FiBL
EXCELLENCE FOR SUSTAINABILITY

Research Institute of Organic Agriculture
Forschungsinstitut für biologischen Landbau
Institut de recherche de l'agriculture biologique






Domestic animals and infectious diseases in organic farming – the need for alternatives to control (resistant) pathogens

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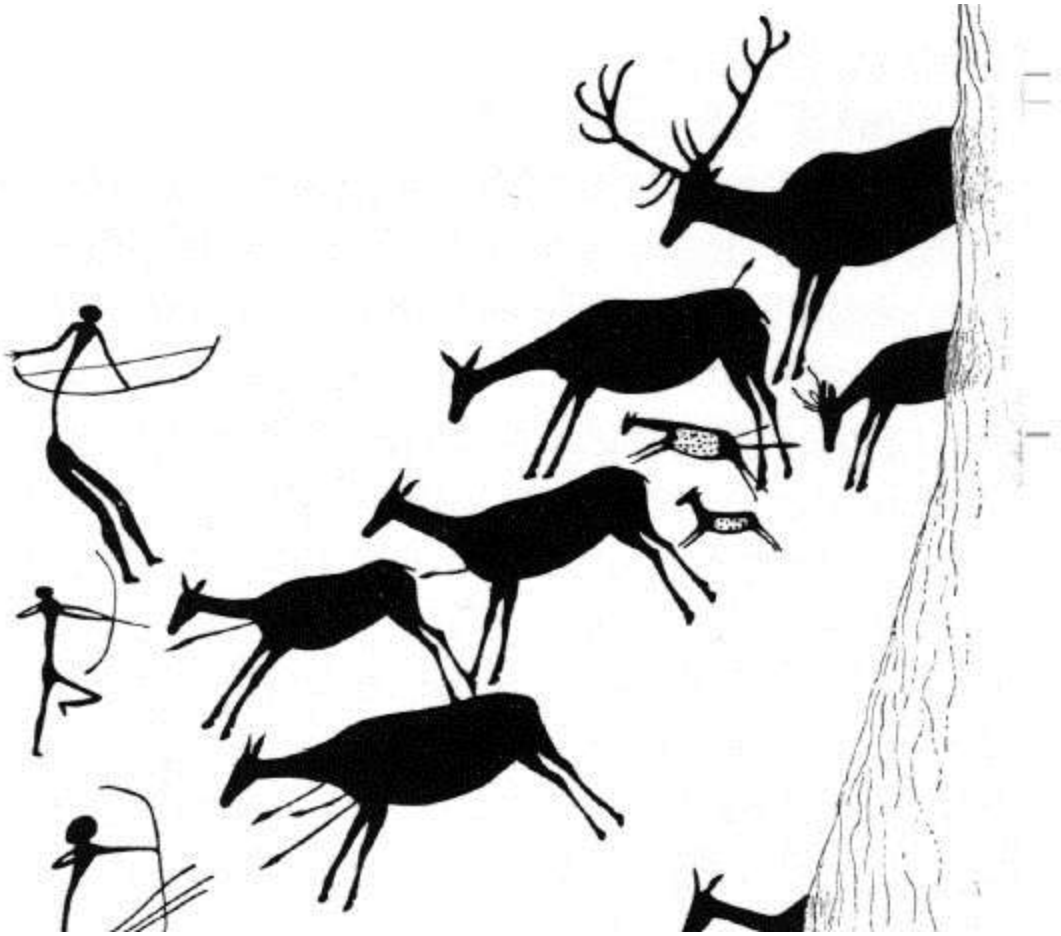
What are they doing?

- Are they organic and sustainable?
- Are they significant?



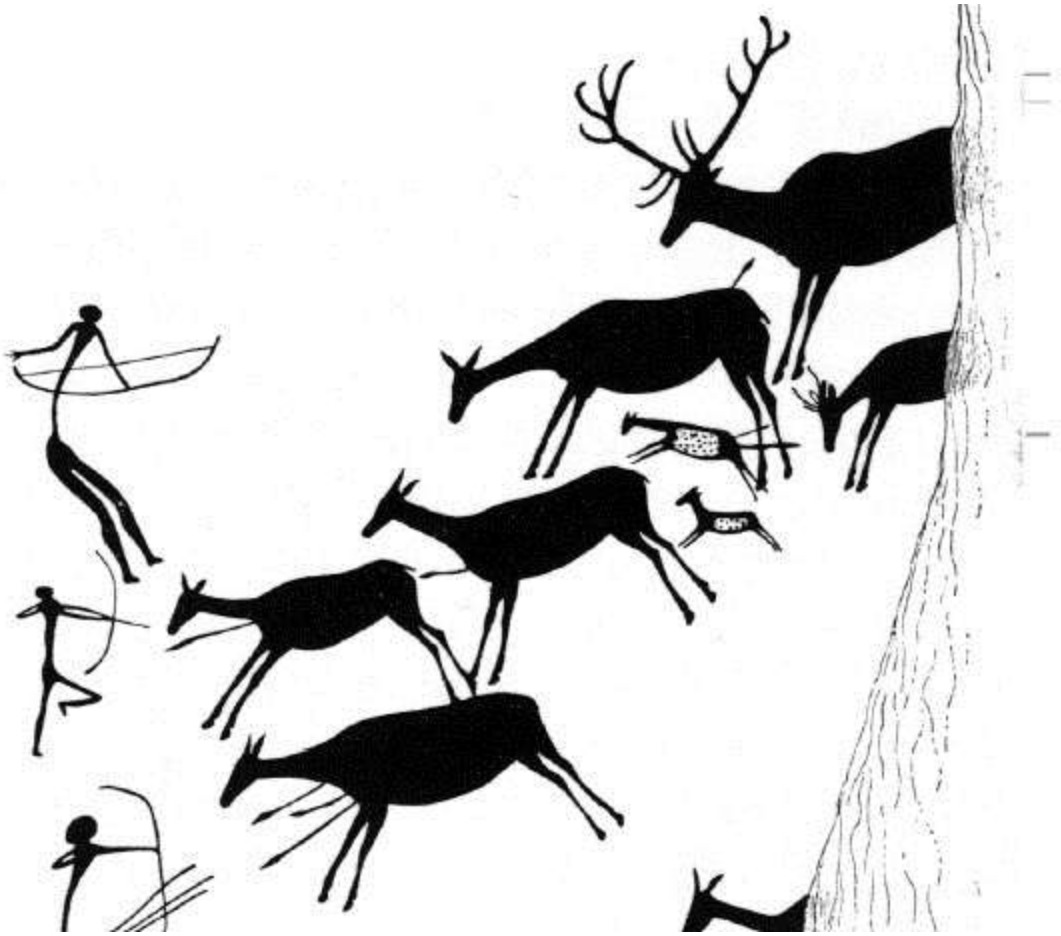
Worlwide human and livestock population (Mio)

›	Human	7200	430 Mio t live weight
›	Cattle	1400	700 Mio t live weight
›	Small ruminants	1900	115 Mio t live weight
›	Pigs	960	96 Mio t live weight
›	Broiler Chicken	60000	60 Mio t live weight

FAO, 2013

Do they have infections?

- Do they have infectious diseases?
- Do they carry resistant microbes?



Causes for infections

- Virus
- Bacteria
- Fungus
- Parasites

- Are they (solely) responsible for infectious diseases?

An infectious disease is allways an imbalance between the (immune system of the) host and the pathogen.

Resistance?

… nothing new!

