

Integrative medical approach to the antimicrobial resistance problem

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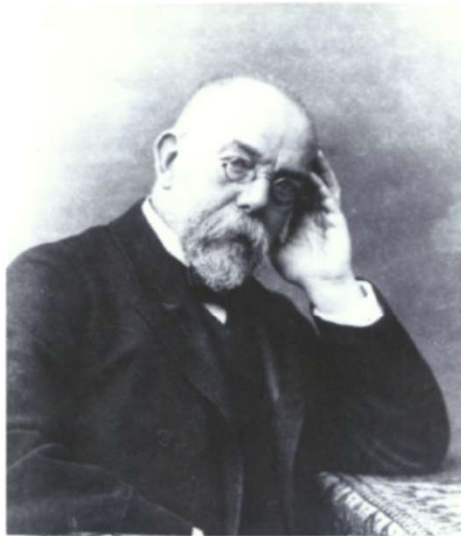
Why Integrative Medicine?

- Essential for organic farms in accordance with EU organic farming regulation
- No residue and inhibitor issues when homeopathy is used
- Valuable supplement to Conventional Medicine
- Starting point for reducing the use of antibiotics
- Used without exception by trained doctors & veterinarians
- Desired by the population

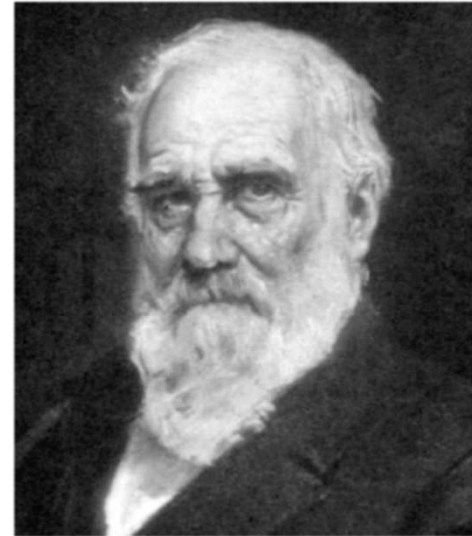
Conventional and Integrative Medicine complement each other

- Pathogenesis: Science of the development of disease
 - Salutogenesis: Science of the development & maintenance of health
(Aaron Antonovsky)
 - Salutogenesis model: - Health is not a condition, but a process
- Risk and protective factors interact
- ➡ The development of disease can best be prevented by understanding and promoting the factors that develop and maintain health.

Koch + Von Pettenkofer



Robert Koch (1843-1910):
“bacteria are the smallest but most
dangerous enemies of mankind”



Max Josef von Pettenkofer (1818-1901)
“germs infect the most susceptible”
(those with poor diet, constitution, etc.);
and he drank a large cholera cocktail without falling ill.

Common goals of Conventional and Integrative Medicine

- Focus on individual organism - biological susceptibility
- Therapeutic use of the body's own immune defense reaction
- Research focus on the body's own immune defense reaction

➔ Integrative Medicine offers therapeutic options

Patient safety through risk governance

DIE ÖSTERREICHISCHE TIERÄRZTEKAMMER

bekannt sich zur integrativen bzw. komplementären Tiermedizin. Um die Bewusstseinsbildung zu stärken, setzt die Tierärztekammer einen Informationsschwerpunkt und veröffentlicht einen Forderungskatalog.



Veterinäre, die integrative Medizin bzw. Komplementärmedizin anbieten, greifen auf ein breites Spektrum von Disziplinen und Behandlungsmethoden zurück, die auf anderen Modellen der Entstehung von Krankheiten und deren Behandlung basieren als jene der Schulmedizin. Integrativmediziner sind akademisch ausgebildete TierärztInnen, die auf der Basis ihres schulmedizinischen Wissens auch Methoden der Komplementärmedizin anwenden.

Die Palette umfasst völlig unterschiedliche Ansätze wie Homöopathie, Akupunktur, Neuraltherapie, Traditionelle Chinesische Medizin (TCM), Chiropraktik, Phytotherapie, Osteopathie.

Die gesetzliche Grundlage zur Ausübung der tierärztlichen Tätigkeiten findet sich im § 12 des TÄG. Die Ausübung integrativer Veterinärmedizin ist an eine vorausgegangene Untersuchung und Diagnosestellung durch eine/n zur Berufsausübung berechnigte/n Tierärztin/Tierarzt mit angemeldeter tierärztlicher Tätigkeit gebunden.

