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ANTIMICROBIAL RESISTANCE – MYTHS AND REALITIES

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ABSTRACT

Antimicrobial resistance and its potential transmission from animals to man has become a major issue, both politically and scientifically, and is leading to greater controls, both in North America and Europe, on how we use antibiotics in agriculture and veterinary medicine. There is deep and sincere concern expressed by the medical profession about the worsening antimicrobial resistance situation in man and the potential that agricultural/veterinary use of antimicrobials is adding to their problem – to a large extent – the 'myth'? Hence there is a call for a 'One Health' approach between human and animal use of antibiotics to try to combat the problem. However, much of the proposed legislation and controls on veterinary medicine is not based on factual assessments but assumptions, and the contribution that agricultural use is making on human antimicrobial resistance problems has not been quantified – the 'reality'?

By analysis of the transmission of infections to man it can be shown that the direct transmission of infections and resistance from pigs to pig farmers/workers of such bacteria as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus suis* are relatively high at 83% and 21%, respectively. *Escherichia coli* transfer appeared to be lower at 4%.

Indirect transmission via meat appears to be a much smaller risk from pigs to the human population. *Campylobacter coli* transmission attribution from pigs to man is 0.3% of all campylobacter cases of food poisoning. Macrolide resistance tends to be higher in pigs but even so the resistance transmission rate in the EU is estimated at 0.00003% or 0.03 people /100,000 population. Similarly, the main salmonella infection, *S.* Typhimurium, found in pigs the transmission attribution of extended-spectrum beta lactamase (ESBL) resistance caused by the use of 3rd and 4th generation cephalosporins can be estimated at 0.00004% or 0.04 people/100,000 population. Recent attribution data of ESBLs transmitted from animals and food to man in the EU suggests that only 0.27% of resistant genes are identical to those found in man and therefore 99.73% are associated with human use of cephalosporins particularly in the hospital situation. Based on Swedish data the attribution of animal and food transmission (all species not just from pork) of ESBL resistance is 0.00022%/year or 0.22 people/100,000 population.

It appears likely that the attribution of antimicrobial resistance by indirect transmission to the general human population is overestimated and unlikely to have significant effects on resistance development in man. Both medical and veterinary doctors need to use antimicrobials responsibly and put infection control programmes in place to ensure that they remain effective for the future.

INTRODUCTION

Antimicrobial resistance and its potential transmission from animals to man has become a major issue, both politically and scientifically and is leading to greater controls, both in North America and Europe, on how we use antibiotics in agriculture and veterinary medicine. There is deep and sincere concern expressed by the medical profession about the worsening antimicrobial resistance situation in man and the potential that agricultural/veterinary use of antimicrobials is adding to their problem – to a large extent – **the 'myth'?** Hence there is a call for a 'One Health' approach between human and animal use of antibiotics to try to combat the problem. However, much of the proposed legislation and controls on veterinary medicine is not based on factual assessments but assumptions, and the contribution that agricultural use is making on human antimicrobial resistance problems has not been quantified – **the 'reality'?**

This paper attempts to quantify the significance of the use of antimicrobials in pigs on human antimicrobial resistance or enables it to be determined on a national basis.

OVERVIEW OF RESISTANCE DEVELOPMENT AND SPREAD

The use of antibiotics, especially when given by mouth, either in feed or in drinking water or tablets etc. may have a direct effect on the bacteria in the gut; i.e. kills them off if they are susceptible. They may be good bacteria or the bad **pathogenic bacteria** that you are trying to treat like *Escherichia coli* or *Brachyspira hyodysenteriae*. This exposure may select for organisms that are either **inherently resistant**, so they don't die, then they multiply because of reduced competition or selects for resistant bacteria that have already **acquired resistance**. Bacteria can acquire resistance either by **mutations** of their DNA (remember they are often growing and multiplying at a very fast rate) and if this mutation is on chromosomes this leads to clonal spread as the bacteria multiply e.g. *Campylobacter coli* and fluoroquinolone resistance. Sometimes they acquire resistance via **plasmids**, which are passed from one cell to another by **conjugation** (almost sexually) and some bacteria like *E. coli* can spread plasmids very readily and these carry potentially **resistant genes** so are spread horizontally to possibly susceptible bacteria or potentially other bacterial species. Less common routes of transmission are by **transformation**; they pick up DNA left by other bacteria or by **transduction** where bacteriophages (viruses) inject the DNA. After treatment, the gut flora stabilises over time and often returns to what it was before. Some bacteria that have resistant genes or plasmids do not always survive or compete very well and naturally die off. Hopefully, the pig has developed immunity or is resistant to further infections.