THE SOIL AS A SOURCE OF MICROORGANISMS ANTAGONISTIC TO DISEASE-PRODUCING BACTERIA*,1

SELMAN A. WAKSMAN AND H. BOYD WOODRUFF
New Jersey Agricultural Experiment Station, New Brunswick, New Jersey

Received for publication April 26, 1940

The ISME Journal (2009) 3, 243–251

www.nature.com/ismej

ORIGINAL ARTICLE

Functional metagenomics reveals diverse β-lactamases in a remote Alaskan soil

Heather K Allen[1,2], Luke A Moe[1], Jitsupang Rodbumrer[1,3], Andra Gaarder[1] and Jo Handelsman[1]
[1]*Departments of Bacteriology and Plant Pathology, University of Wisconsin-Madison, Madison, WI, USA* and [2]*Microbiology Doctoral Training Program, University of Wisconsin-Madison, Madison, WI, USA*

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Aug. 2010, p. 5321–5326
0099-2240/10/$12.00 doi:10.1128/AEM.00123-10

Novel Florfenicol and Chloramphenicol Resistance Gene Discovered in Alaskan Soil by Using Functional Metagenomics ▽

Kevin S. Lang,[1] Janet M. Anderson,[1] Stefan Schwarz,[2] Lynn Williamson,[3] Jo Handelsman,[1]* and Randall S. Singer[4]*
Department of Veterinary and Biomedical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, Minnesota 55108; Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), 31535 Neustadt-Mariensee, Germany; and Department of Bacteriology and Plant Pathology, University of Wisconsin, Madison, Wisconsin 53706

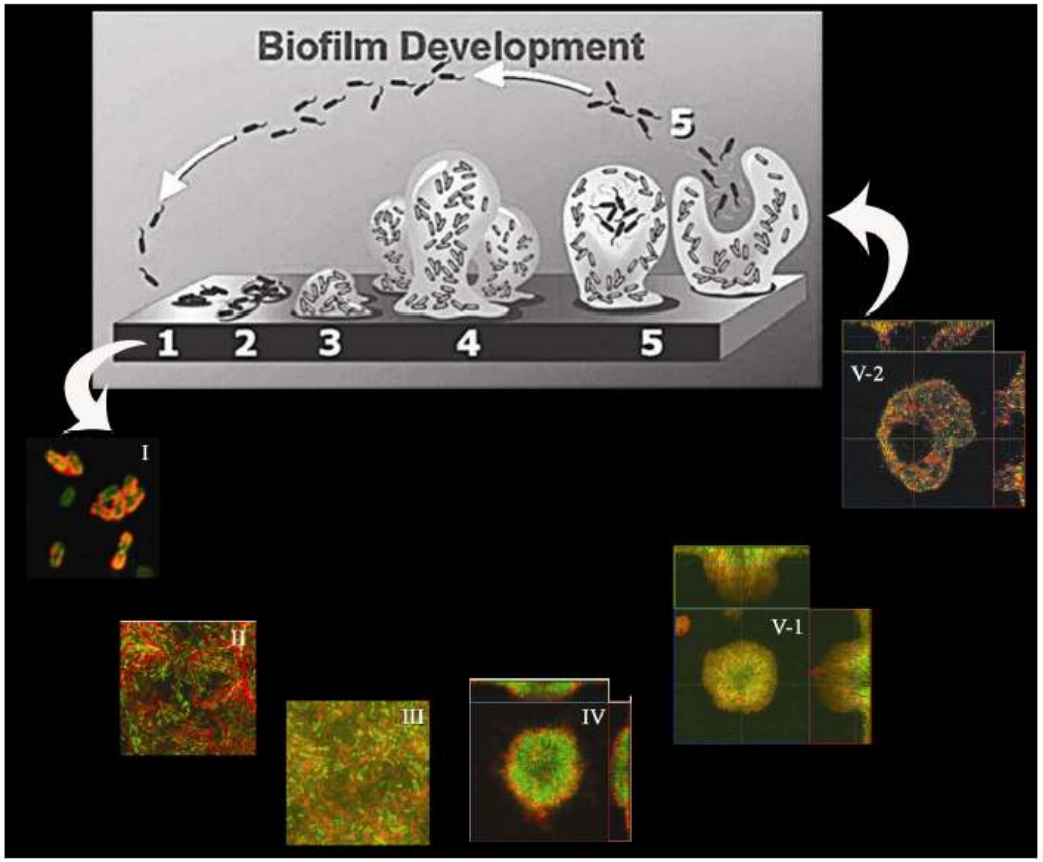
Received 5 February 2010/Accepted 1 June 2010

Functional metagenomics was used to search for florfenicol resistance genes in libraries of cloned DNA isolated from Alaskan soil. A gene that modified reduced susceptibility to florfenicol was identified and designated pexA. The predicted PexA protein showed a structure similar to that of efflux pumps of the major facilitator superfamily.

Vol. 76, No. 15

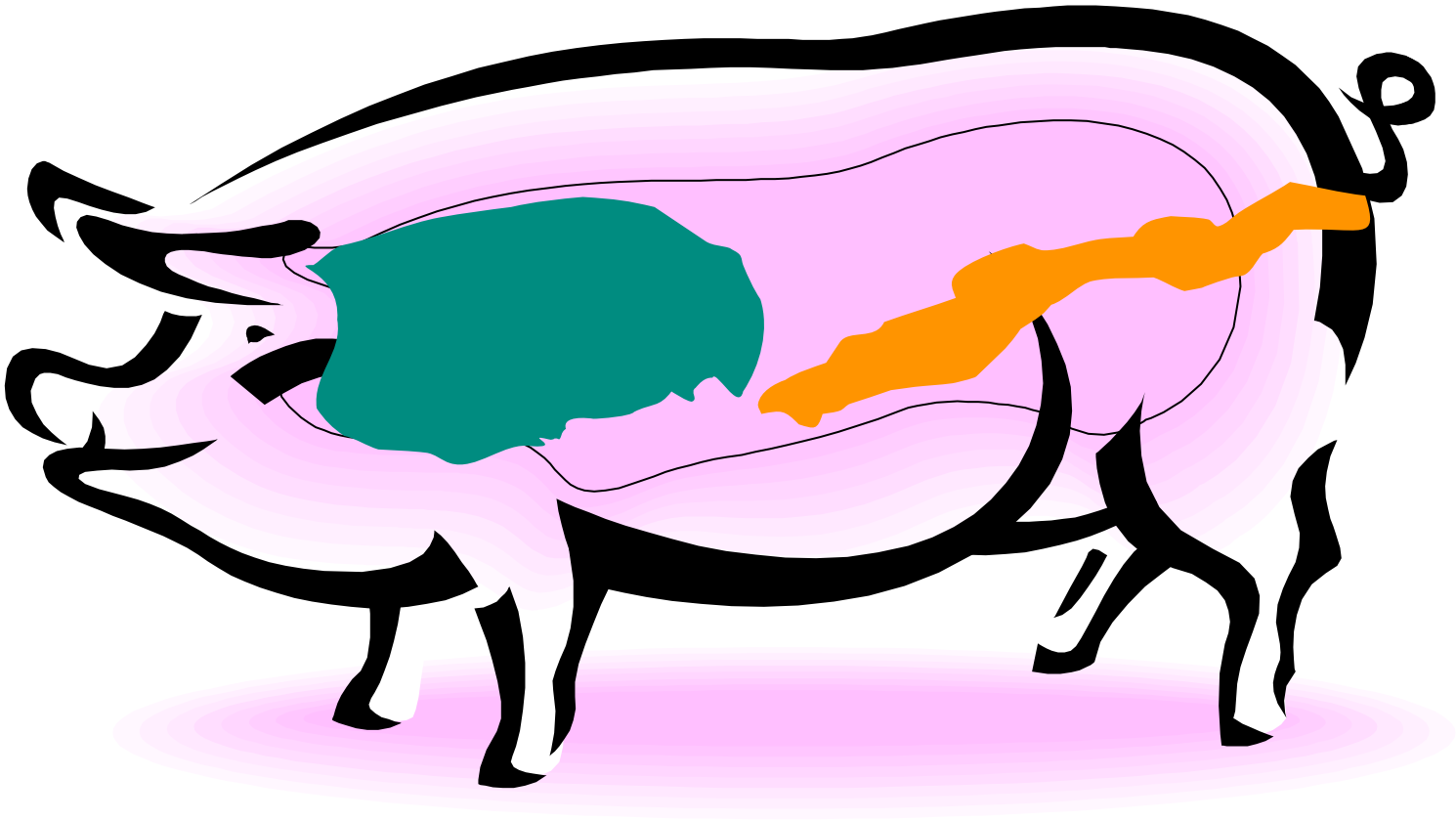
A further good (mikrobial) idea: Biofilm

