydrocannabinolic acid, THCA. THCA does not yet alter consciousness; it only converts to psychoactive THC through sunlight and warmth. The effect is triggered above all by Δ 9-THC. When ingested orally, it disturbs the sequences in the central nervous and cardiovascular systems and causes intoxication. Its main effects are lethargy and tiredness.

Hemp seed, cake, oil, flour and fibre can be used as feed material in the EU if it is produced from authorised hemp varieties. The level of psychoactive Δ 9-THC in authorised varieties may not exceed 0.2 percent. By

way of comparison: so-called drug hemp contains over 1 percent Δ 9-THC. But whereas consumers of drug hemp usually use less than one gram of this, a cow can eat several kilos of industrial hemp every day.

Hemp as animal feed

No reliable data is currently available on the THC transfer from industrial hemp used as feed to foods of animal origin. To date, there have only been laboratory experiments but no practical examinations. The BfR is measuring transfer for the first time, i.e. how much Δ 9-THC actually reaches the food – in this case milk – depending on the varying Δ 9-THC levels in the animal feed. "The feeding and transfer experiments are intended to clarify whether, depending on its THC content, industrial hemp is suitable as a feed material for dairy cows," explains Dr. Markus Spolders, who is coordinating the study at the BfR.

Cannabinoids are distributed in different concentrations in the hemp plant. The leaves and inflorescences have the most glandular hairs which produce the THC-containing resin. The seeds and roots, on the other hand, are free of glandular hairs. Above all hemp seeds and the oil made from them are rich in fat and protein – a long-known feedstuff for cattle, pigs and chickens which has all but completely been displaced in recent years by protein feeds, such as soy and rape. The whole plant, which is rich in raw fibre, would also be a valuable feedstuff provided that the Δ 9-THC levels do not pose a health risk. By-products from the cultivation of industrial hemp could then be fed to dairy cows. Industrial hemp is cultivated in Europe above all to acquire hemp fibres for insulation materials in the automotive and construction industries, or fibres for the manufacture of textiles.

THC transfer to milk

The levels of psychoactive Δ 9-THC analysed in milk vary very strongly. "They depend more than anything else on the industrial hemp variety fed to the animals and the duration of feeding," explains Spolders. "The mean levels lay within a range which was also analysed in a nationwide food monitoring of various hemp-containing foods." The BfR established for these foods that they contain too much Δ 9-THC and that health impairments are therefore possible. This also applies to the level of Δ 9-THC analysed in the milk of the cows from the transfer experiment. Once the hemp silage had been discontinued, the cows behaved normally again; they were bright and lively and resumed rumination. Their milk no longer contained any Δ 9-THC either. ■

Stoned from food?

Hemp in snacks, breakfast cereals and tea – many foods and food supplements containing hemp can be bought in Germany in the meantime. The BfR assessed in a model calculation whether the Δ 9-THC they contain poses a health risk. The results showed that the Δ 9-THC levels measured in the products are often so high that they may have an effect on the central nervous system. They can trigger health risks such as mood swings or tiredness, above all in children and people who eat large quantities of hemp-containing foods. The BfR recommends that manufacturers should further reduce the levels of Δ 9-THC contained in their products.

More information:
BfR Opinion No. 034/2018 of 8 November 2018
(in German)



Digital Tracing

Special software known as FoodChain-Lab is now used if there is an increase in foodborne diseases due to a particular pathogen. It helps to recognise the source of the infections or impurities, with the goal of identifying the “culprit” of a food crisis.

The investigation of the hepatitis A outbreak took several months. Several hundreds of people all over Europe became infected with hepatitis A viruses in May 2013. These viruses cause acute inflammation of the liver and are transmitted from person to person or via contaminated food.

Tracing back the culprit more quickly

“The investigation of the hepatitis A outbreak was the breakthrough for FoodChain-Lab,” reminisces Dr. Armin Weiser, mathematician at the BfR. FoodChain-Lab is software with which data on the sale and distribution of food is recorded. The BfR developed it in the course of the EHEC crisis in 2011 and it can be used to investigate dangerous foodborne outbreaks. The special feature of this software is that it process-

es the huge amount of data collected in the search for clues and visualises the results immediately. Doing this same job manually used to take up a lot of time.

On-site tracing

The search for clues begins with an Excel table into which the authorities enter the most important information on-site. Who ate which foods where and when? Where and when were the foods purchased? The authorities make inquiries in private households, in restaurants and along the entire supply chain with dealers, distributors, manufacturers and primary agricultural producers, all of whom have to present the delivery documents. In this way, a total of 6,227 stations were identified within the investigated goods flows in the course of the trans-European hepatitis A outbreak.



Together with a team of nine, mathematician Dr. Armin Weiser develops and guides software solutions with which foodborne outbreaks can be investigated.

99

The investigation of the hepatitis A outbreak was the breakthrough for FoodChain-Lab.

With this data the scientists used FoodChain-Lab to visualise a map of Europe on which many circles appear. These represent the places on which the data were collected. If a circle is red, an infection occurred there. In this way, it is estimated for every food and every station how great the probability of a connection to the outbreak is. The software also recognises geographical connections. One commonality found during the hepatitis A outbreak was that the people who took ill at all infection sites had eaten deep-frozen blackberries from Bulgaria and redcurrants from Poland.

Networking becoming more and more important

The hepatitis A outbreak shows that the investigation of foodborne outbreaks is becoming more difficult as goods flows become more complex and global, especially in Europe with its single market and free movement of goods. FoodChain-Lab has become an important tool here to simplify collaboration among the different countries so that the source of an outbreak can be identified more quickly. That is why the European Food Safety Authority (EFSA) and the BfR have had an official cooperation agreement in this area since 2017. One of the goals is to further develop the software and make it available to other EU member states for the investigation of future outbreaks. In addition to this, Armin Weiser and his team are holding workshops at European partner authorities to teach personnel how to handle the software. “We would also like to make the software available to official food control authorities,” says Professor Karsten Nöckler, head of the Biological Safety department at the BfR. “By doing so, it would be possible to retrace the flows of goods more quickly both regionally and supraregionally in the event of foodborne outbreaks in Europe, because we would have a uniform data standard.” The success of the training can be seen by the fact that the software is already being used specifically by authorities in the UK and Austria.

Another advantage is that FoodChain-Lab is freely available as open-source software. The BfR has continuously further developed it in recent years and developed new modules. Accordingly, there is a desktop version, and a web-based application is to follow this year. There are also other programs, such as software that helps to find out where bacteria can propagate easily during the food production process.

Demand for tools to support the investigation and analysis of foodborne disease outbreaks will increase. Armin Weiser is sure of this and hopefully states: “We need more colleagues in every institution and local authorities too with a high degree of affinity to software and digital data. That would be a great help towards deploying tools like FoodChain-Lab to great effect.” ■

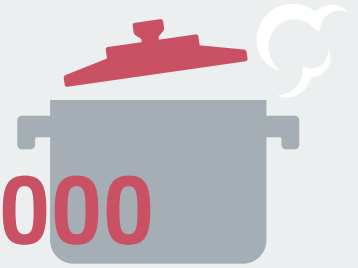
More information:

<https://foodrisklabs.bfr.bund.de/foodrisk-labs>

What's for dinner?

