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Salmonella virchow PT 26 infection in England and Wales: a case control study investigating an increase in cases during 1994

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SUMMARY

An increase in the number of human isolates of *Salmonella virchow* phage type (PT) 26 in England and Wales during 1994 was investigated. A national case control study was conducted which included 88 cases and 182 controls. The cases were mostly young adults (median age 26) and 13 (15%) were admitted to hospital. Acquisition of *S. virchow* PT 26 was associated with the consumption of any chicken (OR 2·5, CI 1·1–5·8), of chicken curry from restaurants and take aways (OR 2·9, CI 1·4–6·1), and of some other diverse types of pre-prepared chicken (OR 3·8, CI 1·9–7·6). Halal chicken was associated ($P = 0{\cdot}006$) with illness in a subset. There were negative associations with contact with animals (OR 0·47, CI 0·23–0·95) and with the consumption of chicken cooked whole (OR 0·37, CI 0·21–0·66). The increase in *S. virchow* PT 26 may be due to changing epizoology and may be an indicator of what will become the dominant salmonella strain in poultry in future years. The increasing incidence of *S. virchow* PT 26 is of particular concern because of its association with more invasive disease in humans.

INTRODUCTION

In spring 1994 there was an upsurge in the number of human isolates of *Salmonella virchow* PT 26 confirmed and reported by the Public Health Laboratory Service (PHLS) Laboratory of Enteric Pathogens (LEP). Eighty-three cases of human infection in England and Wales were reported in 1992 rising to 188 in 1993, and 124 isolates had been identified in the first 5 months of 1994 alone. *S. virchow* is the third most common salmonella serotype isolated from humans in England and Wales (after *S. enteritidis* and *S. typhimurium*). In 1993, PT 26 became the second most common *S. virchow* phage type (after PT 8). Poultry, in particular chicken, is the main reservoir of *S. virchow* and, unlike the commonest *S. virchow* strain PT 8, patients with *S. virchow* PT 26 infection do not usually have a history of travel abroad. The true extent of *S. virchow* PT 26 infection in UK poultry remains unknown but increasing numbers are being reported by LEP.

Cases of infection with *S. virchow* PT 26 in 1994 were predominantly in young adults. Although cases were occurring throughout England and Wales, over half of the cases in the first 5 months of 1994 were reported by four regions: Yorkshire (32), Trent (14), South East Thames (12), and Mersey (10). Most isolates of *S. virchow* PT 26 were fully sensitive to antimicrobial drugs. Isolates showing antimicrobial resistance patterns were clustered in particular geographical areas and were thought likely to be outbreak associated and not sporadic cases.

In view of the high proportion of young adults affected a hypothesis was formed that the upsurge was due to recently marketed raw chicken products made from comminuted chicken. These raw products (e.g. chicken nuggets) are likely to be confused with very

similar cooked products and consumers may be warming rather than cooking these products. Furthermore because they are frequently made from comminuted or compound chicken, salmonellae may be spread widely throughout the raw product and thus be protected from light heating. Three microbiological surveys of chicken nuggets (Dr A. Rampling, personal communication) revealed a high contamination rate, predominantly with *S. enteritidis* and *S. virchow*, the latter being found by LEP to be mainly PTs 26 and 45. Confirmation of the hypothesis could lead to more explicit labelling of these products concerning their cooking requirements.

Patients with *S. virchow* PT 26 isolated during May and June 1994 were contacted by telephone and interviewed using a detailed food questionnaire to assess whether consumption of a particular food or foods was common to those infected. Of the ten patients interviewed using this 'trawling' questionnaire, all but one had definitely consumed chicken prior to illness and four had definitely consumed chicken nuggets.

A further hypothesis was formed that the upsurge in cases of *S. virchow* PT 26 was associated with the consumption of halal chicken. There were three reasons for this. Firstly, many of the cases had Asian names; secondly, *S. virchow* PT 26 was isolated from halal mince during a concurrently running study (Dr R. Gair, personal communication) and thirdly, a disproportionate number of cases showed many of the characteristics of cases involved in an outbreak of *S. typhimurium* DT 104 where a link had been identified between infection and the consumption of halal meat (Dr C. Newman, personal communication) [1].