Figure 1. Scheme of biofilm development in *P. aeruginosa*. Selected images showed how the matrix of Psl polysaccharide (**red** fluorescence) enmeshes bacterial cells (**green** fluorescence) within bacterial communities during biofilm development (**I**: initial attachment; **II**: irreversible attachment; **III**: microcolony formation; **IV**: biofilm maturation; **V**: biofilm dispersion). The figure was used with the permission of the authors [15,27] and modified herein.

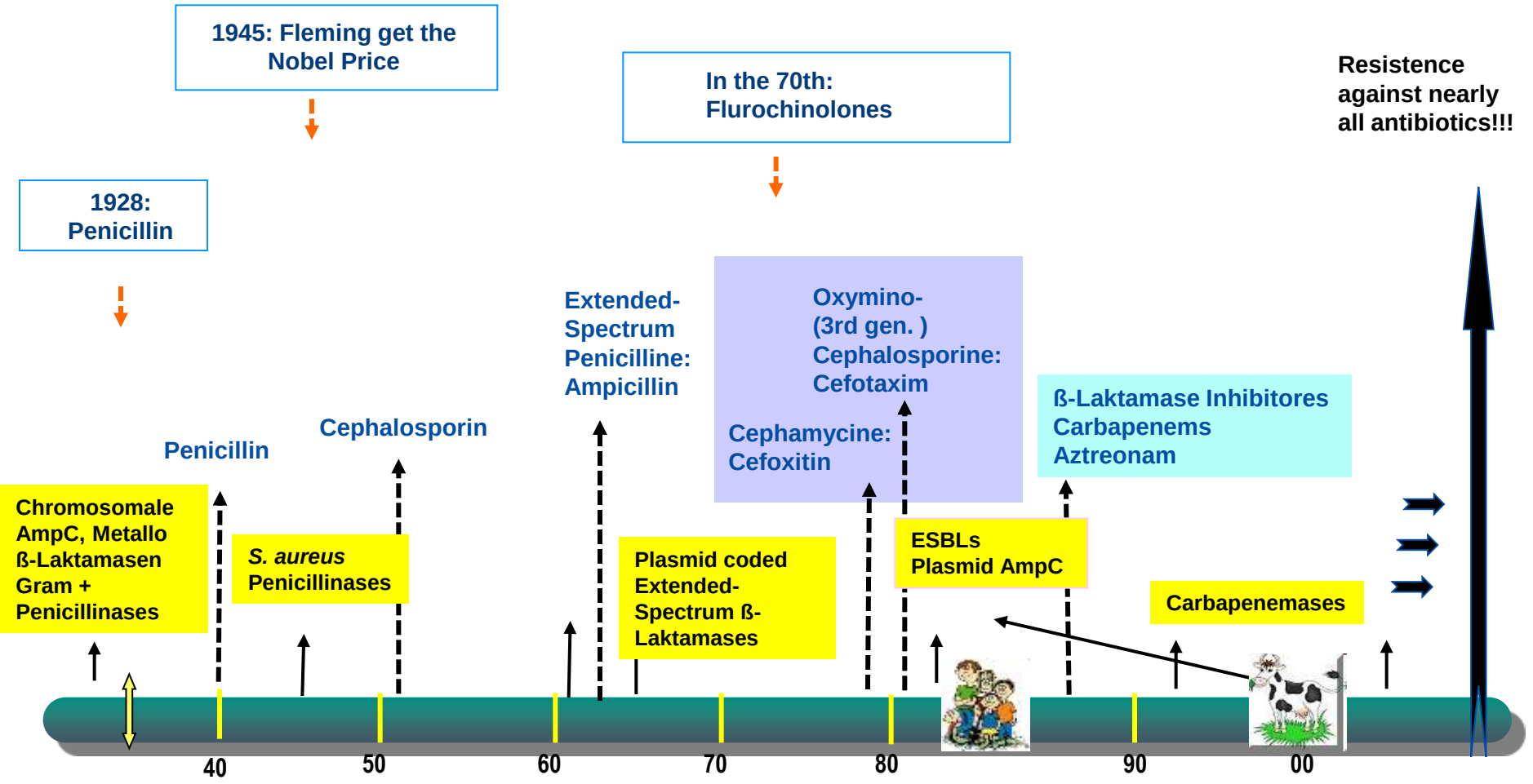


Wei and Ma 2013

What’s the problem?