What is really in our food? The BfR MEAL Study is looking for answers to this question. The study examines for the first time on a large scale in Germany which substances in what amount are contained in prepared food.

60.000



Around 60,000 foods are being processed into meals in the study kitchen in the manner they are typically put onto the plate in Germany – potatoes as mash, chips or fried potatoes, for example. The reason for this is that the levels of substances can change during preparation. Vitamins get lost when cooked and certain potentially health-damaging substances such as acrylamide only occur when preparing food, through intense heating, for instance.

90%



More than 90 percent of the foods most commonly consumed in Germany are being examined in the study. Add to this some rarely eaten foods, such as squid and porcini mushrooms, which can have particularly high levels of undesired substances.

300



The BfR is examining the prepared foods for 300 substances, including desired substances like nutrients, as well as undesired substances like dioxin.



Methylmercury levels more than four times higher were discovered in smoked tuna as opposed to canned tuna. This is one of the first results of the BfR MEAL study. Smoked tuna is eaten far less often in Germany than the canned variety, however.

The study provides answers to the following questions:
Which substances in what amount are contained in our food?
Do contamination levels in food vary by region, season or cultivation method?
How can consumers minimise health risks by themselves through their choice of foods and their preparation?

More information:
www.bfr-meal-studie.de

Food supplements containing piperine

Piperine is a natural compound of different pepper varieties. It is added to certain food supplements, i. a. with the intention of improving the bioavailability of other ingredients. As opposed to ingestion via the normal diet, people who use these supplements ingest piperine in isolated form all at once (as a bolus), without the simultaneous intake of other pepper ingredients. The BfR has assessed health risks of administration of isolated piperine boluses and recommends that adults should not ingest more than 2 milligrams of isolated piperine per day via food supplements. The BfR advises pregnant women not to use products of this kind because embryotoxic effects were observed in animal studies after high bolus doses had been administered over several days. In other studies, test animals' ability to reproduce was impaired following administration over several weeks. In human studies involving lower bolus doses, interactions with drugs occurred. Such interactions may increase the risk of excessive, detrimental enhancement of effects of certain concomitantly administered pharmaceuticals.



© MayerKleinostheim/Stockphoto



Opium alkaloids in food poppy seeds

Poppy seeds have a typical taste and are rich in fat and protein. For this reason, they are often used for the production of bread rolls, cakes and cooking oil. Analyses conducted by food monitoring authorities revealed that food poppy seeds can contain larger quantities of the opium alkaloid thebaine. The health risk posed by the consumption of poppy seeds cannot yet be conclusively assessed by the BfR because, among other things, there is a lack of reliable data on the toxicological effects of thebaine. The BfR recommends the investigation of the hazard potential of thebaine and other opiates that occur in poppy seeds in addition to morphine and codeine. As a basic principle, levels of pharmacologically active opium alkaloids in poppy seeds should be reduced as far as technologically feasible. Mature poppy seeds used for food production do not naturally contain any opium alkaloids, however, during mechanical harvesting they can become contaminated with alkaloid-containing latex stemming, for example, from the capsules.

More information:
BfR Opinion No. 018/2018 of 5 June 2018



Robust insects

Supplying the growing world population with high value protein poses a great challenge. Edible insects could be an answer, but how safe is consuming beetles, locusts & Co? In a joint project with the University of Bremerhaven, the BfR found that larvae of the flour beetle do not accumulate toxins produced by mould fungi (mycotoxins) from their food and that they can even excrete these health-damaging substances. In the study, insect larvae were fed with a cereal-based diet containing the mycotoxin zearalenone. Zearalenone is one of several mycotoxins of significance in cereal. To excrete mycotoxins almost completely would be an advantage of insects over cattle and pigs for which a transfer to meat and milk is observed. Whether these findings are an indication of general detoxification processes is being examined in other studies.

More information:
Niermans et al. 2019. Feeding study for the mycotoxin zearalenone in yellow mealworm (*Tenebrio molitor*) larvae – investigation of biological impact and metabolic conversion. *Mycotoxin Res.* doi: 10.1007/s12550-019-00346-y (Open Access)



Used as a packaging material, in deodorants and in dishes, the metal is found in many products of daily use and in food, too. The BfR is investigating how the nano form of aluminium takes effect in the human body.

Aluminium is the most common metal in the earth crust. As a trace element, it has no known function for the human body, but it is controversial from a health point of view. The principles of action of aluminium on the human body have not yet been fully understood. Add to this the question as to how aluminium affects human health when it is ingested via food in the form of nanoparticles. Generally speaking, special properties are attributed to nanoparticles, such as increased reactivity or additional uptake to human cells. These general statements must be examined and assessed for every single nanomaterial, however, and that is precisely what the SolNanoTOX project is doing.

Aluminium is a common nanoparticle in the environment

SolNanoTOX is a Franco-German cooperation project in which the BfR is involved along with the French ANSES institute and the universities of Rennes and Leipzig, and which is being funded by the German Research Foundation (DFG) and the French Agence Nationale de la Recherche (ANR). In the project, various aluminium-containing nanoparticles are being examined, together with water-soluble salts, representing the most common forms of aluminium in the environment: metallic and mineral aluminium. Metallic particles are aluminium in its pure form, such as manufactured aluminium sheets or foils, whereas mineral particles occur naturally as aluminium oxides.

Solubility determines uptake by the body

Nanoparticles can dissolve in water or biological fluids such as digestive juices, thereby releasing metal ions into their environment. The project observes how digestive juices influence this solubility, because the sol-

ubility of the particles determines how they are taken up by the body. It was established that more metallic aluminium particles dissolve in simulated digestive juices than mineral aluminium particles. The majority of the dissolution takes place in the gastric juice, whereas a re-formation of nanoparticles was measured in intestinal juice (see chart). The uptake of aluminium



© AndreyPopov/Stockphoto

Reduce aluminium intake – how does that work?

Possible ways to reduce aluminium uptake are not using uncoated cooking utensils containing aluminium and not or only briefly wrapping up fatty, acidic or salty foods in aluminium foil. Only coated dishes are recommended as warming trays. Antiperspirants containing aluminium should not be applied immediately after shaving or to damaged skin in the armpits. Deodorants without aluminium salts are also commercially available.

into cultivated intestinal and liver cells was also examined. Whereas dissolved aluminium (aluminium ions) was hardly to be found in the intestinal cells, at least a proportion of the nanoparticles were ingested. Effects on the cells were only observed after the use of high quantities of dissolved aluminium which lay well above the usual uptake quantities.