A case control study was conducted to determine if there was an association between the consumption of chicken, particular types of chicken and chicken products including comminuted and halal chicken, and infection with fully antimicrobial sensitive strains of *S. virchow* PT 26. Information about the increase in *S. virchow* PT 26 isolates and that a national case control study had begun was published in the *Communicable Disease Report* of 1 July 1994 [2].

METHODS

Case definition

A case was defined as a person with a diarrhoeal illness and a faecal isolate of *S. virchow* PT 26 (fully sensitive strain) confirmed by LEP after 13 June 1994.

Cases were excluded: if they had a history of travel outside the UK in the 2 weeks prior to the onset of symptoms; if the onset of their symptoms was before 1 May 1994; if they were under 6 months of age; if they were associated with an identifiable outbreak; and if they had a household contact with diarrhoea in the 7 days before the onset of illness.

Selection of controls

General practitioner (GP) nominated controls were used. GPs of the cases were asked to nominate four controls, at random, for each case from their practice list. In order to facilitate stratified sampling they were asked to select controls of the same sex as the case and within set age bands. Although GP nominated controls might result in selection bias (GPs may 'choose' patients who are more likely to be 'helpful' and to speak English) the advantages of having community controls from the same geographical area and similar socio-economic circumstances were thought to outweigh any possible selection bias by the GPs. Controls were excluded if they reported having recently suffered diarrhoea or if they had travelled abroad in the 2 weeks before the interview.

Study protocol

The consultant for communicable disease control (CCDC) for the district in which each case was resident and each case's GP were informed of the study and asked for permission to contact each case. Cases and potential controls were contacted by letter explaining the study prior to a telephone interview. Cases were asked about their likely food consumption in the 7 days before the onset of their illness and, since this was an unmatched study, controls were asked the same questions referring to the week before the interview. Most cases were contacted and the interview completed within 1 week of the isolate being typed at LEP so minimizing recall bias due to time reference.

Questionnaires

The information from the initial detailed trawling questionnaires, from the bacteriological studies of comminuted chicken products and from observation of over 100 chicken and turkey products on sale as frozen, chilled or ready to eat products in two

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supermarket chains was incorporated into the questionnaire for the case control study. Food histories therefore focused on comminuted chicken products, other chicken products, any other chicken, turkey and turkey products, beef burgers and eggs. Questions about halal meat had not been included in the trawling questionnaire and the halal hypothesis was not formed until the case control study had already begun. In light of the importance of the new information it was decided to add a question about halal chicken but to present the results separately, as a subset. The additional question on halal chicken was only asked of those who had eaten home prepared chicken since it was assumed that respondents would not know if pre-prepared chicken eaten was halal. The definition of halal chicken was left to the respondent.

Data analysis

The questionnaire data were double-entered and the two files compared to minimize data entry error. The data were analysed using Epi-Info 6 for single variable analysis [3] and GLIM 4 for single variable and multivariable logistic regression analysis [4]. Odds ratios and associated *P*-values were calculated to estimate the risk of disease associated with each potential risk factor. Those variables with a *P*-value $< 0{\cdot}2$ on single variable analysis were further analysed using logistic regression in GLIM 4 in order to test for independence of possible risk factors.

RESULTS

Over the 8-week study period from 13 June 1994, 301 isolates of *S. virchow* PT 26 were confirmed by LEP, of which 144 were fully sensitive to antimicrobial drugs. Forty-four patients were excluded from the study (14 had recently travelled abroad, 7 were less than 6 months of age, 6 were associated with 1 outbreak, 5 were asymptomatic, in 6 cases the GP did not give consent to contact the patient, 2 patients did not give consent to be contacted, 2 had a household contact with diarrhoea and no details were available for 2 patients). Therefore 100 patients were contacted by letter of whom 88 were successfully interviewed.

GPs nominated 254 potential controls and successful interviews were carried out with 182. Thus the case control study comprised 88 cases and 182 controls.

Table 1. *Case control study of* S. virchow *PT 26, England and Wales, summer 1994: age groups of cases and controls with number of cases admitted to hospital*

		Hospitalized		
Age (years)	Cases	No.	(%)	Controls
Less than 1	5	0		15
1–4	9	2	(22)	22
5–9	5	1	(20)	7
10–19	2	0		18
20–44	54	7	(13)	94
45–64	12	2	(17)	24
65+	1	1	(100)	2
Total	88	13	(15)	182

Descriptive epidemiology

Forty-nine (56%) of the cases and 111 (61%) of the controls were male. Young adults were mainly affected with 54 (61%) cases occurring in persons aged 20–44 years (Table 1). The age range of cases was 6 months to 78 years, of controls was 6 months to 70 years and in both cases the median was 26 years.