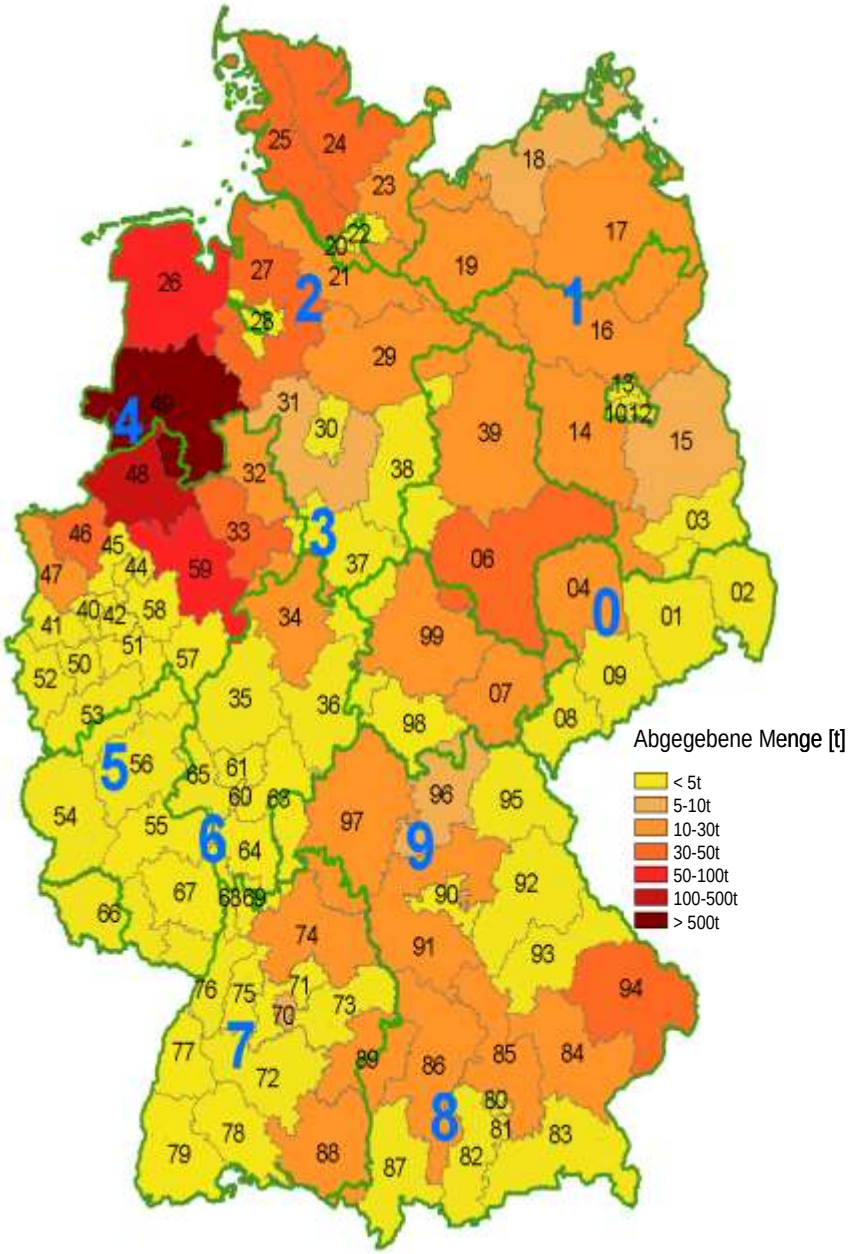


History of antimicrobial resistance



Dr. Norbert Roers, 14. Int. GGTM-Kongress, April 2014

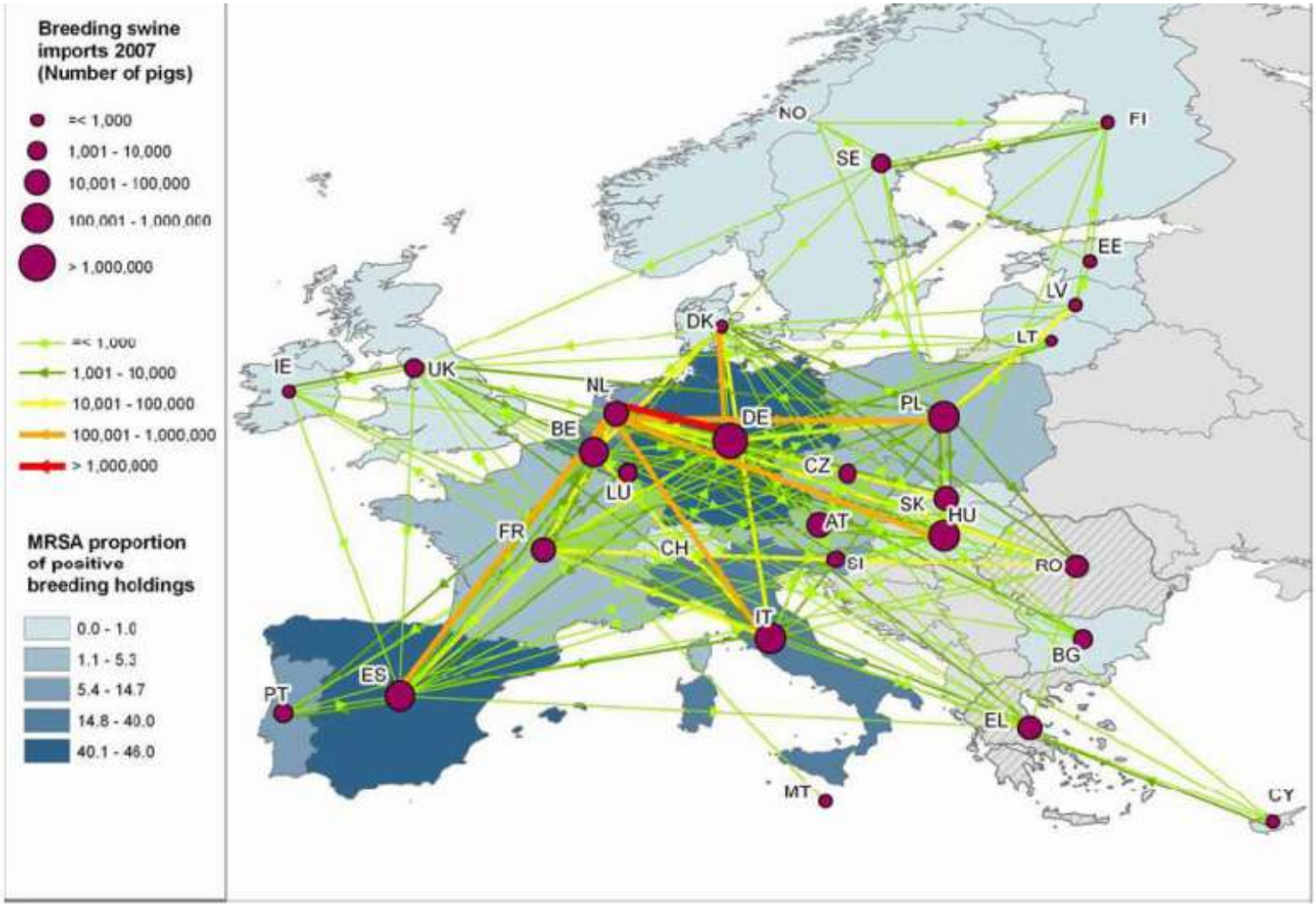
Gutkind et al. 2013;



yearly sold antibiotics for livestock in germany

Dr. Norbert Roers, 14. Int. GGTM-Kongress, April 2014

Resistance - tourism



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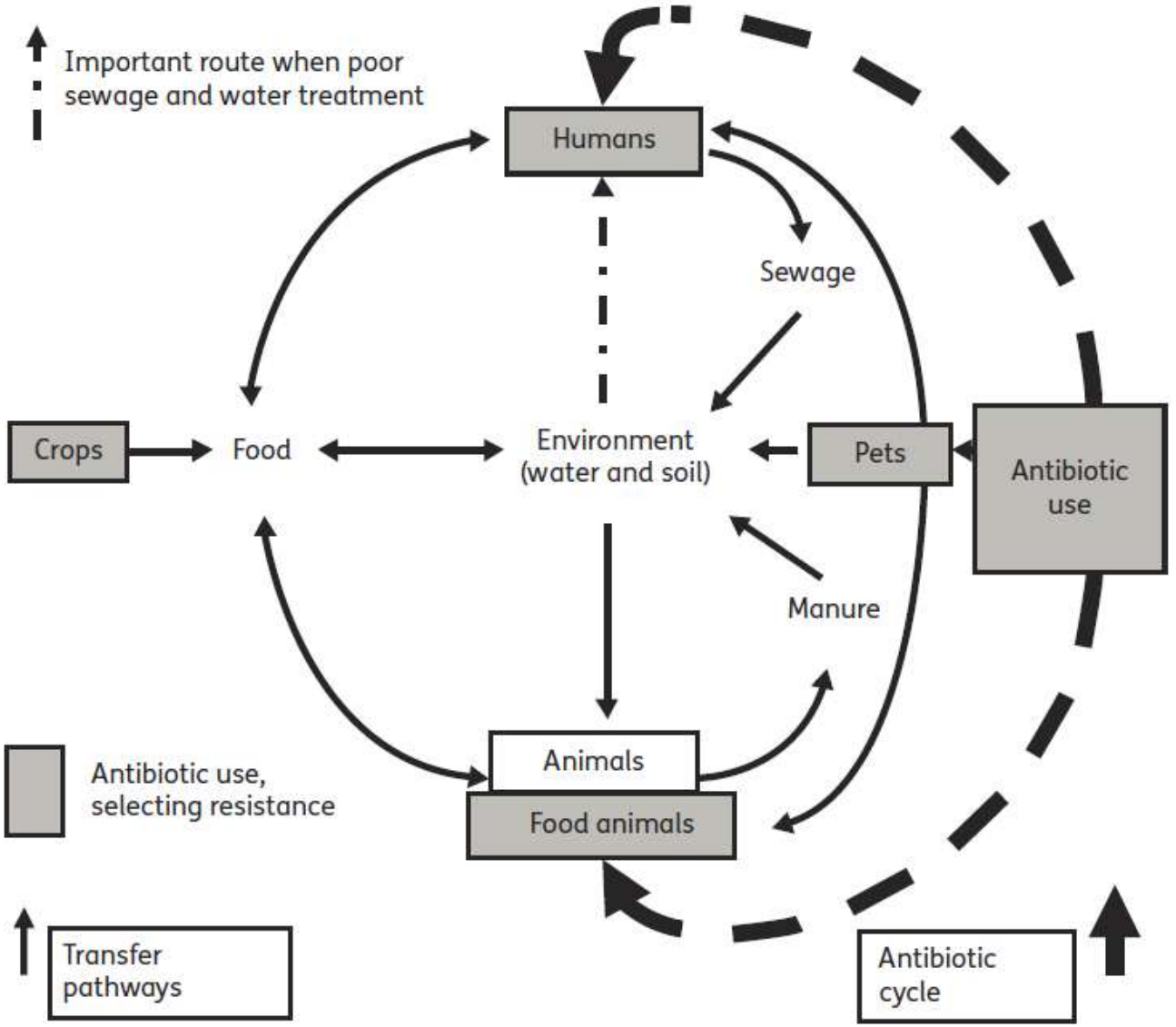