Aluminium in nano form without effect

Although it is not possible to draw any conclusions on the real mechanisms in the body from these assays with cell models, the results of SolNanoTox permit a statement nevertheless: no “nano-specific effect”, i.e. no potentially increased health danger, is to be expected with average aluminium uptake via nanoparticles compared to dissolved ionic aluminium. It is still recommended, however, to generally reduce aluminium intake. ■

More information:

Sieg et al. 2017. Impact of an Artificial Digestion Procedure on Aluminum-Containing Nanomaterials. Langmuir, 33, 10726–10735

www.bfr.bund.de/en > Research > Third party projects of the BfR > Nanotechnology 2017

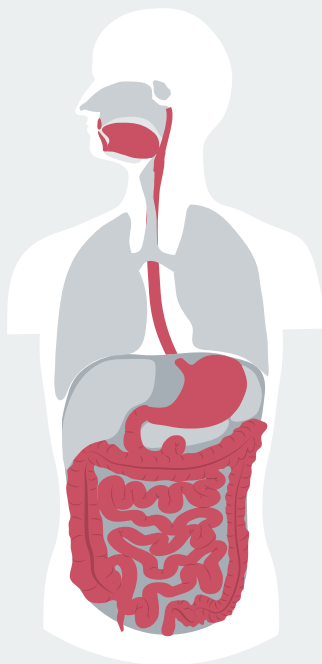


BfR junior research groups

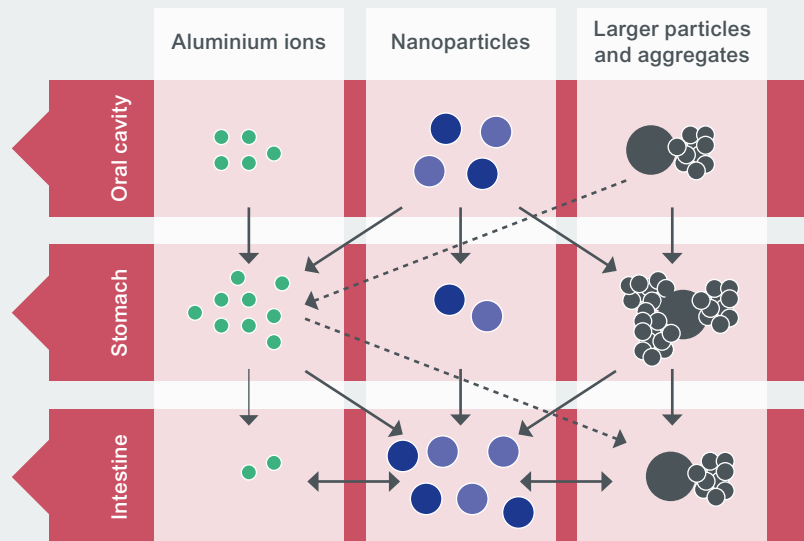
Since 2017, there have been five junior research groups at the BfR which serve to promote research along with the scientific careers of young scientists in selected key areas at the BfR. With the help of toxicological test procedures on cell models of the intestines and liver, the Nanotoxicology junior research group conducts research into nanomaterials which can find their way into the body via food. The junior research group, which also consists of two doctoral candidates and a technical assistant, has been headed by Dr. Holger Sieg (photo left) since August 2017. The junior research group belongs to the Food Safety department at the BfR.

Aluminium nanoparticles in the digestive tract

We ingest aluminium in dissolved form (ions) and as nanoparticles (mineral and metallic forms) via food. The particles can also occur as aggregates. The solubility of the particles determines how they are taken up by the body.



© Body: Tefi/shutterstock.com



The arrows show the transitions between particle form and dissolved form during digestion (thick arrows = clear transitions, thin/dotted arrows = less pronounced transitions).

The new way of smoking

When tobacco is heated instead of burned, it gives off fewer potentially health-damaging substances. Carcinogenic substances can still be produced, however.



Smoking tobacco involves great health risks. More than 90 substances in tobacco smoke are classified as carcinogenic or possibly carcinogenic. Attempts have been made for quite some time to reduce the health risk of smoking. Through technical modifications, tar levels have been lowered by roughly 60 percent since the 1950s. This did not reduce the health risk for smokers, however.

Reducing the amount of potentially health-damaging substances in tobacco smoke is an ambivalent objective. Although the technical standards for tobacco products are often improved, this does not necessarily reduce the health risks – at least not where conventional cigarettes are concerned. To give an example: cigarettes with filter ventilation dilute the mainstream smoke, so the people who smoke these “light” or low-nicotine cigarettes inhale less nicotine – but consequently reach for the packet more often or draw more deeply on the cigarette in order to achieve the same nicotine effect. Light products therefore often involve greater health risks.

New technologies without tobacco burning

Conventional smoking always involves a combustion process, so the options for a comprehensive reduction of potentially health-damaging substances are limited. New technologies are shifting these limits. Electronic cigarettes, for example, dispense completely with tobacco and produce aerosols through the atomisation of liquids. With certain liquids, nicotine can also be inhaled with the vapour. As no combustion takes place and no thermal degradation products occur, the toxicological health risks are lower than they are when smoking tobacco cigarettes, but avoiding tobacco altogether is still the best protection. Tobacco heaters, on the other hand, are tobacco products in which the tobacco strands are not ignited but heated electronically to temperatures of up to 350 degrees Celsius. According to tests conducted by the manufacturers, this technology can reduce the levels of the relevant critical substances in the smoke by 80 to 99 percent.

Tobacco heaters: Fewer harmful substances

In order to establish an independent data basis, the BfR examined the emissions from tobacco heaters currently



on sale in Germany. To do so, a standardised mechanical smoking method was used which roughly imitates human smoking behaviour. The results permitted comparison with the data from other test laboratories and with tobacco cigarettes; emissions from the various heaters could also be compared. The tests conducted by the BfR confirm that levels of relevant carcinogenic substances such as benzene and 1,3 butadiene are reduced by more than 99 percent in the smoke from tobacco heaters compared to cigarettes. The reduction for acetaldehyde, formaldehyde and other carbon compounds was roughly 80 to 90 percent. However, the tobacco heaters only gave off slightly less nicotine than conventional cigarettes.

Health significance not yet known

Whether lower health risks are also to be expected from the lower levels of potentially harmful substances is not yet clear. Although model calculations show a 90 percent reduction in tumour potency for the aerosols of tobacco heaters compared to cigarette smoke, which equates to the inhalation of smoke diluted by a factor of ten, the models are based on dose-response relationships in which it is determined experimentally for in-

dividual substances from which dose an effect is to be expected. It is difficult to derive the actual risks from this as even low doses can cause cancer and synergy effects are conceivable.

