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Human Deaths and Third-Generation Cephalosporin use in Poultry, Europe

To the Editor: Globally, antimicrobial drug resistance is rapidly rising, with resultant increased illness and death. Of particular concern is *Escherichia coli*, the most common bacterium to cause invasive disease in humans (1). In Europe, increasing proportions of bloodstream infections caused by *E. coli* are resistant to third-generation cephalosporins (1,2).

Resistant *E. coli* can be transmitted to humans from animals. A large proportion of resistant isolates causing human infections are derived from food animals (3–6). However, lack of data has made it difficult to quantify the proportion of antimicrobial drug resistant *E. coli* infecting persons through food sources and the resultant effects on human health. Recent data from the Netherlands now make such estimates possible (2,6). The additional illness and death among humans resulting from bloodstream infections caused by third-generation cephalosporin-resistant *E. coli* (G3CREC) has been calculated for Europe (2). In the Netherlands, there were 205 G3CREC cases during 2007 (4% of all *E. coli* bloodstream infections) (2). Another study in the Netherlands revealed that 56% of the resistance genes in G3CREC in humans were identical to genes derived from *E. coli* isolated from retail chicken samples (6). Using the findings of Overdeest et al. (6) and de Kraker et al. (2), we calculated that, in the Netherlands, infections in humans

with G3CREC derived from poultry sources were associated with 21 additional deaths. G3CREC-related illness also resulted in 908 hospital bed-days needed to treat persons with these antimicrobial drug resistant bloodstream infections. If these values were extrapolated to all of Europe (i.e., if 56% of G3CREC were derived from poultry), 1,518 additional deaths and an associated increase of 67,236 days of hospital admissions would be counted as a result of cephalosporin and other antimicrobial drug use in poultry.

To more accurately estimate the associated increased deaths among persons resulting from third-generation cephalosporin use in poultry, detailed data from more countries is essential. Needed data include records of antimicrobial drug use and resistant bacterial strains found in food animals and domestic and imported foods. However, we already know that G3CREC is rapidly rising in many countries, and in Europe, the infection rate is likely to have tripled from 2007 to 2012 (2). Globally, billions of chickens receive third-generation cephalosporins in ovo or as day-old chicks to treat *E. coli* infection, a practice that has resulted in large reservoirs of resistant bacteria. In Canada, this practice has been associated with substantial increases in resistance to third-generation cephalosporins in *Salmonella enterica* serovar Heidelberg isolates detected in humans. (7). The United States Food and Drug Administration recently prohibited the off-label use of cephalosporins, including prophylactic uses, in major food animal species, including poultry (8).

The number of avoidable deaths and the costs of health care potentially caused by third-generation cephalosporin use in food animals is staggering. Considering those factors, the ongoing use of these antimicrobial drugs in mass therapy and prophylaxis should be urgently examined and stopped, particularly in poultry, not only in Europe, but worldwide.

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Autochthonous Human Schistosomiasis, Malaysia

To the Editor: In Malaysia, the only histologically diagnosed autochthonous cases of human schistosomiasis were reported in the 1970s, all in rural aborigine (Orang Asli) populations (1–3) (online Technical Appendix Figure 1, wwwnc.cdc.gov/EID/article/19/8/12-1710-Techapp1.pdf). The fact that the infection had been found only among aborigines had led to the proposal of a distinct unknown schistosome with an animal reservoir causing sylvatic infections (2,3). Consequently, during the 1980s, *Schistosoma malayensis* n. sp. was described from intermediate snail (*Robertsiella* sp.) and final mammalian hosts (*Rattus muelleri* and *R. tiomanicus* [4]). *S. malayensis* is closely related to *S.*

mekongi and differs genetically from the latter by $\approx 10\%$. Both species differ from *S. japonicum* by 25% (5), and adult and ova morphologies are similar (4). Few transmission sites for this new *S. japonicum*–complex schistosome species were identified in rural areas (4). We report after 30 years the histologic finding of *S. malayensis*–like eggs in the liver of a Malay man and discuss public health implications.

A 29-year-old male nonaboriginal Malay from Subang Jaya in Selangor State, Peninsular Malaysia, had died suddenly of an intoxication in 2011. According to his mother, he had reported hematuria and dysuria during adolescence. Similar symptoms had reoccurred 10 years later, accompanied by constipation. The patient had never been outside of Malaysia, and he had gone bomb fishing for many years in Sungai Lepar Utara, a river near his village (Felda Tekam Utara, Jerantut, Pahang; 3°52'30"N, 102°49'2"E). No tests on blood or feces were performed before his death. An autopsy was conducted in Sungai Buloh Hospital, and gross pathology showed a normal heart, kidneys, and brain. The lungs were edematous and congested. The liver also was congested, but no macroscopic lesions were seen. Toxicology investigations showed methadone and a derivative in his blood and urine. During a routine histologic examination, several granulomas with intensive lymphocyte, monocyte, and eosinophil infiltration surrounding clusters of ovoidal eggs were found in the liver (Figure; online Technical Appendix Figure 2). Serial sectioning showed that the eggs contained miracidia and had the overall appearance of *S. malayensis*–like ova 50 μm long \times 28 μm wide. The ova were not operculated and had no bipolar plugs; the thin yellowish shell was not striated, but a knob-like structure was seen laterally. Morphologic differential diagnoses included eggs of *Capillaria hepatica* (bipolar striated ova in liver), *Dicrocoelium* (slightly

smaller operculated ova typically found in feces or bile), and the similar *Eurytrema* (thick-walled operculated ova in feces).