Cases reported being ill for between 2 and 30 days with a median of 10 days. All 88 cases visited their GP and all reported diarrhoea (with bloody stools in 22 (25%)), 73 (83%) reported fever, 68 (77%) abdominal pain and 39 (44%) reported vomiting. Thirteen cases (15%) were admitted to hospital (Table 1). The median length of stay for cases admitted to hospital was 6 days (range 1–21 days).

Analytical epidemiology

The results of the single variable analysis of foods consumed and the risk of illness showed that consumption of any chicken (OR 2·5, CI 1·1–5·8), of chicken curry from restaurants and take aways (OR 2·9, CI 1·4–61), and of some other diverse types of pre-prepared chicken (OR 3·8, CI 1·9–7·6) were significantly associated with illness (Table 2). Consumption of halal chicken showed an association ($P = 0{\cdot}006$) with illness in the subset who were asked this question. Consumption of comminuted chicken products, filled chicken, Chinese and barbecue style chicken, chicken pieces, beef burgers, turkey and eggs were not associated with illness. Consumption of chicken cooked whole, and contact with animals were negatively associated with illness.

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Table 2. *Case control study of* S. virchow *PT 26, England and Wales, summer 1994: single variable analysis*

Food	Cases*		Controls*		OR	95% CI	*P* value (Yates)
	Ate	Didn't eat	Ate	Didn't eat			
Beef burgers	25	59	63	119	0·8	0·5–1·5	0·5
Any chicken	76	9	141	41	2·5	1·1–5·8	0·03
Chicken nuggets	5	77	13	169	0·8	0·3–2·7	1·0
Mini kievs	1	84	2	180	1·1	0–15·6	1·0†
Chicken gougons	1	83	0	182	—	—	—
Chicken shapes	1	83	3	179	0·7	0·03–8·0	1·0†
Chicken burgers	10	74	13	169	1·8	0·7–4·6	0·3
Filled chicken	7	77	10	172	1·6	0·5–4·7	0·5
Chicken drummers	1	84	1	181	2·2	0–81·3	1·0†
Chicken curry	21	62	19	163	2·9	1·4–6·1	0·003
Chinese style chicken	5	77	12	170	0·9	0·3–3·0	0·9
Barbecued chicken	12	74	17	165	1·6	0·7–3·7	0·4
Other pre-prepared chicken	28	57	21	161	3·8	1·9–7·6	0·00005
Other chicken	41	44	92	90	0·9	0·5–1·6	0·7
Halal chicken‡	4	63	0	158	—	—	0·015
Turkey	11	75	24	157	1·0	0·4–2·2	0·9
Eggs	53	32	126	56	0·7	0·4–1·3	0·3

* Case control study comprised 88 cases and 182 controls but not all respondents answered each question.
† Fisher's exact.
‡ See text.

Table 3. *Case control study of* S. virchow *PT 26, England and Wales, summer 1994: consumption of any chicken/chicken products in the week before illness/interview*

Number of times chicken/ chicken products eaten in week	Cases		Controls	
	No.	(%)	No.	(%)
0	11	(13)	41	(23)
1–2	42	(48)	97	(53)
3–4	31	(35)	41	(22)
5+	4	(4)	3	(2)

χ^2 test for linear trend = 8·88, $P = 0·0029$.

Any chicken

Consumption of any chicken, was associated with illness. Many cases had consumed several chicken meals in the week preceding the onset of their illness and so an analysis for trend [5] was performed, comparing those who ate no chicken, those who ate chicken 1–2 times, those who ate chicken 3–4 times and those who ate it 5 or more times in the week questioned (Table 3). From this analysis there was evidence of a trend and no evidence to suggest that the trend was non-linear (χ^2 test for linear trend = 8·88, $P = 0·0029$). Therefore increasing frequency of consumption of chicken and chicken products significantly increased the risk of illness.