Tobacco abstinence is the best way to protect health

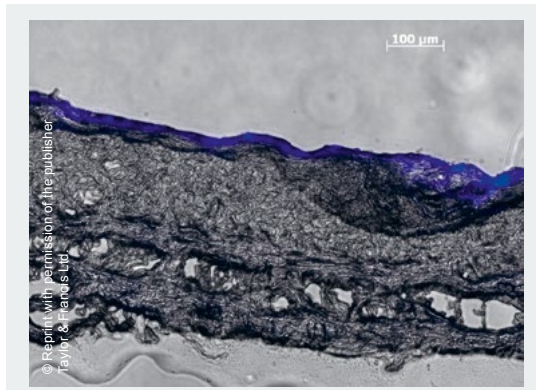
Due to the considerably lower quantities of potentially damaging substances released from tobacco heaters, the BfR expects reduced risks overall for smokers – provided that they succeed in switching completely to tobacco heaters. A quantitative estimation or assessment of the remaining health risks is not yet possible, however, for individual diseases such as cancer. Tobacco heaters do not reach the risk levels experienced by non-smokers. That can only be achieved through tobacco abstinence. ■

More information:

Mallock et al. 2018. Levels of selected analytes in the emissions of “heat not burn” tobacco products that are relevant to assess human health risks. *Arch Tox* 92: 2145. doi: 10.1007/s00204-018-2215-y (Open Access)

Permeable protective barrier

Which substances get through the skin in what amounts? Experiments at the BfR simulate how potentially health-damaging substances penetrate our largest contact organ.



Substances permeate the skin

Microscopic image of a section of human skin after contact with the material of a hammer handle containing polycyclic aromatic hydrocarbons (PAHs).

Substances can make their way into the body through many different pathways. The three most important ones are the digestive tract, the lungs and the skin. Uptake via the skin is a domain that has hardly been explored up to now with regard to risk assessment. Methods are being sought by means of which the dermal absorption of substances can be realistically estimated.

Toxic hammer grip

In 2009, headlines such as “Poison in hammer handles” and “Poison from the one euro shop” gave the public quite a scare. High levels of polycyclic aromatic hydrocarbons (PAHs) had been detected in numerous consumer products made of elastic polymeric materials, such as bike handlebar grips, gardening shoes and the shafts of many tools. Several of these, such as benzo[a]pyrene (B[a]P), are carcinogenic. As long as these substances remain in the material, they do not pose a risk to health, but what happens when people work with the tools or wear the rubber shoes all day long?

There were no science-based answers to these questions, as there was a lack of examinations and suitable tests. In a research project, the BfR developed a method with which quantities of B[a]P that are transferred from the elastic material of a hammer handle to the skin can be realistically examined upon skin contact. This approach could also clarify whether, just like other substances, B[a]P also penetrates into the deeper layers of the upper skin (epidermis) and the corium (dermis) that lies below.

Experiments with Franz cells

Tests with Franz cells were the starting point. The principle of this test is that a material sample lies directly

on a piece of animal or human skin. The skin acts as a membrane with the epidermis tending upwards and the dermal side in contact with a receptor liquid (see chart on page 34). A test run usually takes several hours. “This method is the gold standard in examinations of dermal absorption,” says project leader Dr. Christoph Hutzler. It is commonly applied in the testing of cosmetics and pharmaceutical substances. The method has hardly been relevant up to now in toxicological tests of materials. “We were able to show, however, that apart from friction or pressure, the Franz cell test imitates migration in real skin contact with hammer handles fairly well.”

Experiments were conducted with material samples from various hammer handles and a toy tyre containing known quantities of B[a]P. Epidermis from human donor skin was used as a membrane in order to establish the most realistic exposure scenario. Pig’s epidermis, artificial human epidermis cultivated in a laboratory and a synthetic membrane were used for comparison purposes. Food chemist Dr. Nastasia Bartsch conducted the experiments. After 24 hours, during which the system was kept at 33 degrees Celsius, she determined the quantities of B[a]P which entered the skin. Result: 102 nanograms B[a]P were present in one square centimetre of human skin caused by skin contact with a hammer handle containing 166 milligrams of B[a]P per kilogram material. During the process, four fifths of the migrated B[a]P remained in the outermost layer of the epidermis, the stratum corneum, and one fifth permeated to the deeper layers. Some of it even diffused into the receptor liquid.

In conclusion, B[a]P overcame the protective barrier of the epidermis and reached the dermis below that is crisscrossed with fine blood vessels. Consequently, it was concluded, the substance can also find its way into the blood circulation via these blood vessels.

A look through a fluorescence microscope revealed the permeation pathway. A blue fluorescence signal that is typical of PAHs can be seen in the images of wafer-thin skin samples from the Franz cell. This means that PAHs accumulate in the stratum corneum after contact with the hammer grip and diffuse further from this reservoir into the deeper skin layers.

New substances targeted

What happens on a cellular basis upon skin contact with B[a]P containing materials? This question was recently addressed in experiments using molecular biological methods. B[a]P from the hammer handle damages the genetic material in the nucleus of intact skin cells. This finding is of concern, because it can contribute to the development of skin cancer. For this reason, Germany succeeded on EU level in ensuring that limit values have now been set to restrict the occurrence of this potentially health-damaging substance in consumer products made of rubber or plastic. In the meantime, the team headed by Christoph Hutzler has expanded the examination method to include other critical substances present in plastics. A close eye is being kept here on various plastic additives, such as plasticisers, antioxidants and their breakdown products, which occur through the ageing of the material. The first results show that these can also overcome the outer skin barrier and permeate to the deeper skin layers to varying extents. ▀

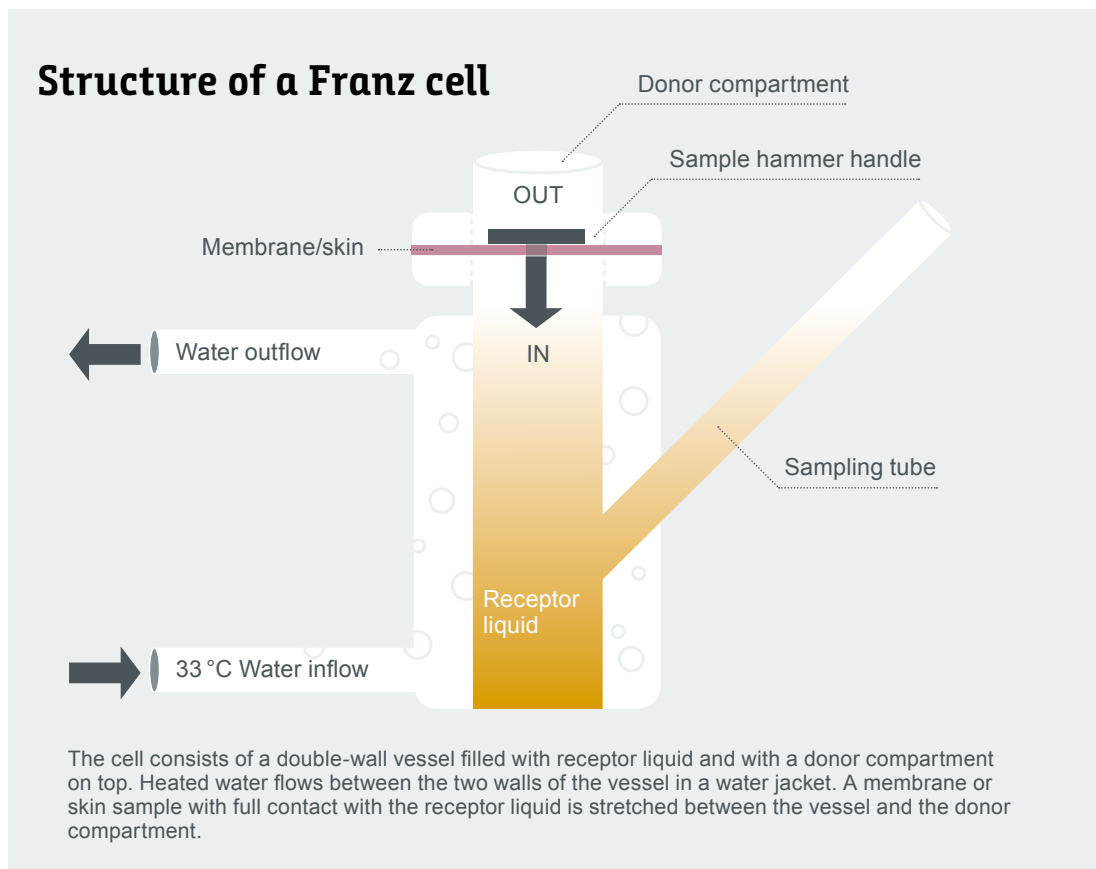
Prediction model suitable for routine use