- Fachtierarzt / Specialist for veterinary homeopathy
- Fachtierarzt / Specialist for acupuncture and neural therapy
- Fachtierarzt / Specialist for chiropractic
- OETK-Diplom / Diploma of the Austrian veterinary chamber for phytotherapy

Homeopathic medicinal products are medicinal products and are subject to strict regulations

- According to the Austrian Medicines Act (AMG), homeopathic medicinal products are regarded as medicinal products
- Single homeopathic medicinal products without indication 100% are identical for humans & animals
- Registration of homeopathic medicinal products without indication is regulated in EU Directive 2001/83 & AMG
- EU Regulation on Veterinary Medicinal Products 2019/6 repeals regulation of veterinary homeopathy at national level

Regulation in the Austrian Veterinary Medicines Control Act

- In Austria, the use of homeopathic medicinal products in animals is regulated by the Veterinary Medicines Control Act (TAKG)
- Paragraph 4 (6), (8) & 4b (3):
 - (6) By way of derogation from paragraphs 2 and 5, homeopathic medicinal products, the active substances of which are included in Annex II to Regulation (EEC) No 2377/90, may be administered under the responsibility of a veterinarian (exception from the cascade)
 - (8) If it is a homoeopathic medicinal product, ..., a waiting period is not necessary

Regulation in the EU Organic Farming Regulation

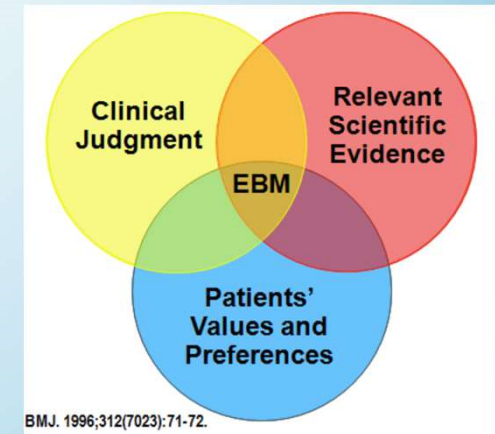
Regulation (EU) 2018/848 on Organic Production and Labelling of Organic Products:

- 1.5.2.3. ..., and phytotherapeutic and homeopathic medicinal products shall be used in preference to treatment with chemically synthesised allopathic veterinary medicinal products, including antibiotics,
 - According to TAKG in Austria & AMG in Germany single homeopathic medicinal products can be used for animal therapy regardless of the cascade
- ➔ This is the only way to meet the requirements of the EU Organic Farming Regulation

Three major components of evidence-based medicine (EBM)

The definition of EBM requires integration of three major components for medical decision making:

1. Individual practitioner's clinical expertise
2. Patient's preference
3. Best external evidence (Sackett et al., 1996)



Medicine is a practice-oriented empirical science (WHO definition)

Review programme shows effectiveness of homeopathy

Review programme of Mathie et al. (2014, 2017, 2018, 2019)

- For individualized homeopathy: effects on all quality levels can be recognized according to Cochrane criteria, even in methodologically high-quality studies
- Mathie et al. (2014): Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis. *Syst Rev* 3: 142.

Overview of the Review Programme

- 131 original research articles
- 13 RCTs with minimal bias risk
- 5 RCTs high reliable evidence
- 10 RCTs homeopathy vs placebo
- OR 1.68 (CI 1.25–2.24; P<0,001)

13 RCTs with minimal risk of bias
(incl. 5 RCTs with 'Highly reliable evidence')

Indiv./Plac. (publ. 2014)	Bell	2004	Fibromyalgia
	Chapman	1999	Brain injury
	Jacobs	1994	Childhood diarrhoea
	Jacobs	2001	Otitis media (acute)
	Jacobs	2005	ADHD
	Thompson	2005	Menopause after breast cancer
Non-Indiv./Plac. (publ. 2017)	Coliau	2012	Menopausal syndrome
	Padilha	2011	Lead poisoning
	Smigel	2010	Post-operative pain
	Taylor	2000	Perennial allergic rhinitis
Indiv./OTP (publ. 2018)	Weiser	1998	Vertigo
	Weiser	1999	Seasonal allergic rhinitis
Non-Indiv./OTP (publ. 2019)	Peckham	2014	Irritable bowel syndrome

June 2019

4 of 5 systematic reviews positive for homeopathy

Chronologically before Mathie et al.'s review programme:

- 5 systematic reviews with meta-analyses on different indications & all homeopathic methodologies published
- 4 of which positive for homeopathy

Meta-analysis of veterinary homeopathy

Meta-analysis of veterinary homeopathy by Mathie and Clausen (2015)