Schistosomiasis is endemic in many developing countries and infects >207 million persons living in rural agricultural areas (6). In Asia, *S. japonicum*, *S. mekongi*, and *S. malayensis* cause human infection (7), with *S. japonicum* being the most dangerous. In Malaysia, *S. malayensis*, in addition to *S. spindale*, *S. nasale*, *S. incognitum*, *Trichobilhazia brevis*, and *Pseudobilharziella lonchurae*, is known to occur in wildlife (8). The first known case of human schistosomiasis in Malaysia was discovered in 1973 during an autopsy of an aborigine. *Schistosoma* eggs resembling those of *S. japonicum* were found in liver tissue (1). A subsequent retrospective autopsy study revealed additional cases with these *Schistosoma japonicum*–like ova in the rural aboriginal population, resulting in an overall prevalence of 3.9% (2). Several attempts to recover eggs from feces from the Orang Asli population in peninsular Malaysia (3), a biopsy-positive Orang Asli (3), and serologically positive persons (9, and others) were unsuccessful, however, which was attributed to the zoonotic nature of *S. malayensis* and thus missing adaptation to the human host. Whether hematuria, a typical sign of *S. haematobium* infection, as seen in the patient reported here also was caused by *S. malayensis* disease remains unclear because symptoms of the latter have not been reported. Serologic surveys for schistosomiasis in peninsular Malaysia showed prevalences of 4%–25% in selected rural populations (9). Because infected *Robertsiella* snails had been found almost exclusively in small rivers (4,9–habitats like the Sungai Lepar Utara River in our current report—we suspect that the patient most likely became infected while fishing. The travel history may not be accurate

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Technical Appendix

Technical Appendix Table 1. Estimated numbers of deaths associated with chicken derived 3rd generation cephalosporin resistant *Escherichia coli* (G3CREC) blood stream infections in Europe* in 2007†

Country	Population incidence of E. coli blood stream infections per 100,000 population	Population incidence of 3rd Generation cephalosporin SENSITIVE E. coli blood stream infections per 100,000 population	Population incidence of G3CREC (RESIST) blood stream infections per 100,000 population	% G3CREC	No. cases of G3CREC	No. cases of chicken associated G3CREC‡	Excess deaths from G3CREC	No. excess deaths caused by chicken-associated G3CREC‡	Excess no. bed-days from G3CREC (x 1,000)	Excess no. bed-days from chicken-associated G3CREC‡ (x 1,000)
Austria	30	27.3	2.7	9%	226	127	40	22	1.8	1.0
Belgium	19.8	19	0.8	4%	84	47	15	8	0.7	0.4
Bulgaria	7.7	5.9	1.8	23%	139	78	25	14	1.1	0.6
Croatia	27.8	27	0.8	3%	38	21	7	4	0.3	0.2
Cyprus	27.2	21.9	5.3	19%	45	25	8	4	0.4	0.2
Czech Rep.	27.7	25.8	1.9	7%	198	111	35	20	1.6	0.9
Denmark	49.1	47.6	1.5	3%	81	45	14	8	0.6	0.3
Estonia	16.4	16.3	0.1	1%	2	1	-	-	0	0.0
Finland	30.4	29.8	0.6	2%	32	18	6	3	0.3	0.2
France	49.7	48.7	1	2%	617	346	110	62	4.9	2.7
Germany	28.5	26.2	2.3	8%	1,921	1,076	343	192	15.2	8.5
Greece	12.4	11.4	1	8%	110	62	20	11	0.9	0.5
Hungary	11.8	11.2	0.6	5%	59	33	11	6	0.5	0.3
Iceland	34.9	33.6	1.3	4%	4	2	1	1	0	0.0
Ireland	40.7	38.7	2	5%	88	49	16	9	0.7	0.4
Israel	57.4	49.3	8.1	14%	558	312	100	56	4.4	2.5
Italy	17.7	15.7	2	11%	1,149	643	205	115	9.1	5.1
Latvia	6.7	5.7	1	15%	23	13	4	2	0.2	0.1
Lithuania	11.2	10.4	0.8	7%	27	15	5	3	0.2	0.1
Luxembourg	58.9	56.5	2.4	4%	11	6	2	1	0.1	0.1
Malta	28.8	25.1	3.7	13%	15	8	3	2	0.1	0.1
Netherlands	30	28.8	1.2	4%	205	115	37	21	1.6	0.9
Norway	61.2	59.9	1.3	2%	59	33	10	6	0.5	0.3
Poland	7.5	7.3	0.2	3%	64	36	11	6	0.5	0.3
Portugal	40.5	36.4	4.1	10%	431	241	77	43	3.4	1.9
Romania	3.6	2.6	1	28%	225	126	40	22	1.8	1.0
Slovenia	43.2	41.5	1.7	4%	35	20	6	3	0.3	0.2