Examinations with Franz cells are elaborate and not suited as routine tests, so is there an easier way to establish exposure values? Sweat simulant testing, which is otherwise the method commonly used for materials with skin contact, dramatically underestimates dermal exposure. If the aqueous simulant contains 20% ethanol, as shown by experiments conducted by the BfR, the material gives off the same quantity of B[a]P into the simulant compared to the human skin exposure in the Franz cell test. This prediction model developed by the BfR has been tested on national and European level and used as an examination method in the national monitoring programme. It is suitable for estimating the health risk of materials containing PAHs which have contact with the skin.

More information:

Bartsch et al. 2016. Skin permeation of polycyclic aromatic hydrocarbons: A solvent-based in vitro approach to assess dermal exposures against benzo[a]pyrene and dibenzopyrenes. *J Occup Environ Hyg* 13(12): 969–979. doi: 10.1080/15459624.2016.1200724

Dissertation paper: Nastasia Bartsch. 2019. Polymer additives, contaminants and non-intentionally added substances in consumer products: Combined migration, permeation and toxicity analyses in skin. <https://refubium.fu-berlin.de > dissertations FU>



“Biological plant protection is a challenge”

Crop plants are an essential part of human life. The Julius Kühn-Institute (JKI) is conducting research into the basic requirements for their safe and sustainable cultivation. The first President of the JKI, Dr. Georg Friedrich Backhaus, on the safety of plant-based foods and feeds.



Dr. Backhaus, the BfR assesses whether foods pose a risk to health. The JKI deals with plant genetics, plant health, cultivation methods and plant protection among other things. What are examples of common work areas?

A milestone during my time as president was the joint research projects on issues of potential bioterrorism, above all pathogens and pests on plants. I also remember the investigation of the EHEC crisis in the early summer of 2011. Working in a joint group, we examined how it was possible for disease-causing germs from the animal kingdom to find their way into vegetable plants like bean sprouts. When it became clear that sprout seeds were the likely source, we asked ourselves how great the risk was of this ever happening again. I am very grateful for the outstanding cooperation between the two institutes over many years and I wish for further intensification of this good relationship in the future.

How are the JKI and BfR cooperating in plant protection?

The roles are clearly distributed. The JKI assesses the efficacy, phytotoxicity and risks for bees, beneficial arthropods and sustainable plant cultivation of active substances and formulated plant protection products, and the BfR assesses the health risks for humans and animals. We cooperate closely, however, where the protection of users and uninvolved third parties - bystanders - is concerned. For example, we conducted joint experiments to calculate the spray drift when applying plant protection products, confirmed the data and results and developed distance values for bystanders. The results of this cooperation found access into the European approval process. A project is currently running to visualise the possible exposure of people in residential areas using

geographical information systems. By doing so, we want to determine the risk potential when plant protection products are used in the vicinity of living areas.

A ban on chemical-synthetic plant protection is often demanded. What do the biological alternatives look like?

The concept of plant protection on a biological basis poses fresh challenges to research institutes and assessment authorities. Biologicals, or biological plant protection products, often use bacteria and viruses, or else they consist of the metabolites of microorganisms or plant constituents. Products of this kind have to be tested and assessed just as seriously as synthetic plant protection products if they are to substitute them in agriculture and horticulture, but to date there are hardly any assessment methods available. The BfR and JKI will have to develop and standardise them on a scientific basis. Only then will we be able to conduct the necessary professional evidence-based assessments. Furthermore, there are still no official assessment methods in Germany for beneficial arthropods, such as beneficial insects and mites, which are artificially introduced into cropping systems for biological pest control.

Dr. Georg Friedrich Backhaus is an agricultural scientist who specialises in horticultural sciences and phytomedicine (the science of plant diseases and plant damage). Backhaus was president of the Federal Biological Research Centre for Agriculture and Forestry from 2002 to 2008. He became the first president of the Julius Kühn-Institute, which was re-established as the Federal Research Centre for Cultivated Plants in 2008. Backhaus was a member of the BfR Scientific Advisory Board from 2006 and retired in December 2018.

The transfer of substances from soil to plants used for food can also pose a health risk. What is the JKI working on?

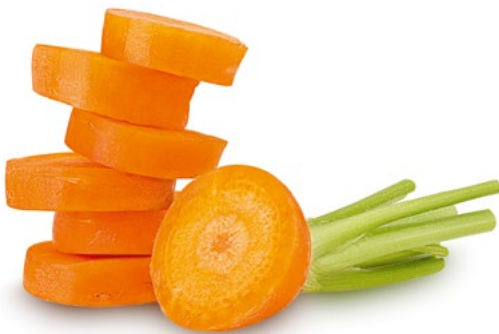
One of the things we're looking at is heavy metals in soil, especially in the root zone, introduced by fertilisers or plant protection products. An example of this is copper, which is also used in organic farming. It's not only about soil biodiversity issues and the sustainable use of soils and arable areas, it's also about whether the substance transfers from the soil into plant-based foods and whether people come in contact with it. When do higher copper levels in plant-based foods become a health concern? We need the BfR's toxicological expertise here so that we can counteract this, if necessary, by taking certain agronomical measures to minimise the uptake of copper or other undesired substances via plant-based foods. ■

SPECTRUM

Does processing alter the pesticide content?