- Limited evidence of the effectiveness of veterinary homeopathy versus placebo shown
- $P=0.01$ for $n=15$, pooled $OR=1.69$ ($CI=1.12-2.56$)

Arbitrary exclusion from studies distorts outcome

- Consideration of all high-quality studies of evidence class 1a and 1b (= basis for compliance with scientific standards)
- Approximately 90% of all studies must be excluded in order to present homeopathy as ineffective (Hahn, 2013)
- Arbitrary & scientifically untenable reduction of studies led to negative results

Examples:

- Review by Shang et al. (2005) (Frass et al., 2006)
- 2. Australian NHMRC report (2015) (Fisher, 2017)
- Both are the basis of the EASAC Statement (2017) (Fisher, 2017)

Secrecy of positive first Australian NHMRC report

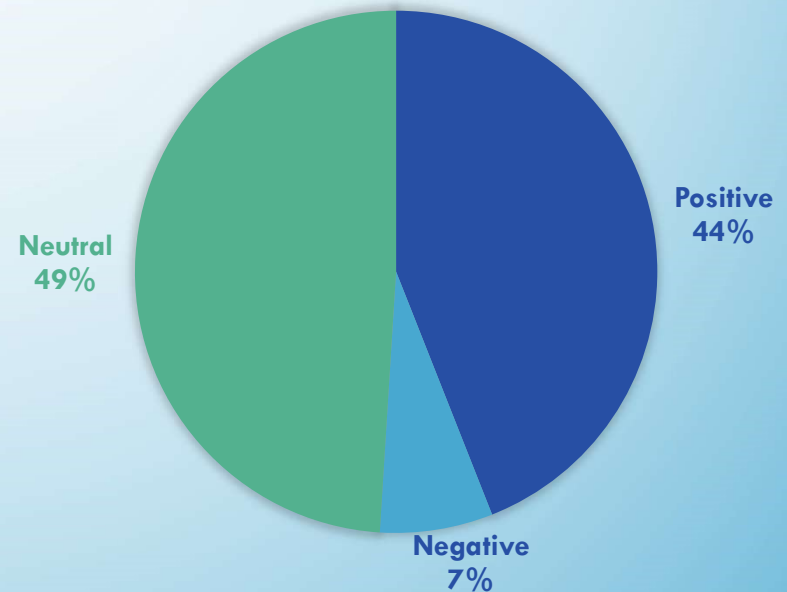
- First Australian NHMRC report from 2012 finally available to the public
- Written by Prof. Karen Grimmer
- Already showed promising evidence of the effectiveness of homeopathy in 5 indications (infections of the upper respiratory tract, otitis media, etc.) in 2012
- CEO NHMRC Prof. Anne Kelso:
„Contrary to some claims, the 2015 review did not conclude that homeopathy was ineffective.“ (26.8.2019)
- Evidence confirmed several times since then

Evidence on conventional therapies

Result of the Cochrane Review of 1,016 systematic reviews of conventional therapies (El Dib et al., 2007):

Positive: 44%
Negative: 7%
Neither benefit
nor harm: 49%

Homeopathy belongs to the group of therapies that are effective but need to be better researched



Phytotherapy within the respiratory tract as a strategy against antimicrobial resistance



Consortium

Danube University
Krems

Charité Berlin

Università degli
Studi di Firenze

Kottas Pharma
GmbH

Considerations

- Microorganisms > ability to adapt > develop resistance to drugs
- Direct impact on human and animal health
- Carries a heavy economic burden due to higher costs
- Currently no didactic materials on this topic available to teachers and learners (complementary medicine)

Aim

- Interdisciplinary and transnational development of:
- Highly qualified abilities for future players in health care sectors
 - Acquire and submit corresponding knowledge
 - One health strategy

EU Working Group “Appropriate use of antibiotics: the role of CAM treatment strategies”

- “... Preliminary studies have shown that ... CAM practices and hospitals have lower antibiotic prescription rates and lower resistance rates compared to conventional practices ...
- In order to ... reduce mis- and overprescribing of antibiotics ..., the available practical expertise and scientific knowledge on CAM strategies must be explored and systemized
- The working group will ... focus on the development of an evidence and expertise based decision-making tool for ... doctors and the implementation of this tool in the European countries”

EU Working Group staffed by renowned conventional and integrative physicians and researchers from other fields