Garcia-Alvarez et al., 2012

What's the problem?

Veterinary Parasitology 186 (2012) 70–78

Contents lists available at SciVerse ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

An inconvenient truth: Global worming and anthelmintic resistance

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[b] Department of Statistics, George Mason University, Fairfax, VA, USA

What's the problem? … we select «the best»!

- **Antibiotics and antiparasitics are a cheap production factor (but – how long?)**
- **High worldwide livestock density and flow**
- **High antibiotic use in livestock and in human**
- **Oral application and following «feaces tourism»**
- **Intraspecies, interspecies and intergenus transfer of resistance genes in the world of (patho- and apathogene) bacteria**

How to guaranty a high health status of organic livestock

- **Breeding robust animals**
  - **Species-specific feeding, housing and management including preventive herd health management**
    - **Complementary medicine (for instance phytotherapy)**
      - **Chemical synthetic drugs and antibiotics in case of emergency**

Organic livestock

- Exact and representative population data are missing
  - EU: ≈ 3% of the ruminants; < 1% pigs and poultry
- Exact and representative data are missing both for organic as well as for non-organic livestock:
  - Prevalence of (infectious) diseases … ?
  - Use of antibiotics and antiparasitics … ?

Preventive herd health management - an option?

- **ANIPLAN project (EU)**
- **Effects of paddock management on internal parasites in laying hens (CH)**

Ivemeyer et al., 2008; Ivemeyer et al., 2012; Maurer et al. 2013

ANIPLAN - animal health and welfare planning principles

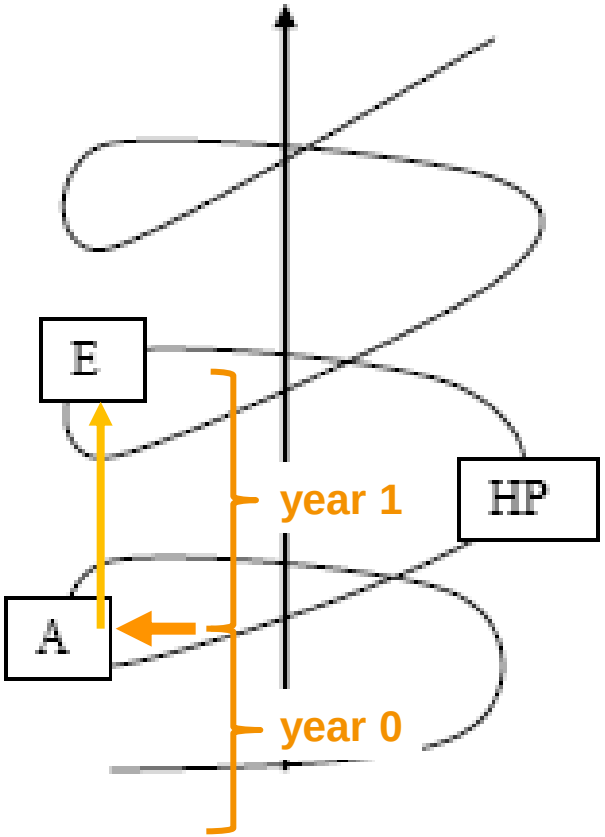
1. Continuous development and improvement
   - Identify current status and risks (using animal and resource based parameters)
   - Evaluation and target setting
   - Promotive, preventative and responsive strategies and action
   - Review
2. Farm specific
3. Farmer ownership (setting targets, accounting for aspirations, setting planning agendas)
4. External person(s) should be involved (to provide unbiased advice/support)
5. External knowledge
6. Within framework of organic principles (systems approach)
7. Written documentation
8. Acknowledge existing positive aspects of health and welfare also

Analyses in ANIPLAN

influences on development of health, welfare **and use of medicines**, e.g. farmers‘ goals, farmers‘ satisfaction with farmer field schools **and specific advise effects**

development of health, welfare **and use of veterinary medication between first and second assessment**