Peeling, cooking, leavening – processing methods have an influence on the levels of pesticide residues in food. Whether marmalade or beer contain higher or lower residue levels than the raw orange or the malt is determined in processing studies. The BfR has evaluated a number of these studies on behalf of the European Food Safety Authority (EFSA) and derived specific processing factors for many different pesticide-food combinations. The processing factor indicates the factor by which the pesticide residue increases or decreases through the typical processing of food. In this way, a European database currently containing data on 143 different active pesticidal substances has been built up. These factors help to improve the risk assessment and provide monitoring authorities with the first indications of whether a processed food was made from a raw product which complied with the maximum legally permitted residue level of a pesticide.

More information:
www.bfr.bund.de/en > A-Z index: processing factors



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Don't put bamboo utensils in the microwave

Whether it's multiple use coffee-to-go cups or the set of dishes with the animal motif, the trade has a large range of "bamboo ware" on offer for children as well as adults. The brightly coloured dishes are light and breakproof and contain bamboo fibres as a filler. From a health point of view, however, these products are not all suitable for use as dishes because of the plastics that are used. Melamine resins made from melamine and formaldehyde are often used in the manufacture of bamboo ware. The BfR has established that excessive quantities of these substances transfer from the dishes to the food at high temperatures and can therefore pose a risk to health. According to the information given by the manufacturers, food in bamboo dishes may not be heated in the microwave for this reason. By the way, advertisements for bamboo ware sometimes bear statements such as "contains no plastic" or "100% natural". These markings are misleading, because they do not take into consideration that these products are also made of plastic, state laboratories and consumer protection centres complain.

More information:
www.bfr.bund.de/en > A-Z index: melamine

Lashing out

Eyelash growth serums promise long, thick eyelashes. They are marketed in Germany as cosmetic products. The active substances they contain are based on the endogenous hormone Prostaglandin F. A BfR safety assessment revealed that lash boosters of this kind constitute a health risk. The BfR bases its findings among other things on clinical studies and long-term observations with a drug authorised in the US for the treatment of reduced eyelash growth containing an active compound structurally related to Prostaglandin F. Hyperpigmentation of the skin and eyelashes was observed along with itchy, reddened eyes, changes in the structure of the fatty tissue on the eyelid and reduced intraocular pressure. In addition to this, brown pigment can permanently accumulate in the iris. Consumers can identify eyelash growth serums containing prostaglandins if an ingredient has "prost" as part of its name.



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What does

... a National Poisoning Registry actually do?

A National Poisoning Registry continuously and comprehensively records all cases of poisoning in a country. Poisoning Registries have been established in neighbouring countries, such as France and the UK, for quite some time. The German federal government is planning to set up such Registry at the BfR in the course of the current legislative period. Today, cases of poisoning are only partially recorded in this country, for example through medical doctors' reports to the BfR or notifications to regional Poison Information Centres. It will be the task of a National Poisoning Registry to compile and maintain this information on a national level.

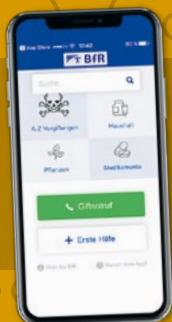
The importance of this kind of monitoring for consumer protection and product safety can be illustrated using the example of liquid laundry detergent capsules (LLC) – highly concentrated washing liquids contained in pods with water-soluble film wrapping. By collecting and evaluating information on cases of poisoning, a strongly increased risk of poisoning with LLC was detected for children some years ago. As a consequence, new safety regulations such as child-impeding package closures and improved warning notices for parents on the packaging have been implemented. The National Poisoning Registry will monitor the effectiveness of these new safety measures and will help to recognise similar high-risk products in a timely manner.

Before the Registry is implemented, tools and procedures are being developed in a pilot study. On behalf of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety in collaboration with the Society for Clinical Toxicology (Gesellschaft für Klinische Toxikologie, GfKT) and the German Poison Information Centres, a systematic collection of poisoning case data was tested for selected product groups, such as e-cigarettes, waterproofing sprays, and fish contaminated with ciguatoxins (leading to Ciguatera fish poisoning). The legal framework for the permanent cooperation and exchange of case data between the Poison Information Centres and federal authorities was reviewed in a legal expert report. The results of the study will be presented at a symposium in September 2019.

More information:

Feistkorn et al. 2019. Gesundheitsberichterstattung über Vergiftungen in Deutschland – Wissenschaftliche Untersuchung zur Einrichtung eines nationalen Monitorings von Vergiftungen in Deutschland. Bundesgesundheitsbl. 62(3):341-349 doi: 10.1007/s00103-019-02886-1 (Open Access, in German only)

Symposium on the pilot study on 24 September 2019. Information will be available here, as of August 2019: www.bfr-akademie.de



BfR app "Poisoning accidents among children"

Good to know: The BfR app "Poisoning accidents among children", which is available for free download, offers precautionary advice on how to protect children from poisoning as well as emergency assistance. An emergency call to a Poison Information Centre is also possible directly from the app. Free download for Android and iOS: www.bfr.bund.de > Presse > BfR-Apps

At the German Centre for the Protection of Laboratory Animals at the BfR Professor Dr. Lars Lewejohann is investigating how the living conditions of laboratory animals can be improved. The scientist is also a professor at the Institute of Animal Welfare, Animal Behavior and Laboratory Animal Science at Freie Universität Berlin.



Understanding Mice

Professor Dr. Lars Lewejohann conducts research into the behaviour of laboratory animals at the BfR. His goal is better living conditions for the animals – and better science at the same time.

It's all go in the cage. A ball of fur the size of a chestnut crawls through a length of transparent plastic pipe to a higher-level platform, another one is drinking at the water trough. These are house mice, scientific name *Mus musculus*, with black fur, long tail, erect ears and cute little button eyes.

In the dim light, the mice scurry through the two by two metre cage with its high plateaus, tunnels, boxes and separated areas, all of which the animals find interesting. "The mice live here almost as they do in the wild," says behavioural biologist Lars Lewejohann about the large enclosure. "They can explore their surroundings without having to worry about predators and they are provided with food – a mouse's paradise."

This paradise isn't just for the mere sake of it, however, it's part of a research project by Professor Lewejohann and his team. The scientist works at the German Centre for the Protection of Laboratory Animals at the BfR. At the Institute's Marienfelde location, he examines how the living conditions of laboratory animals can be improved. Refinement is the term used for this.

Replacement, Reduction, Refinement

Refinement is one of the three pillars of the 3R principle along with the replacement and reduction of experiments with animals. With "3R" – replace, refine, reduce – microbiologist Rex Burch and zoologist William Russell drew attention to the situation of laboratory animals around 60 years ago. "We've already achieved a lot for the animals," is how Lewejohann

describes the current situation, "but we are still not where we could and should be".

The greatest possible gain in findings with the lowest possible level of animal suffering is the researcher's credo. "Better animal husbandry is not a contradiction to good research," says Lewejohann. For the biologist, one does not exclude the other, they complement each other. Good conditions for laboratory animals lead to natural behaviour and thereby to realistic scientific results.