- Erik W. Baars. MD, MSc Epidemiology, PhD Senior Researcher Healthcare, Louis Bolk Institute. Professor Anthroposophic Medicine, University of Applied Sciences Leiden
- Willem van Leeuwen. Microbiologist. Professor Innovative Molecular Diagnostics, University of Applied Sciences Leiden
- George Lewith. Professor of Health Research at the University of Southampton
- Roman Huber. MD, Professor, University of Freiburg
- David Martin. MD, Professor of Pediatrics, Tübingen University

Recent research shows potential

Review Integrative Medicine & Antimicrobial Resistance (AMR) (Baars et al., 2019):

- Potential of Integrative Medicine, including homeopathy, to reduce the use of antibiotics evident
- Need for further research to provide further high-quality evidence on (cost) effectiveness



Study in sepsis patients demonstrates effectiveness

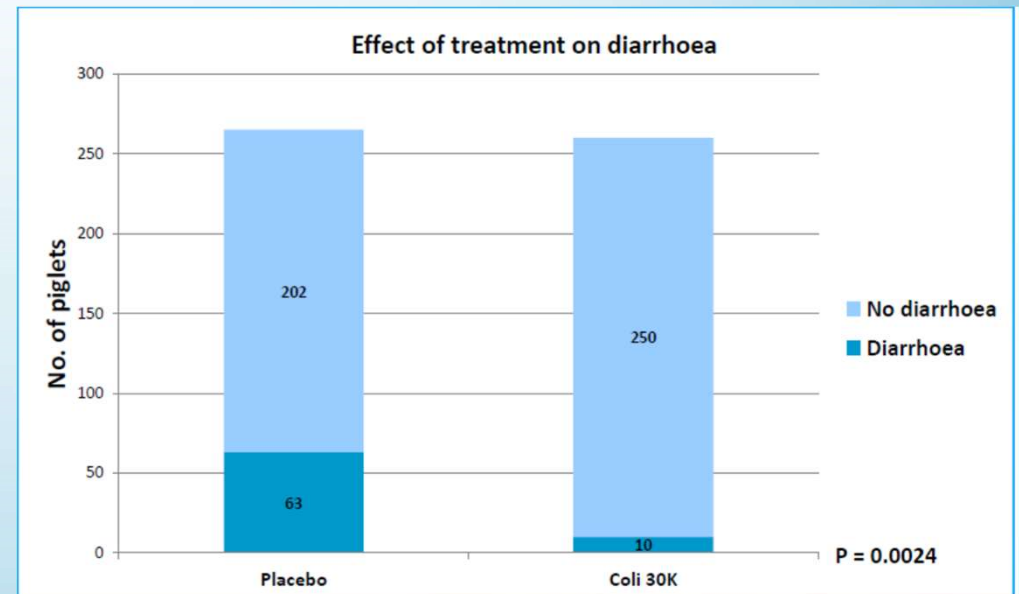
Randomized, double-blind, placebo-controlled study (Frass et al., 2005):

- Intensive Care Unit: 70 patients with severe sepsis
- In addition to the standard therapy homeopathic medicinal product or placebo
- Day 180 survival in homeopathically treated group statistically significantly higher than in placebo group
- $p = 0.042$; Kruskal-Wallis Test; $p = 0.0248$; Chi Square Test in ITT Analysis

Effectiveness in prophylaxis of diarrhea in piglets

Randomized, placebo-controlled, double-blind study (Camerlink et al., 2010):

- Homeopathy in E. Coli diarrhea in piglets
- Homeopathic group significantly fewer piglets with diarrhea; $p = 0.0024$
- Less severity of the disease, diarrhea of shorter duration



Farm wanted for piglet study

- Randomized, placebo-controlled, double-blind study in ETEC-induced weaning diarrhea
- Farm without use of antimicrobials or zinc when weaning with spatially separated pens
- Fisher's exact test for primary endpoint diarrhea yes/no
- 1 weaning group - 145 weaned piglets (after dropout) needed
- With an average effect strength to be tested of 0.3, a fixed $\alpha=5\%$ and power=95%.
- Promising financial support

Systematic review indicates effectiveness of homeopathy in preventing and treating mastitis in cows

Systematic review (Zeise und Fritz, 2019):

- 32 studies on mastitis in cows from 1982 - 2016 analysed according to quality score
- 8 studies show quality score of $\geq 2.5/5$ and were used for analysis:



These high-quality studies indicate the effectiveness of homeopathy



One study also shows a reduction in the use of antimicrobials of up to 75% (Merck, 2004)