influences on basic situation e.g. management, resources



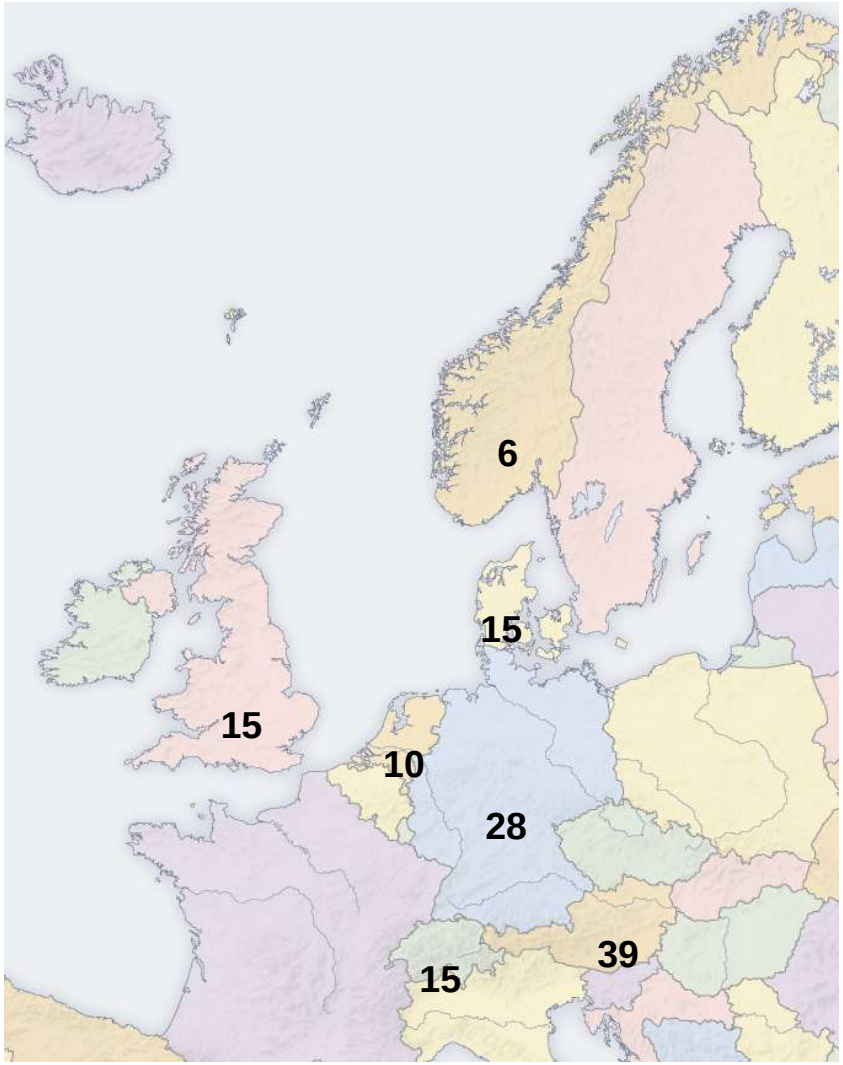
A= Assessment

HP= Health planning

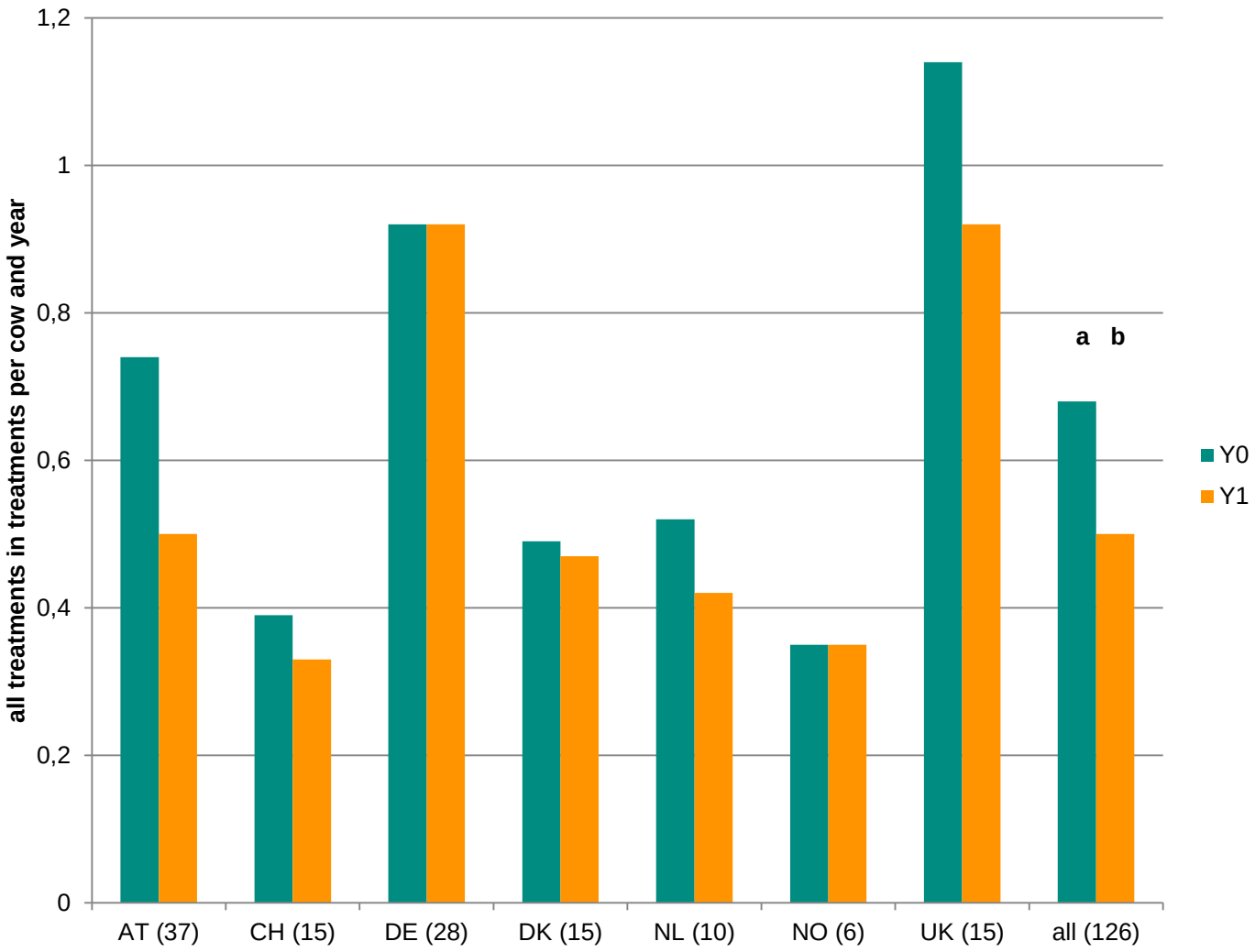
E= Evaluation

Farms and data

- 132 farms in 7 countries
  - 39 farms in AT, 15 farms in CH, 28 farms in DE, 15 farms in DK, 10 farms in NL, 6 farms in NO, 15 farms in UK (not all data were available from all countries)
  - no representative selection; selection in CH, DE and NL from existing projects or farm-networks
- All analyses conducted on farm level
- Production: Daily milk yield (DMY), average lactation number (LN), milk composition (%fat, %protein) as means of all test-day results over one year.
- Herd size: Number of cows = Number of test-day measurements in one year / 9 (when 11 measurements per year and about 6 weeks dry-off)