Generally, in pig medicine we use a lot of oral antimicrobials via feed or drinking water; hence many of the bacteria we find in the gut carry a higher level of resistance. Resistance is often higher in young or weaned pigs where they have been treated but by the time they go for slaughter the resistance is less (Table 1). This is important to reduce potential indirect transmission of resistance via meat contamination.

We also use oral antibiotics to treat respiratory diseases such as *Mycoplasma hyopneumoniae* (enzootic pneumonia), *Actinobacillus pleuropneumoniae*, or systemic diseases like *Streptococcus suis* (strep meningitis) of *Haemophilus parasuis* (Glässer's disease). Generally, resistance is lower against these infections but the gut flora is exposed

at the same time, hence tetracycline resistance is very high in *E. coli* (around 80%) but relatively low in *A. pleuropneumoniae* (24%).

Table 1. Comparison of antimicrobial resistance (%) in *E. coli* by age group in the UK (VMD, 2015).

Antimicrobial	**Neonatal pig**	**Post-weaning**	**Adult**
Ampicillin	49	61	35
Amoxicillin+ clavulanic acid	0	4	0
Cefpodoxime (3G)	0	1	0
Spectinomycin	51	52	24
Streptomycin	40	63	25
Neomycin*	5	2	12
Apramycin	3	37	6
Enrofloxacin	18	6	6
Tetracycline	77	82	59
Trimethoprim+ sulpha	49	64	29

Key: * not available UK

We also use oral antibiotics to treat respiratory diseases such as *Mycoplasma hyopneumoniae* (enzootic pneumonia), *Actinobacillus pleuropneumoniae*, or systemic diseases like *Streptococcus suis* (strep meningitis) or *Haemophilus parasuis* (Glässer's disease). Generally, resistance is lower against these infections but the gut flora is exposed at the same time, hence tetracycline resistance is very high in *E. coli* (around 80%) but relatively low in *A. pleuropneumoniae* (24%, Table 2).

Table 2. Antimicrobial resistance (%) in the EU to *A. pleuropneumoniae, S. suis* and *H. parasuis* (El Garch et al, 2015).

Antimicrobial	***A. pleuropneumoniae***	***S. suis***	***H. parasuis***
Amoxicillin	11	1	1
Amoxicillin+ clavulanic acid	0	1	0
Ceftiofur (3G)	1	2	0
Tulathromycin	0	67e	0
Tiamulin	0	85e	0
Tilmicosin	1	67	0
Florfenicol	1	0e	0
Enrofloxacin	1	1	0
Tetracycline	24	88	3
Trimethoprim+ sulpha	2	10	3

Key: e = estimate.

If low preventive levels or growth promotion levels are used this also increases the exposure of the gut flora, which may lead to greater resistance. So saying however, some bacteria acquire resistance quicker than others e.g. *E. coli* and some antibiotics develop resistance more slowly e.g. aminoglycosides such as neomycin and apramycin.

Some antibiotics given by injection are excreted primarily by the kidney (amoxycillin, ceftiofur) and thereby do not have such an impact on gut flora. Others, like enrofloxacin and tiamulin are metabolised and excreted mainly by the liver and bile duct directly into the gut and again can expose the gut flora to the drug. The former kidney excretors are good for kidney infections caused by *E. coli* and the liver excretors are often good for treating gut infections, like enrofloxacin and *E. coli* and tiamulin and *B. hyodysenteriae* (swine dysentery).

There is concern about **multiple resistance** development to pig pathogens by veterinarians and farmers e.g. we have multiple resistant *B. hyodysenteriae* in the EU, resistant to all licensed antimicrobials, which has made it necessary to depopulate herds. However, the main public concern about resistance in pigs in particular, is the potential transference of resistance, whether via **zoonotic bacteria**, which cause disease in man such as *Salmonella* or *Campylobacter* spp and make them more difficult to treat, or by **commensal bacteria**, such as *E. coli* and *Enterococcus* spp, which may transmit resistance via plasmids and genes to the human gut flora but may not cause disease directly in man. *Staphylococcus aureus* has become a recent concern, as it can colonise a pig's nose and may spread to man. In many countries in the EU and also N. America, many pig farms carry the methicillin resistant form (**MRSA**) in particular CC398. The bacterium can colonise the pig's nose and live there quite happily and may not cause disease, however it can colonise a human nose also but usually for a short time; it can cause disease in man but hospitals that screen patients are very worried about it coming into the wards and being spread to other patients or contaminating wounds of the carriers post surgery.