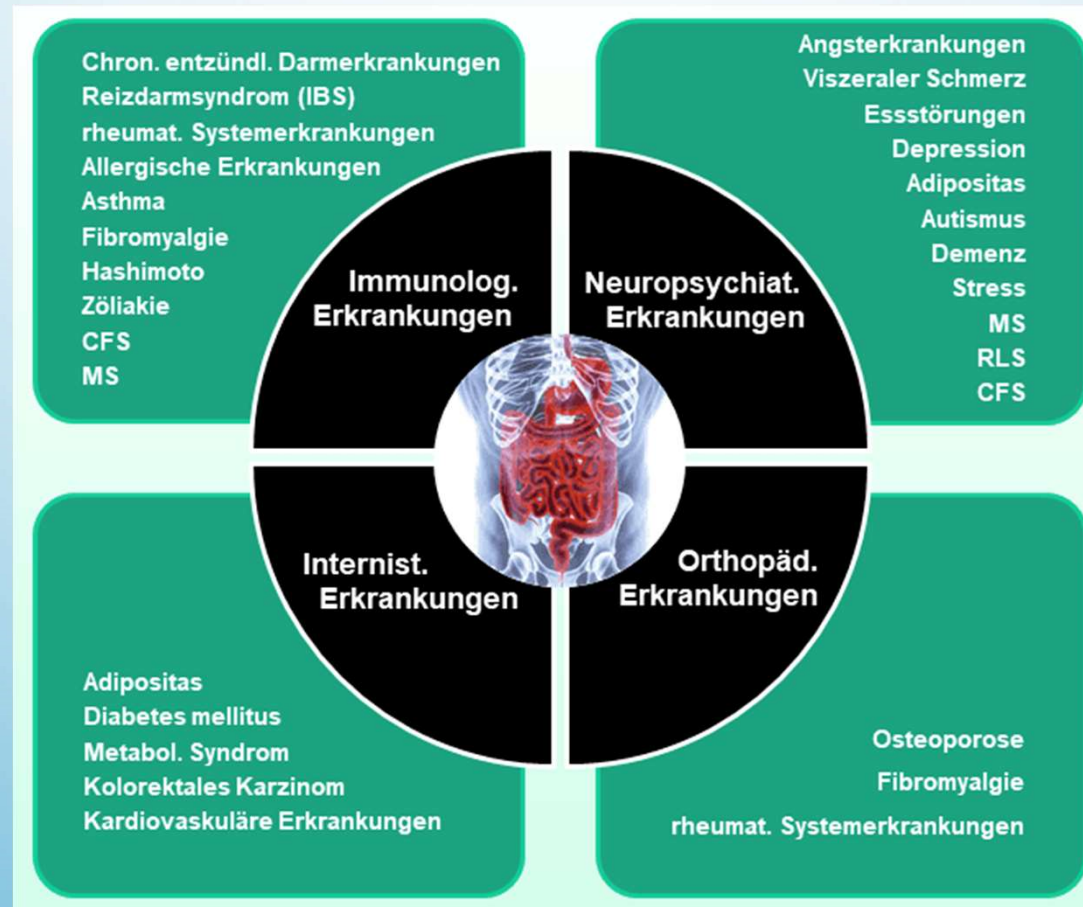
Significant reduction of the antimicrobial treatment incidence in the farm

Kometian project in Switzerland (Maeschli et al., 2019)

In the case of integrative medical care, especially homeopathic care:

- Antimicrobial treatment incidence in the farm decreased significantly (33%) from 27 to 18 treatments per 100 animals in the first year
- $p < 0.001$; Wilcoxon-signed-rank Test

Clinical relevance of the microbiome



Conclusions

- Cooperation:
between clinics and experts in homeopathy in our responsibility to our patients
- Research:
request by European Commission in European One Health Action Plan Against AMR for further research in such promising areas as Integrative Medicine
- National health policies and systems:
according to their Traditional Medicine Strategy 2014 – 2023 the WHO urges member states to include Integrative Medicine in their national health policies and systems



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Take Home Messages

- Integrative Medicine offers potential for reducing the use of antibiotics
- The basic prerequisite for the effectiveness of homeopathy is the selection of the simile by appropriately trained homeopathic doctors/veterinarians
- Legal basis for homeopathy
EU Reg 2019/6, EU Organic Farming Reg 2018/848, TAKG, AMG, EU Dir 2001/83
- The basic prerequisite for fulfilling the requirement of the EU Organic Farming Regulation is a larger number of veterinarians trained in homeopathy and phytotherapy
- Risk Governance through Fachtierarzt / Specialist for veterinary homeopathy, acupuncture & neuraltherapy, chiropractic, Diploma of the Austrian veterinary chamber for phytotherapy



Thank you for your attention!