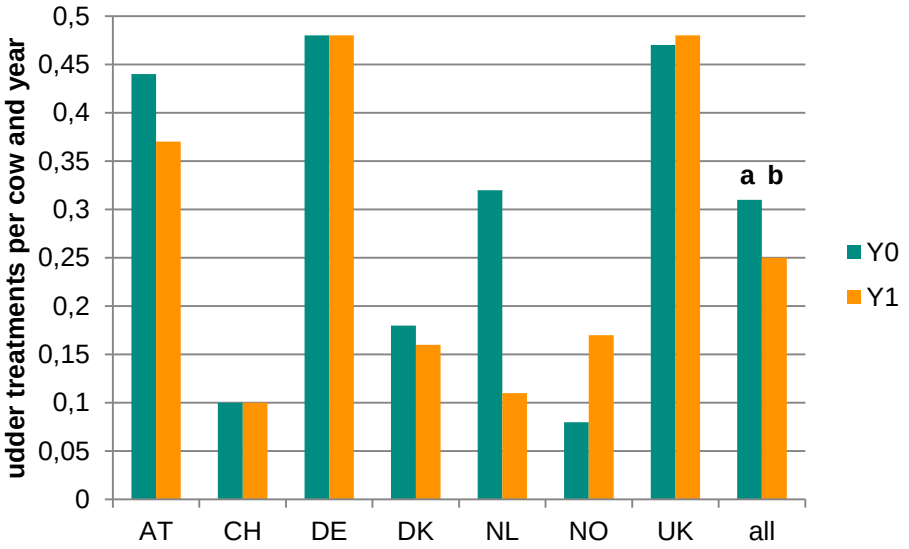


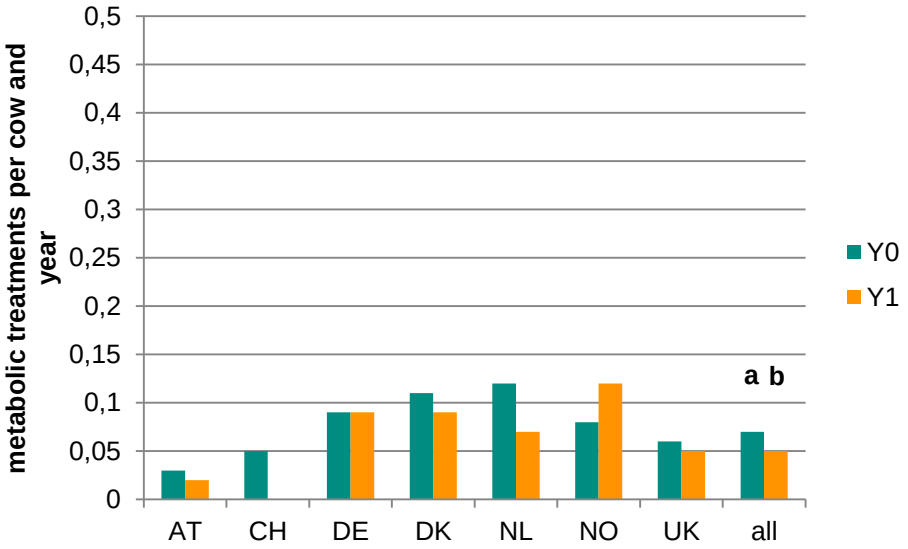
Treatments in Y0 and Y1 - all treatments (medians)



a, b: results from Wilcoxon-test for paired samples;
a b show a significant development

Treatments in Y0 and Y1 – in categories (medians)





a, b: results from Wilcoxon-test for paired samples;
a and b show a significant development

Udder health

Variable (n farms)	Factor	Effect level	DF	F	*P*	
Health						
SCS	Rep	Within	1	5.58	**0.020**	Y0 > Y1
	Country	Between	5	10.39	**<0.001**	
	fa_udder	Between	1	3.56	0.062	
	Rep*fa_udder	Within	1	1.42	0.237	
	Rep*country	Within	5	0.80	0.554	
	Country*fa_udder	Between	5	0.79	0.560	

Paddock Management in laying hens

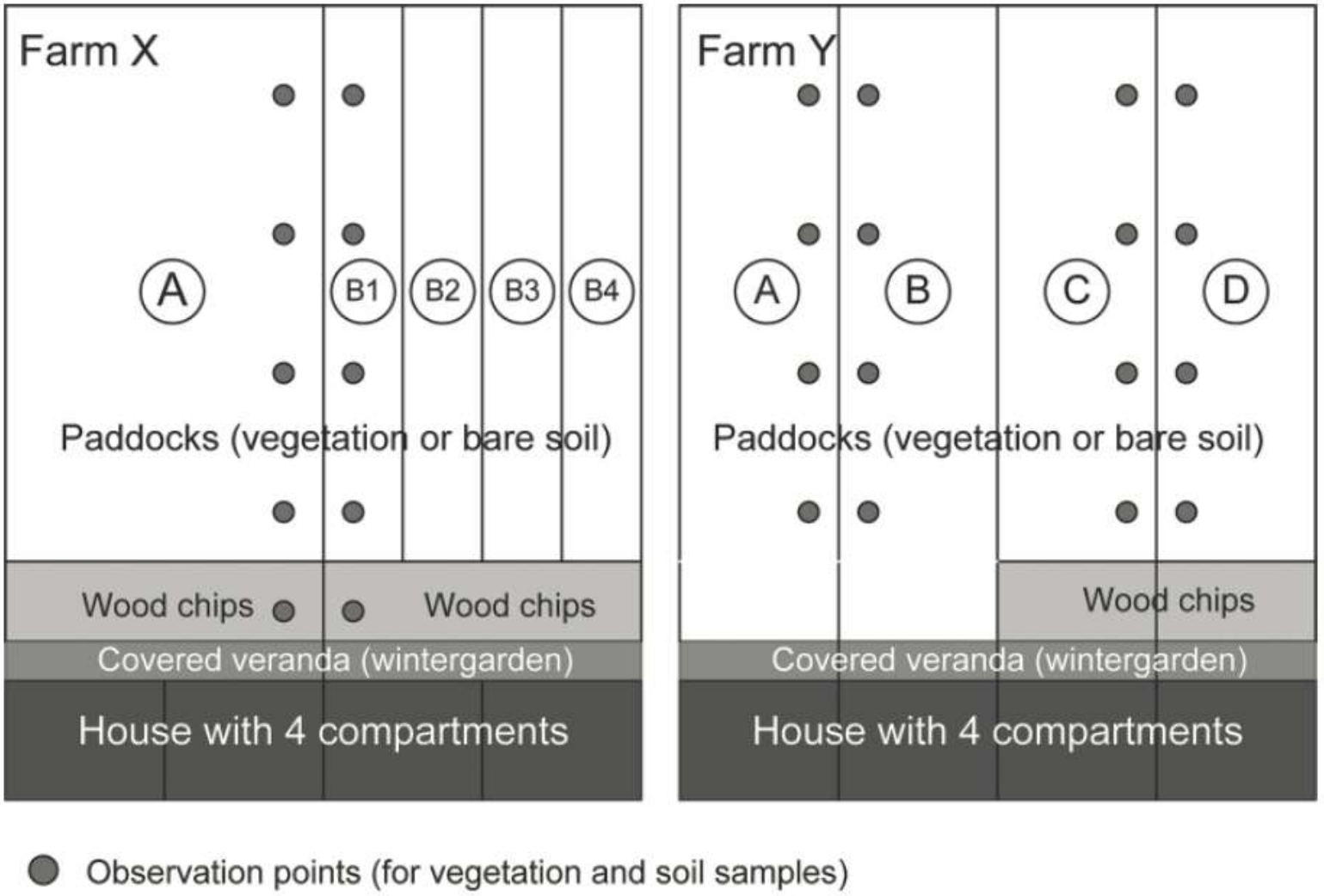


Figure 1. Sketch of experimental setup at farms X and Y. Capitals in circles (A–D) denote paddocks; paddock B on farm X is subdivided into 4 runs (B1–B4). Sketches are not true to scale.

Paddock Management in laying hens

- **No significant effect of the management regimens on worm burdens (Ascaris galli, Heterakis gallinarum, capillaria spp.) at the end of laying period**

- **Heterakis or Ascaridia fecal egg counts were significantly reduced on a rotationally used paddock and on paddocks with wood chips in the area close to the pop holes compared with unmanaged paddocks**

Phytotherapy - an option?

- Phytotherapy – one of the oldest therapeutic measures
- „Oldest source“: an analyse of pollen in an Irakian grave about 60‘000 B.C.
- For a long time without differentiation between human and animals
- Traditional therapy measure in several regions and cultures
- Unbroken tradition e.g. in asia

Secundary plant metabolites

Substances in small amounts which fulfill specific and very diverse „jobs“ for the plants

Why do plants do this?

Plants cannot run (away) !!!