Early death in the wild

The scientist does not succumb to illusions about the animals leading a pleasant life in freedom. "It would be naïve to assume that all wild animals are 'happy', because the stress of survival is extreme," explains Lewejohann. "Parasites, disease and predators are constant dangers and most mice die prematurely in the wild. There is a reason why they produce so many young!" As the keepers of the animals in captivity, however, humans have to accept responsibility.

What does the mouse want? This question has been driving Lewejohann ever since he embarked on his scientific career. He tries to understand the rodents and see things from their point of view. This can only be done by closely studying their behaviour and thereby their decisions and then subjecting these to scientific interpretation. Does the animal prefer coarse or fine nesting material, does it want to be "challenged", how is boredom expressed and how can it be prevented? And do mice have something resembling a personality?

If you can answer these questions, the animals' living conditions can be improved specifically.

The nature of the mouse

House mice are sociable; the nocturnal rodents snuggle up closely together in their nests and groom one another. The little mammals are still individuals, however, and Lars Lewejohann even attributes a kind of individual personality to the animals. This is all the more astonishing as the mice used in the experiments are practically identical from a genetic point of view. It would therefore seem obvious that the rodents would not only be as identical as two peas in a pod with regard to their genetic make-up but also with regard to their character. This does not appear to be the case, however.

Biologists and psychologists have discovered some amazing things in recent years about the animals' abilities, intelligence, memory and even their moral behaviour. The idea that mice could have an individual nature is no longer all that unusual (and already an established fact for fans of Tom and Jerry or Mickey Mouse).

Discoverers and laggards

The animals can be distinguished by their behaviour inside their large enclosure. The mice, which are tagged with transponders (small transmitters), are registered

via a system of antennae which provides information on where they are and which routes they have taken. There are mice which "get around a lot", as Lewejohann says. They patrol the terrain, presumably driven by a desire for adventure and the fun of playing as they slide almost recklessly down through plastic pipes. Others are more reserved; cautiously and apparently ready for whatever might happen, they cover a comparatively small area.

A further experiment deals with the animals' mentality. An acoustic signal at the water dispenser indicates reward, another punishment. Once the mice have learnt this, they are confronted with mixed tone sequences. This is an ambivalent signal which has to be interpreted by the animals. The rodents react in different ways. The "optimists" can't be held back and head for the dispenser, whereas the "pessimists" fear the worst and stay away from it. Both of these behaviours have their advantages and may have evolved as strategies for this reason. What the animals experience immediately before they hear the ambivalent signal can also contribute towards whether they tend to react optimistically or pessimistically, however. "In this way, we can 'ask' the mice how stressful they find certain experiments, for instance," says Lewejohann, whose research is also sponsored by the German Research Foundation (DFG).

Another project is dedicated to the research of boredom. Stereotypes – always the same behavioural patterns –, a disturbed day-night rhythm (house mice are normally





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Some mice are driven by a desire for adventure and the fun of playing.

active at night) and “eating attacks” are interpreted as signs of dulling and disinterest. Lars Lewejohann and his team have come up with some ideas here to disperse the animals’ lethargy. Tricky “problem boxes”, for example, which can only be opened with skill in order to relinquish the reward they contain. Along with swings, exercise games and little houses with rotatable roofs. Some of these toys are self-built or originate from a 3D printer. Video games for mice are also being tested in the meanwhile, Lewejohann reports.

The pivotal question: What does the animal want?

The scientist’s motivation is almost tangible – to find out what the animal wants. His approach combines the topic “Improvement of animal tests” with psychology, brain research and medicine in its attempt to find out more about mental deterioration (dementia) and isolation, which mice can presumably suffer from too.

An example of the bandwidth of his scientific work is Lewejohann’s involvement in the Berlin research project “Science of Intelligence” in which he participates as a professor of Freie Universität Berlin. In this cluster of excellence sponsored since recently by the German Research Foundation, scientists from very different areas of specialisation have got together to dedicate themselves jointly to the subject of intelligence, be it animal, human – or artificial. Many disciplines are represented, from philosophy, psychology and biology to robotics and computer science. Understanding intelligence is in their view one of the great challenges of the present, and the overcoming of interdisciplinary boundaries an important step towards meeting them together.

It may appear paradox to conduct animal tests while taking a very critical view of them at the same time, but Lewejohann is enough of a realist to know that tests in the development of drugs, for example, will continue to be indispensable for quite some time. “Testing drugs directly on humans before trying them out on animals is not a road we can go down,” he says. “Our goal is to structure tests which cannot yet be replaced in such a way that they benefit the animals if this is at all possible. What also applies here is that the people who conduct animal tests must also review their own actions again and again – a great demand.” ■

More information:

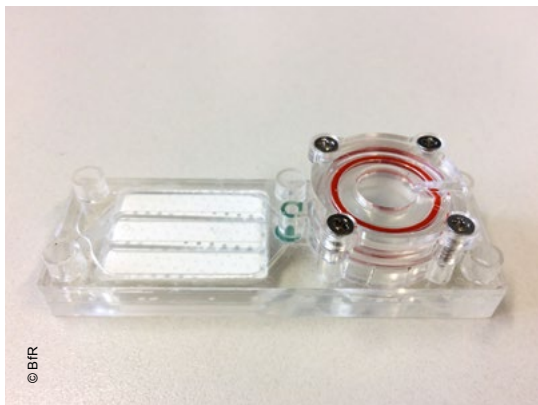
Habedank et al. 2018. Severity assessment from an animal's point of view. *Berl Münch Tierärztl Wochenschr* doi 10.2376/0005-9366-18007

SPECTRUM

Bones on a small scale

Bones not only provide mechanical support and thereby shape our body, they can be considered a dynamic and vital tissue. Blood is produced in the bone marrow, while bone diseases such as osteoporosis can considerably restrict movement and quality of life. Researchers at the BfR are now developing a “bone on a chip”. The model contains the most important cell types of bone, cultivated on a very small scale under physiologic conditions. “Organ-on-a-chip” technology makes it possible to investigate diseases, test potentially toxic substances and reduce the number of animal testing. The research team at the German Centre for the Protection of Laboratory Animals at the BfR is part of “EUROoC”, a recently founded European research network which trains up-and-coming scientific talents and further develops organ chips.

More information:
www.eurooc.eu



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Science also learns from its mistakes

Scientific studies should always be published, irrespective of their results. This is one of the conclusions of a research project conducted by the German Centre for the Protection of Laboratory Animals at the BfR. In this project, it was examined on the basis of a mathematical model what influence individual criteria of study design and publishing have on further research. One outcome was that even studies without results confirming the original hypothesis speed up the gain in knowledge. If results are reasonable and repeatable, this helps to prevent unnecessary follow-on experiments (and additional animal experiments) which would not stand up to further examination. False conclusions of studies can be easily refuted in this way. That published studies are repeatable cannot be taken for granted: depending on the survey, 51 to 89 percent of the results published in bioscientific studies cannot be reproduced by other researchers.