DIRECT SPREAD

Methicillin-resistant *Staphylococcus aureus* (MRSA)

The direct spread of MRSA from pigs to man has been a major issue. **Ninety percent** of MRSA CC398 human carriers and infected patients in Denmark (DANMAP, 2011) were associated with pig farming, either workers/farmers or veterinarians and their families. In Germany, colonisation was reported at **83% in pig farmers** and 4.3% of their families (Cuny et al, 2009). Additionally, 36% of pig veterinarians and 14% of slaughterhouse workers (Blaha et al, 2009) had nasal colonisation. The spread beyond to the general population was very limited. The methicillin-susceptible form (MSSA) has been around for a long time in humans but somehow got into pigs and it is postulated that the widespread use of 3rd generation cephalosporins in the 2000's probably **selected** for MRSA in piggeries. Methicillin or related compounds are not used in pig medicine but once it has the *mec*A gene it is resistant to all beta-lactam (penicillin-based) antibiotics. The pig associated MRSA is usually tetracycline resistant and has been found to have a chromium/zinc resistance *cra* gene associated with the *mec*A gene. Both tetracyclines and zinc oxide are widely used in many pig-producing countries but these are not **primary selectors** of methicillin resistance but may be **co-selectors** if they have the resistance genes as well as they may kill off susceptible bacteria, enhancing the survival of the resistant bacteria.

In Denmark, there is great concern about the spread of MRSA from pigs to man. The Danes (DVFA, 2014) identified that in 2013, 68% of finisher herds were MRSA positive and colonisation with MRSA CC398 in man was increasing rapidly to 643 cases (30.7%)

of overall MRSA colonised patients and infection and clinical disease associated with CC398 was 156 cases (**16.8%**) and of these, bacteraemias were **1.8%** and actual deaths were lower at approximately **0.8%** (Table 3). All mortalities had a number of serious underlying diseases.

Table 3. Epidemiology of direct contact infections from pigs to stockmen – MRSA Denmark.

Chain	Example	Contact population (Denmark)	General population (Denmark)
Organism	**MRSA**		
Source	Pig (68% herds)	20 million killed	
Host	Man	25,000 **pig workers**	5.5 million
Route	Inhalation dust		
Susceptibility of host	High	High	High
Colonisation	83%	14,100 (56.4%)	0.26%
Infection	16.8%	156 (1.1%)	0.0028%
Disease incidence	16.8%	156 (1.1%)	0.0028%
Resistance transfer (%)	100	100	100
Treatment failure incidence due to resistance	0.8%	1.25 (0.8%)	0.000023%
Mortality incidence	0.8%	1.25 (0.8%)	0.000023%

The potential direct spread of the pig MRSA to stockmen can be very high and therefore **methicillin resistance** spread to stockmen is also high. By comparison, the spread amongst the general Danish population is incredibly low and potential infection rate is **0.0028%** in comparison with **1.1%** in stockmen.

Streptococcus suis

Barlow et al (2003) in the UK reported that **21% of pig stockmen** were seropositive to *S. suis* type 2; there were approximately two clinical cases/year over a 20 year period and approximately 12.5% of cases died from the infection. One death was in a case who was asplenic (immunocompromised). Approximately, 20-30% of UK pig farms are affected by *S. suis* infections. Interestingly, almost all of the isolates in the UK cases were penicillin susceptible, the main antibiotic used for treatment, so penicillin resistance transfer *per se* was not the issue and could be considered as effectively zero.

Direct transmission of *S. suis* to pig farm workers can be considered high at 21% causing seroconversion but infection transmission amongst the general public is low at 0.0032% and penicillin resistance transfer is zero (Table 4).

Escherichia coli

In contrast, Nijsten et al. (1996) in the Netherlands found that the antibiotic resistance of *E. coli* in faecal samples of pig farmers was significantly lower than samples obtained from pigs. The resistance patterns of only **4% of farmer *E. coli*** were the same as pigs from the same farm. DeBeen et al. (2014) did show that direct transmission of *E. coli* carrying

plasmids and extended-spectrum beta lactamase (ESBL) resistance genes could be transmitted from pigs to farmers.

Direct spread of bacteria from pigs to farmers can be considered high and as a consequence, the potential risk of the direct spread of antimicrobial resistance can also be considered high.

Table 4. Epidemiology of direct contact infections from pigs to stockmen – *S. suis* UK.