- **Protection against diseases (bacterials, fungi, virus), insects and other herbivores**
- **Communication**
- **Reproduction**

Ivemeyer et al., 2008; Ivemeyer et al., 2012; Maurer et al. 2013

Secundary plant metabolites

- 1‘000‘000 existent
  - 100‘000 known
    - only 10‘000 well analysed

- Plant extracts are «Multi Componant Compositions» and «Multi Target Drugs»

  - based on 700 millions of years[1] ”experiance” in coexistance with microorganism
    - Virus, Bacteria, Fungus, Parasites
    - Successfull also to react on Biofilms

  - Activating of vertebrates immune system and metabolism

1 Heckman et al., 2001

Ethnoveterinary research in Switzerland

2011: Zürich, Aargau und Schaffhausen
2011 – 2012: Projekt ZHAW: Graubünden
2012: Appenzell Innerhoden, Appenzell Ausserrhoden, Thurgau und St. Gallen
2013: Zug, Schwyz, Glarus, Uri, Obwalden und Nidwalden

2013 – 2014: Tessin (part of a veterinary PhD),
2014: Basel Landschaft, Basel Stadt, Bern, Luzern, Solothurn (two master thesis)
2015 – 2016: Fribourg, Jura, Neuchâtel, Valais, Genf, Vaud (three master thesis)

Impressionen 2013

Ethnoveterinary Research in Switzerland

Year	canton	Number of interviews (persons)	Recipies with one plant species	plant species	most common mentioned plant species	application
2011	AG, ZH, SH	21 (24)	123	43	*Matricaria recutita* L., *Calendula officinalis* L., *Symphytum officinale* L., *Coffea arabica* L.	150
2012	TG, SG, AI, AR	38 (50)	315	76	*Matricaria recutita* L., *Calendula officinalis* L., *Rumex obtusifolius* L., *Urtica dioica* L.	428
2013	GL, NW, OW, SZ, UR, ZG	49 (63)	230	68	*Matricaria recutita* L., *Calendula officinalis* L. *Utrica dioica* L., *Coffea arabica* L.	278
ges.	13	108 (137)	668	109		856

› **Ongoing project**

Schmid et al., 2012; Disler et al., 2014; Walkenhorst et al., 2014

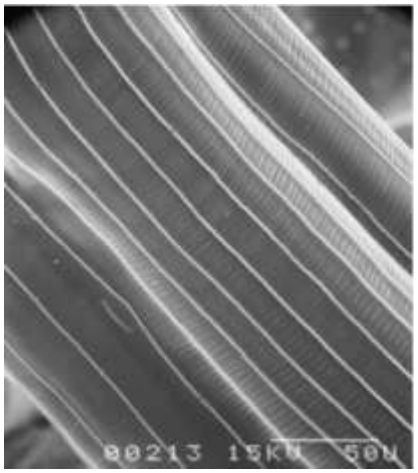
Tanniferous fodder: Ex. Sainfoin

- **Excellent fodder legume**
- **Contains Condensed Tannins**
- **Prodelphinidine / Procyanidine**

- **Mueller-Harvey *et. al.* 2006**
- **Hoste *et. al.* 2006**
- **Häring *et. al.* 2007**
- **Theodoriou *et. al.* 2011**

Anthelmintic effect of Sainfoin

1. Fecundity of female worms – egg output ↓ and nematicidal effect in some studies
2. Establishment of L3 larvae
3. Development of free living stages?



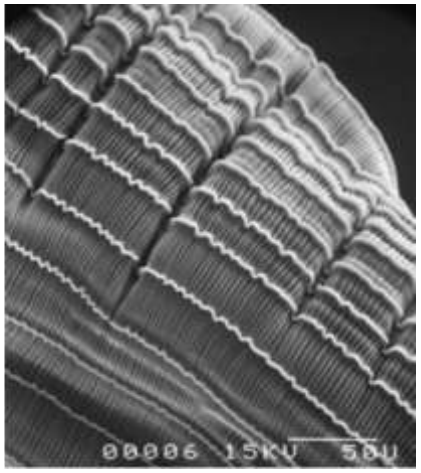
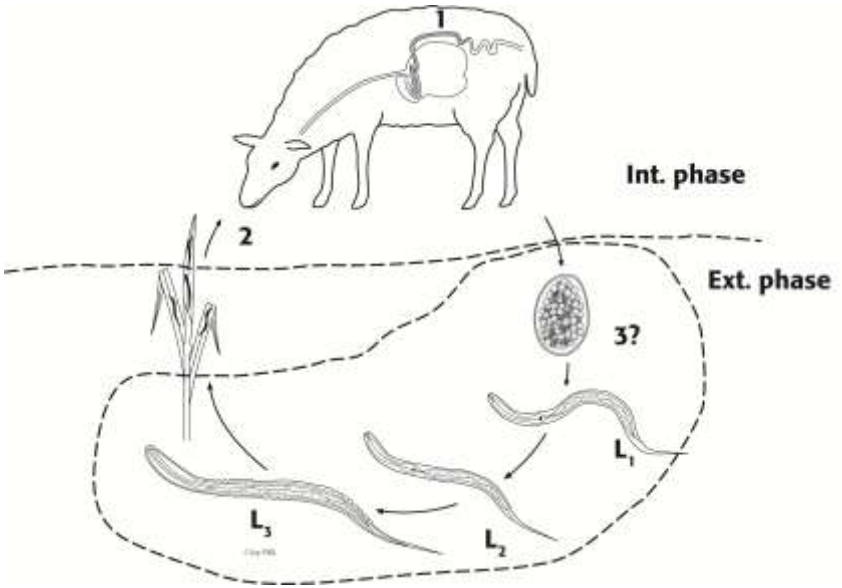


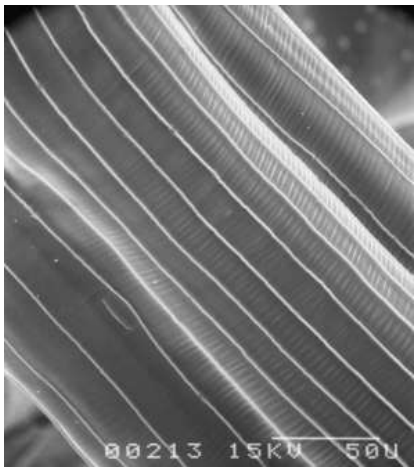
Photo: Cintli Martinez Ortiz de Montellano (INRA Toulouse)

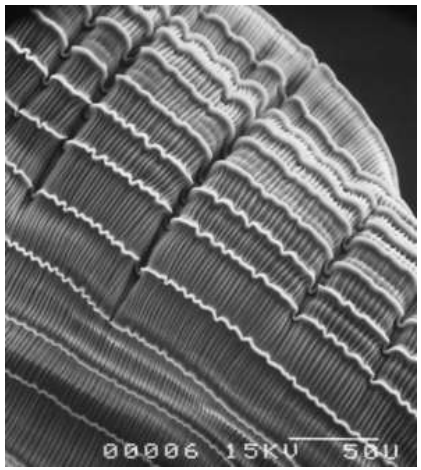


Sainfoin – results

Trial	Focus	Feeding period	Tannin concentration	Effect on GIN
Lambs[1]		16 Days	6.12 % DM	+++
Ewes[1]	PPR	25 Days	5.74% DM	+++
Goat		20 Days	4.34 % DM	+
Goat		22 Days	4.34 % DM	-
Goat	PPR	60 Days	4.31 % DM	+

Photo: Cintli Martinez Ortiz de Montellano (INRA Toulouse)





[1] Werne et al., 2013 a and b

Conclusions

- «Resistance» is an (very) old and not the only mechanism of microoganisms to compete inside the microorganisms world
- Through a tremendously risen density of livestock (and human) - living under suboptimal conditions - and an extensive use of antimicrobials the expansion of pathogens as well as resistances was an expectable consequence.
- The demands of organic agriculture how to keep and manage livestock offer several important aspects - with main emphasis on prevention - how to keep livestock healthy without using antibiotics and antiparasitics as an production factor.
- Results of recent pharmaceutical, pharmacological and (human) clinical research confirm oftentimes the meaningfulness of the traditional use of medicinal plants, specific veterinary research in the field of phytotherapy is highly needed.


Thank you very
much for your
attention !