Other pre-prepared chicken

'Other pre-prepared chicken' was a category which included all pre-prepared chicken and products not listed individually in the questionnaire (i.e. not chicken nuggets, mini-kievs, shapes, burgers, sticks, drummers, gougons, filled chicken, curry, Chinese or barbecue style chicken). This category was diverse and the numbers were too small for meaningful analysis – but included 'Southern fried' type chicken, sandwiches, chicken pies, baby food, drumsticks and kebabs. Apart from six 'Southern fried' type products there was little homogeneity in this group. The association between consumption of 'other pre-prepared chicken products' and illness was most marked for products eaten from a take away or at home compared with those eaten elsewhere (Table 4). There was no evidence that younger or older ages were more likely to eat 'other pre-prepared chicken' and no age effect was found on the association between consumption of 'other pre-prepared chicken' and illness.

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Table 4. *Case control study of* S. virchow *PT 26, England and Wales, summer 1994: single variable analysis (Epi Info)*

	Cases*		Controls*				
	Ate	Didn't eat	Ate	Didn't eat	OR	95% CI	*P* value (Yates)
Chicken curry							
From a take away	15	71	9	173	4·1	1·6–10·7	0·002
From a restaurant	8	78	4	178	4·6	1·2–18·9	0·02†
At home	1	85	4	178	0·5	0·02–5·1	1·0†
Other pre-prepared chicken							
From a take away	13	72	7	175	4·5	1·6–13·2	0·002
From a restaurant	0	86	1	181	—	—	1·0†
At home	13	73	11	171	2·8	1·1–7·1	0·03
Other	7	77	2	180	8·2	1·5–59·2	0·01†

* Case control study comprised 88 cases and 182 controls but not all respondents answered each question.
† Fisher's exact.

Chicken curry

Consumption of pre-prepared (i.e. not home made) 'chicken curry' eaten in a restaurant or from a take away was significantly associated with illness (Table 4). No significant association was found between illness and consumption of pre-prepared chicken curry eaten at home or elsewhere.

Halal chicken

Consumption of 'halal' chicken suggested a possible association with illness in the subset of 24 cases and 69 controls who were asked (Table 2). Four cases and no controls had eaten halal chicken. This was a significant difference ($P = 0{\cdot}006$) and remained so when the analysis was extrapolated to represent all 133 people who had eaten home prepared chicken ($P = 0{\cdot}015$). Because of the small numbers, confidence intervals and odds ratios were undefinable.

Chicken cooked whole

Consumption of 'chicken cooked whole' was shown to have a protective effect on illness (OR = 0·47, CI 0·23–0·95, $P = 0{\cdot}035$). This was whole chicken which was not pre-prepared, whether eaten at home or elsewhere. In most cases it was prepared and eaten at home.

Forty-five cases and 135 controls reported contact with animals. This was significantly negatively associated with illness (OR 0·37, CI 0·21–0·66, $P < 0{\cdot}0005$).

Table 5. *Case control study of* S. virchow *PT 26, England and Wales, summer 1994: multivariable analysis final model*

	OR	95% CI	*P* value
Age	1·009	0·99–1·03	0·40
Sex			
Male	1·00*		
Female	1·42	0·73–2·76	0·30
Chicken nuggets			
No	1·00*		
Yes	1·00	0·24–4·17	1·00
Chicken burgers			
No	1·00*		
Yes	1·91	0·66–5·52	0·24
Chicken curry			
No	1·00*		
Yes	3·35	1·46–7·69	0·005
Chinese chicken			
No	1·00*		
Yes	0·95	0·25–3·68	0·94
Other pre-prepared chicken			
No	1·00*		
Yes	4·16	1·93–8·97	0·0003
Halal chicken			
No	1·00*		
Yes	†	†	0·001

* Baseline category.
† undefinable, see text.

The variables which showed some association with infection ($P < 0{\cdot}2$) were then entered into a multivariable logistic regression analysis. These results confirmed the findings of the single variable analysis in that chicken curry (OR 3·35, CI 1·46–7·69), other pre-prepared chicken (OR 4·16, CI 1·93–8·97) and

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halal chicken ($P = 0{\cdot}001$) remained independent risk factors for illness (Table 5). The association between chicken curry and illness remained when the analysis was adjusted for age and sex ($P = 0{\cdot}005$).