Chain	Example	Contact population (UK)	General population (UK)
Organism	***S. suis***		
Source	Pig	10 million slaughtered	
Host	Man	10,000 pig workers	65 million people
Route	Direct		
Susceptibility of host	Low - moderate	Low - moderate	Low - moderate
Colonisation	21%	2,100	0.0032%
Infection (seroconversion)	21%	2,100	0.0032%
Disease incidence	0.02%	2 (0.048%)	0.000003%
Resistance transfer (%)	0	0	0
Treatment failure incidence due to resistance	0	0	0
Mortality incidence	12.5%	0.25 (0.095%)	0.0000003%

INDIRECT SPREAD

Campylobacter coli

Campylobacter spp are currently the most frequently transmitted enteric infections transmitted from animals to man, mainly by contaminated food and the environment (EFSA/ECDC, 2014a). *Campylobacter jejuni* infections are the most common in man accounting for approximately **94.4%** and *C. coli* for approximately **5.6%** (Mughini Gras et al., 2012) in a Dutch case control study. Chickens have a similar proportion of *Campylobacter* species to humans and cattle are predominantly *C. jejuni* too. Pigs however, carry predominantly *C. coli* and Burch (2002) concluded that using macrolide (erythromycin) resistance as a marker, pig *C. coli* were unlikely to contribute significantly to human *C. coli* infections. Carcass contamination of pork with *Campylobacter* spp is also very low at 0.6% but chicken carcasses are high at 31% (EFSA, 2011). Mughini Gras et al. (2012) looked at a combined case control and genetic source attribution analysis for both *C. jejuni* and *C. coli* in the Netherlands, using multi-locus sequence typing (MLST). Overall, they attributed cases, 66.2% to chicken, cattle 20.7%, sheep 2.5%, **pigs only 0.3%** and environment 10.1%.

The susceptibility of *C. jejuni* to the fluoroquinolone, ciprofloxacin, is relatively low but the susceptibility to macrolides (erythromycin) is comparatively high (EFSA/ECDC, 2014b, Table 5). In contrast the susceptibility of ciprofloxacin to porcine *C. coli* is higher but erythromycin lower.

Therefore, based on the Mughini Gras et al (2012) attribution, a likely EU assessment (EFSA/ECDC, 2014b) of resistance attribution to humans of the 214,268 reported cases from *Campylobacter* spp infections can be made for pigs and poultry for macrolides (Table 6).

Table 5. Resistance* (%) of *Campylobacter* spp to antimicrobials in the EU.

Species	Ciprofloxacin	Erythromycin	Gentamicin	Tetracycline
C. jejuni				
Human (14MS)	54.1	1.4	0.2	28.3
Chicken (10MS)	44.1	0.4	0.7	34.1
Chicken meat (8MS)	59.5	1.8	0.7	47.5
Cattle (5MS)	32.9	0.6	0.2	43.5
C. coli				
Human (14MS)	42	15.1	1.8	49.7
Chicken (6MS)	78.4	11.2	4.1	73.1
Chicken meat (6MS)	82.7	16.5	1.7	57.3
Pigs (5MS)	32	23.9	2.9	76.8

(EFSA/ECDC, 2014b) *Human data used clinical breakpoints, whereas animal data used epidemiological cut-off breakpoints, so not directly comparable. MS = Member States

Table 6. Comparison of *Campylobacter* spp transmission by pigs and chickens to humans and macrolide resistance in the EU.

Chain	Example	Population (EU)	Example	Population (EU)
Organism	***Campylobacter***		***Campylobacter***	
Source	**Pig**	250 million	**Chicken**	6.7 billion
Host	Man	500 million	Man	500 million
Route	Meat	Meat	Meat	Meat
Susceptibility of host	High	High	High	High
Colonisation	Low	Low (5.6% Cc)	High	High (94.4% Cj)
Infection	0.3%	214,268* cases	66.2%	214,268* cases
Disease incidence	0.3%	643 cases (0.00013%)	66.2%	141,845 cases (0.028%)
Resistance transfer	23.9% (Macro)	154 (0.00003%)	1.8% (Macro)	2553 (0.0005%)
Treatment failure incidence due to resistance	ND	ND	ND	ND
Mortality case incidence	0.03%	0.2 cases (0.00000004%)	0.03%	28.2 cases (0.000006%)

Key: Macro = Macrolide *Reported cases of campylobacter in man; Cc = *C. coli*; Cj = *C. jejuni*; ND = No data.