More information:
 Steinfath et al. 2018. Simple changes of individual studies can improve the reproducibility of the biomedical scientific process as a whole. PLOS One 13(9): e0202762 (Open Access)

Pharmacologically effective substances in animal experiments

Laboratory animals are administered pharmacologically effective substances such as tamoxifen and tetracycline in order to inactivate specific genes in various tissues at defined times. Animal models for the examination of certain diseases and underlying mechanisms are produced in this way. The legal classification of this procedure is problematical, as tamoxifen is also approved for the treatment of hormone-active tumours in humans, and its use is strictly regulated by the German Medicines Act. If its provisions applied, it would not be allowed to use tamoxifen for gene knockout in animal experiments. The National Committee for the Protection of Animals used for Scientific Purposes has now assessed the legitimacy of the use of tamoxifen in animal experimentation. The result: tamoxifen is permissible as a genetic tool and, in this case, its use is subject to the Animal Welfare and not the Medicines Act.

More information:
 Chmielewska et al. 2019. Legal aspects of the application of the pharmacologically effective substance tamoxifen in the conditional gene knockout in the experimental animal mouse [Rechtliche Aspekte der Anwendung des pharmakologisch wirksamen Stoffs Tamoxifen bei der konditionellen Genausschaltung im Versuchstier Maus]. Natur und Recht. 41: 26–32 (Open Access, in German)



Quick advice for animal welfare

A large group of experts supports the National Committee

Heart disorders, cancer, Alzheimer's or dementia – animal experiments are still necessary for a better understanding of serious diseases and development of new therapies. Genetically modified mice which contract tumours or whose brains are susceptible to an inherited variant of Alzheimer's are used, for example. Projects of this kind are of great importance for medicine and science. But how should they be assessed from the point of view of animal welfare? “We are involved in particular with the question of how much distress the animals experience due to the genetic modification,” says private lecturer Dr. Bettina Bert, “and what has to be done to improve their wellbeing”.

Ms. Bert, veterinarian at the German Centre for the Protection of Laboratory Animals at the BfR, works for the “National Committee for the Protection of Animals used for Scientific Purposes” (“National Committee” for short). One of the legally stipulated tasks of this independent committee is to advise licensing authorities and animal welfare bodies in Germany on questions relating to the care, breeding and accommodation of laboratory animals. Expert opinions are prepared for these consultancy tasks in line with the “3R principle” which stipulates that laboratory animals should be substituted whenever possible, their numbers reduced and their welfare improved (replace, reduce, refine). The example of genetically modified laboratory animals shows how challenging the severity assessment of animal experiments is in this age of rapidly developing methods, such as the “CRISPR” gene editing scissors. The National Committee can now obtain very competent advice in matters of this kind: a pool of experts consisting of 127 specialists from Germany and Austria supports it. The inaugural event of the pool of experts was held at the BfR on 11 October 2018.

“We have made very good experiences with workshops at which ten to twelve specialists discuss a topic thoroughly during two or three days,” reports Bettina Bert on the work of the pool of experts. The jointly drafted results are published by the National Committee in scientific journals, for example. “All of the specialists have been appointed as members of the pool of experts due to their outstanding expertise and not because they belong to a specific institution,” explains Bert. “We also place the greatest value on transparency; possible conflicts of interest must of course be disclosed.”

More information:

www.bfr.bund.de > German Centre for the Protection of Laboratory Animals > National Committee on Animal Welfare Law

INTERNATIONAL

Delegation trip to Moscow

In September 2018, a delegation from the Federal Ministry of Food and Agriculture, including employees of the BfR and other bodies, travelled to Moscow. In addition to discussions with representatives of agriculture and consumer protection, visits were made to the Skryabin Moscow State Academy for Veterinary Medicine, the Russian Academy of Science and the Moscow Timiryazev Agricultural University to discuss opportunities for future cooperation.

Cooperation with Chile

In August 2018, the BfR signed a cooperation agreement with the Chilean Food Safety and Quality Agency (ACHIPIA). The cooperation focuses on risk assessment and the revision of expert opinions for non-professionals. BfR president Professor Andreas Hensel visited the Scientific Committee of ACHIPIA and the National Commission for Scientific and Technological Research (CONICY) in Chile and also held discussions with the FAO representative for Latin America and the Caribbean, Mr. Julio Berdegué.



Crisis exercise in Sarajevo

How do you prepare for a crisis? At the end of 2018, 32 participants from food safety authorities in Bosnia and Herzegovina (BiH) practiced the investigation of a foodborne disease outbreak in an interdisciplinary plan game. The strengths and weaknesses of the existing structures in BiH were analysed as the basis for applying for a partnership project with authorities in the EU. The BfR organised parts of this practical workshop.

Cooperation with China

The BfR conducted a workshop on the subject of food safety with the Chinese Academy of Inspection and Quarantine (CAIQ) in Beijing in April 2019. At the same time, the CAIQ and BfR renewed a memorandum of understanding with the goal of intensifying future cooperation in the field of risk assessment. The CAIQ is a public research institute which officially supervises markets in China and conducts research in many areas, including inspection methods for the control of foods and products.

Project Safe Pork – courses in Vietnam

Within the scope of a project sponsored by the Federal Ministry for Economic Cooperation and Development, the BfR held training workshops in Vietnam at the end of 2018. Together with participants from monitoring authorities and control laboratories from Laos, Cambodia and Vietnam, specialists from the BfR prepared strategies at the National Institute of Veterinary Research on how to optimise local detection methods for trichinae in meat samples.

DAAD scholarship student from Kenya

Kenyan DAAD scholar Martin Wainaina Kimari started his three-year PhD project at the BfR in December 2018. He is to examine the epidemiology of brucellosis in humans and animals in Kenya: findings on prevalence, molecular typing of isolates, determination of outbreak sources and identification of risk factors for brucellosis infections. This is being done in cooperation with the International Livestock Research Institute, which has its head office in Nairobi, Kenya, and Freie Universität Berlin.



EVENTS



Consumer protection forums at the BfR

The tried and tested “BfR Consumer Protection Forum” is set to run three times in 2019, starting off on 6/7 June with the subject of microplastics, continuing on 13/14 June with “Generation 65+” and ending on 7/8 November with a discussion on the subject of bacteriophages. The focus on the first day is on the level of available scientific knowledge, as well as risk assessment and aspects of regulation. Stakeholders such as associations, science, politics and NGOs take centre stage on the second day.

You can find out more about this and other events at: www.bfr-akademie.de

INTERNAL

Fresh wind

By focusing on research and further academic qualification, new structures have been created within the BfR: five junior research groups have been established since 2017. Three new study centres dealing with the topics of total diet studies, genome sequencing and One Health were set up at the end of 2018. In addition to this, several new specialised units have been built up within the departments hand in hand with the increase in personnel since 2014.

More information:
www.bfr.bund.de/en > The Institute



SUBSCRIPTION:
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