DISCUSSION

This case control study showed an association between illness due to *S. virchow* PT 26 and consumption of several food items. These were consumption of any chicken (with a dose–response effect), chicken curry eaten in a restaurant or from a take away, 'other pre-prepared chicken' and a possible association with the consumption of halal chicken. Any recall bias which might have resulted from the time lag in taking food histories from cases, perhaps demonstrated by the higher proportion of missing responses amongst cases compared with controls, would tend to bias against detecting a difference, thus strengthening the associations found.

The median age of cases was 26 years and this preponderance of young adults differs from the usual age distribution of infections with salmonellae which mainly affect pre-school children and the elderly [6]. Young adults are more likely to eat ready made and take away foods and to eat in restaurants. Older adults may be more likely to eat chicken cooked whole at home, which was found in this study to be negatively associated with the acquisition of *S. virchow* PT 26. This hospitalization rate was 15% which is low compared with rates of about 20% usually reported for salmonellosis [1, 7–9]. This low rate is particularly surprising since *S. virchow* has been described in the literature as one of the more pathogenic invasive salmonellae with a high incidence of bacteraemia [10–16]. The low morbidity associated with *S. virchow* PT 26 in this study may also be related to the age range of the cases. These were young people, less likely than older people to have other factors predisposing to blood stream invasion.

The association between infection with *S. virchow* PT 26 and consumption of chicken is not surprising, given that the main reservoir of *S. virchow* is poultry, and the association is strengthened by the finding that the likelihood of illness was dose related. Although the controls may have eaten a chicken meal in the week before interview, it was clear that many of the cases had eaten chicken on several occasions in the week before onset of illness.

The association with chicken curry may be related to the association with halal chicken. It is not known what proportion of chicken curry eaten from restaurants is halal chicken but it is likely to be greater when compared with chicken from other outlets. The association between curried chicken and illness may be due to a very high level of *S. virchow* contamination in the raw chicken, to incorrect storage, defrosting or cooking of the product or to cross contamination in the kitchen. Although only four people knew that they had eaten halal chicken they were all cases. Another case who was vegetarian regularly prepared halal chicken for her children.

The production and distribution of halal meat in the UK is complex. Halal meat is defined as meat which has been slaughtered according to Islamic law. Bona fide halal meat is sold from registered shops and is often consumed within 24 h of slaughter. There is anecdotal evidence that some meat not sold within 24 h may enter a 'second class' poultry meat chain where it, together with meat from other sources, is stored incorrectly and eventually sold cheaply (Dr C. Newman, personal communication). There is a need for a clearer understanding of these aspects of the poultry meat trade, including any microbiological and public health implications. A lesson from this study is that trawling questionnaires should incorporate a question on halal meat.

The food stuff most closely associated with illness in this study was 'other pre-prepared chicken'. This category contained such diverse chicken products that it was not possible to analyse the results further. It was clear that most were 'fast foods', some may have contained comminuted chicken and many were 'Southern fried'. This deep frying technique might have been expected to cook chicken adequately but instructions may not be properly followed or the raw chicken may also be heavily contaminated.

No association was found between illness and the consumption of comminuted chicken products which had been thought to play some part in the increase in isolations of *S. virchow* PT 26. The case control study and the hypothesis generating questionnaire contained a lot of detail on foods, especially comminuted chicken products, and if one brand or specific item was responsible for the increase it was unlikely to have been missed.

The analysis revealed two factors negatively associated with the acquisition of *S. virchow* PT 26. These were contact with animals and the consumption of chicken cooked whole. The association between animal contact and protection against *S. virchow* PT 26 is hard to explain. Consumption of chicken

cooked whole has been found to be protective in other salmonella studies [1, 7]. People who cook chicken whole at home may be more aware of the risks of salmonella and may defrost and cook the chicken more carefully than those who eat pre-prepared products.

The increase in *S. virchow* PT 26 has been accompanied, for the first time in years, by a slight fall in cases of *S. enteritidis* PT 4 [17, 18]. This may be due to changing epizoology in poultry and may be an indicator of what will become the dominant salmonella strain in poultry and in terms of human isolates in future years. The increasing incidence of *S. virchow* PT 26 is of particular concern because of its association with more invasive disease. The findings from this study require further follow up with more intensive investigation of the sources of sporadic and outbreak associated cases of *S. virchow* PT 26.

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