Macrolide resistance is transmitted by pigs to man at a very low rate of **0.00003% or 0.03 people /100,000 population** and the incidence or potential macrolide resistance transfer from chickens is also low **0.0005% or 0.5 people/100,000 population**. This is in accord

with the European Medicines Agency's categorisation of macrolides (EMA, 2014) as a lower risk family of antimicrobials in their Category 1, in contrast to the World Health Organisation's (WHO, 2011) assessment of being a Highly Critically Important Antibiotic (HCIA).

Salmonella spp

The incidence of reported salmonella cases has been steadily falling in the EU since 2004 when it was 195,947 cases (EFSA/ECDC, 2010) until 2012 when it was 91,034 cases (EFSA/ECDC, 2014a), a 54% fall, following the introduction of vaccine and hygiene measures in poultry flocks. The main effect has been a reduction of the incidence of *S. enterica* Enteritidis, which contaminated meat and eggs but *S.* Typhimurium cases, the main pig isolate, have stayed much the same (Table 7).

In the EU, in contrast, the main human salmonella serovars were **41.3% *S*. Enteritidis** and **29.3% *S*. Typhimurium and monophasics** (EFSA/ECDC, 2014a). Pigs are commonly associated with *S.* Typhimurium but phage typing of GB isolates tells a different story that possibly only one third **(9.8%)** are pig associated(AHVLA, 2014) and therefore **51.1%** are chicken associated (both *S.* Enteritidis and *S.* Typhimurium).

The antimicrobial resistance patterns for *S.* Typhimurium have been reported in EFSA/ECDC (2014b, Table 8).

Table 7. Isolation of the most common salmonella serovars in humans and animals (%) in GB (AHVLA, 2014).

Serovars	Human	Pig	Chicken	Cattle
S. Enteritidis	27.7	-	-	-
S. Typhimurium	11.0	33.1	-	5.0
Monophasic S. Typhimurium	10.1	43.3	-	3.5
S. Infantis	3.0	-	-	-
S. Newport	2.6	-	-	-
S. Virchow	2.3	-	-	-
S. Stanley	1.8	-	-	-
S. Kentucky	1.6	-	-	-
S. Paratyphi (Java)	1.5	-	-	-
Others	38.2	23.6	100	-

Table 8. A comparison of antimicrobial resistance (%) to human and animal *S.* Typhimurium isolates (EFSA/ECDC, 2014b).

Antimicrobial	Human (19MS)*	Pig (5MS)**	Chicken (5MS)**	Cattle (7MS)**
Ampicillin	66.6	76.7	39.5	34.5
Cefotaxime (3G)	0.9	2.3	4.0	0.4
Ciprofloxacin	2.2	7.5	17.7	9.1
Gentamicin	3.0	3.7	1.6	1.1

Key: MS = Member States; 3G = 3rd generation cephalosporin; *Clinical breakpoint; **Epidemiological cut-off value.

The estimation of transfer of cefotaxime (3G) (ESBL) resistance from pigs and chickens to man via *Salmonella* spp infections is summarised in Table 9.

Table 9. Comparison of *Salmonella* spp transmission by pigs and chickens to humans and cefotaxime 3G (ESBL) resistance.

Chain	**Example**	**Population (EU)**	**Example**	**Population (EU)**
Organism	***Salmonella* spp**		***Salmonella* spp**	
Source	**Pig**	250 million	**Chicken**	6.7 billion
Host	Man	500 million	Man	500 million
Route	Meat	Meat	Meat	Meat
Susceptibility of host	High	High	High	High
Colonisation	Low	Low	High	High
Infection	9.8%	91,034* cases	51.1%	91,034* cases
Disease incidence	9.8%	8,921 (0.0018%)	51.1%	46,518 cases (0.0093%)
Resistance transfer	2.3% (cefotaxime)	205 (0.00004%)	4% (cefotaxime)	1,860 (0.00037%)
Treatment failure incidence due to resistance	ND	ND	ND	ND
Mortality case incidence	0.14%	12.4 cases (0.0000025%)	0.14%	70 cases (0.000014%)

Key: ND = No data; *Reported cases of salmonella in man (EFSA/ECDC, 2014a).

The estimated transmission rate of cefotaxime (3G) resistance via *Salmonella* spp from pigs to man is **0.00004% or 0.04people/100,000 population**. For chickens the transmission rate is higher at **0.00037% or 0.37people/100,000 population**. On this basis ESBL resistance transmission can be considered very small even for chickens.