Country	Population incidence of E. coli blood stream infections per 100,000 population	Population incidence of 3rd Generation cephalosporin SENSITIVE E. coli blood stream infections per 100,000 population	Population incidence of G3CREC (RESIST) blood stream infections per 100,000 population	% G3CREC	No. cases of G3CREC	No. cases of chicken associated G3CREC‡	Excess deaths from G3CREC	No. excess deaths caused by chicken-associated G3CREC‡	Excess no. bed-days from G3CREC (x 1,000)	Excess no. bed-days from chicken-associated G3CREC‡ (x 1,000)
Spain	44.7	41.6	3.1	7%	1,385	776	247	138	10.9	6.1
Sweden	49.1	48.1	1	2%	90	50	16	9	0.7	0.4
Turkey	14.8	8.9	5.9	40%	4,440	2,486	793	444	35.1	19.7
UK	38.8	34.2	4.6	12%	2,821	1,580	504	282	22.3	12.5
Europe (31 countries)	28.2	25.6	2.6	9%	15,183	8,502	2,712	1,519	120.1	67.3

*Countries include European Union member states, excluding Slovakia, both candidate countries (Croatia and Turkey), 2 European Free Trade Association countries (Iceland and Norway), and Israel.

†See (1).

‡56% of resistance in G3CREC is derived from poultry (2).

Technical Appendix Table 2. Poultry meat consumption in European Union, 2000–2009*

Country	Food supply quantity (kg/capita/yr)									
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Austria	17.1	17.9	17.3	16.8	18	18.3	16.8	17.5	17.1	17.9
Belgium	19.8	22.3	25.6	22.1	22.2	25.6	23.6	25.1	24.4	21.5
Bulgaria	16.9	18.5	21.7	15.8	17.6	18	18.8	19.9	21.3	21.4
Cyprus	29.3	29.7	30.3	28.9	28.9	30.2	24.7	26.8	28.2	26.9
Czech Republic	22.3	24.2	22.9	23.4	25.5	26.4	26.4	24.6	24.7	25.1
Denmark	17.3	20.3	20.2	18.3	16.9	19.7	19.1	20	22.7	18.9
Estonia	17.6	19.7	21.4	21	15.5	16.1	16	17.3	17.8	19.4
Finland	13.7	15.7	17	17.8	18	17.9	17.3	18.8	19.9	18.8
France	26.5	27.7	25.8	24.6	24.4	20.9	20.2	21.1	21.2	22.3
Germany	12.9	14.3	13.3	13.7	14.8	14.8	14.3	15.5	17.1	17.3
Greece	13.3	16.1	15.2	20.6	17	18	14	13.5	13.6	13.7
Hungary	34.1	34	37.1	34.1	34	33.1	28.9	27.5	27.6	26.4
Ireland	30.9	28.1	27.5	27.5	27.8	32.2	28.1	26.1	27.6	26
Italy	18.9	18.3	18	15	15.7	15.4	13.5	15.8	17	17.3
Latvia	10.3	11.8	15.5	16.3	18.4	19.1	20.4	20.5	21	19.5
Lithuania	9.8	11.1	13.2	14.8	20.2	22.6	24.4	24.9	24.9	22.6
Luxembourg	13.8	17.8	15.2	16.8	16.2	15.7	14.4	15.7	17.5	16.6
Malta	15.5	17.7	19	20.7	23.9	21.9	22	24.4	25.1	26
Netherlands	12.6	14.1	12.2	10.9	23	20.6	15	14.4	27.2	22.7
Poland	14.5	17.1	19.6	18.3	19.4	20.4	20.2	21.1	18.5	21.4
Portugal	26.6	28.3	24.6	21.5	22.9	23.8	23.4	26.3	27.6	28.7
Romania	13	15.9	19.4	19.4	19.1	20.7	19	19.3	18.6	21
Slovakia	12.6	12.4	18.2	18.7	18.2	19.9	19.7	18	18	17.4
Slovenia	29	24.1	22.5	23.2	20.6	22.8	20.3	19.9	24.6	26.5
Spain	25.3	26.2	30.2	29.7	26.8	26.9	25.8	27.3	25.3	27.5
Sweden	10.2	11.2	13.2	12.7	12.9	14	13.9	14.8	16.1	15.4
United Kingdom	28.5	29.2	29.1	29.8	31	30.8	30.8	29.1	28.2	32.2

*Data from (3). EU human poultry consumption from FAOSTAT, the FAO statistical database (<http://faostat.fao.org/?lang=en>).

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