Escherichia coli

There have been a number of reports in the EU looking genetically at ESBL resistance genes found in urinary tract infections and blood-borne infections in man and comparing them from ESBLs found in animals and food (Wu et al, 2013, SVARM, 2015; DANMAP, 2015; Burch, 2015).

These results demonstrated that **2/747 (0.27%) ESBL resistant genes** were identical to genes found in animals and food and that **745/747 (99.73%) were attributable to human** use of 3rd and 4th generation cephalosporins in man (Table 10). Surprisingly, the Danes concluded in their report that "consumption of meat may currently be considered an insignificant source for the human infections" (DANMAP, 2015). Using the SVARM (2015) data the attribution rate of ESBLs from animals to human infections was 1/379 (0.26%), which represents on a transmission rate basis that the number of clinical cases potentially caused by ESBL containing *E. coli* from food/farm animals = 21.2/8,161 cases or an infection rate of **0.00022%/year** on a 9.5 million population basis. This represents **0.22 people/100,000 population** out of 85people/100,000 population which would normally get infected, i.e. an extremely low infection rate.

Table 10. Combined results ESBL resistance gene attribution from animals and food and those in clinical infections in man (Wu et al, 2013, SWARM, 2015; DANMAP, 2015).

Reference	Member States involved	No. human ESBL genes tested	No. of animal ESBL genes identical	Percentage animal/human ESBL genes identical
Wu and others, 2013	UK Netherlands Germany	127	0	0
SVARM, 2015	Sweden	379	1	0.26
DANMAP, 2015	Denmark	241	1	0.41
Total	**5**	**747**	**2**	**0.27** (SD ± 0.21)

RISK ASSESSMENT SUMMARY

A comparison of risk assessments for transfer of infectious agents and antibiotic resistance transfer from pigs to man are summarised in Table 11.

Table 11. Comparison of risk assessments for transfer of infectious agents and antibiotic resistance transfer directly from pigs to farmers or indirectly from meat to man.

Direct transmission to farmers			
	Colonisation (%)	Disease (%)	Resistance (%)
MRSA	83	16.8	100
S. suis	21	0.02	0
E. coli	4	0	4
Indirect transmission to population			
Campylobacter spp	0.00013	0.00013	0.00003 (macrolide)
Salmonella spp	0.0018	0.0018	0.00004 (ESBL)
E. coli	Low	Low	0.00022 (ESBL)

In comparison, direct transmission from pig to farmer is potentially very high, depending on the organism and the infection on the farm. Indirect transmission from meat to man is apparently very low.

CONCLUSIONS

The direct transmission of infectious agents from pigs to man, working and caring for the animals, is unfortunately very high. It also depends on which bacteria are present on the farm. The transmission of MRSA to farmers and veterinarians appears to be very high. Fortunately, colonisation in man is not long lived and there is a low incidence of infection and disease with it. Similarly, for *S. suis*, the transmission probably in the air and dust is also very high and the colonisation and seroconversion is also high but the incidence of disease is low. *Escherichia coli* probably can be easily transmitted by faecal and dust

contact to the farmer and may be ingested. Fortunately, colonisation is comparatively low and infections are low but the spread of plasmids and resistance genes does occur.

Indirect transmission via pig meat and its products would appear to be very low. Only 0.3% of human *Campylobacter* spp infections are attributed to pigs. Macrolide resistance may be a little higher than say in poultry but overall the infection rate and resistance transmission rate is very low. Salmonella in man is changing in the EU with an over 50% reduction, mainly of the chicken infection *S.* Enteritidis. Sero-typing of *S.* Typhimurium, the main pig strain, shows that both poultry and cattle contribute also and it is not just pigs that carry it. ESBL resistance is not high so actually the transmission rate of this important resistance is low. Recent data regarding ESBL resistance transmission by *E. coli* also demonstrates a very low transmission rate from food to man and causing infections in man. There is a different epidemiology of resistance transmission spreading in man because of the high usage of cephalosporins in man and the transmission of infectious agents and their resistance genes particularly in hospitals (Overdevest, et al, 2011).

Antibiotics must be used responsibly in pigs and the future legislation is likely to reduce their use by banning growth promotion and moving them under veterinary prescription. In the EU we are going further by banning prophylactic use and restricting in-feed medication. The 'myth' that antibiotic use in pigs causes a huge amount of resistance in man does not stand up to close scrutiny and hopefully the 'reality' will be taken on board by legislators to prevent over-restriction of the use of antibiotics in veterinary medicine and endangering the health, welfare and productivity of pig production.

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