OPEN

The Effect of Childhood Infection on Hearing Function at Age 61 to 63 Years in the Newcastle Thousand Families Study

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Objectives: It is known that childhood hearing function can become impaired after the occurrence of specific infections. However, evidence on the effect of common childhood infections on adult hearing function is limited. The objective of the study was to identify whether associations exist between the occurrence of common childhood infections in a UK birth cohort and hearing function across different frequencies at age 61 to 63 years.

Design: The Newcastle Thousand Families study is a birth cohort of all individuals born in May and June 1947 to mothers resident in Newcastle upon Tyne, United Kingdom. Of the original cohort members who had an audiometry test at age 61 to 63 years, 333 had data available on infections during their first year of life and 296 on infections up to their fifth year of life. These data were analyzed using linear regression in relation to adult hearing function across differing frequencies in isolation.

Results: After adjustment for sex, overcrowding in the first year, having had an ear operation, and having worked in a loud environment, significant negative associations were identified between adult hearing and tonsillitis at 250 Hz (p = 0.013), 1 kHz (p = 0.018), 6 kHz (p = 0.012), and 8 kHz (p = 0.033); otorrhea at 4 kHz (p = 0.005), 6 kHz (p = 0.003), and 8 kHz (p = 0.002); bronchitis (two or more episodes) at 2 kHz (p = 0.001), 3 kHz (p = 0.005), 4 kHz (p = 0.009), 6 kHz (p < 0.001), and 8 kHz (p < 0.001); and the total number of severe respiratory infections in the first year at 2 kHz (p = 0.037), 3 kHz (p = 0.049), 4 kHz (p = 0.030), 6 kHz (p < 0.001), and 8 kHz (p = 0.006). That is, individuals who had tonsillitis, bronchitis (twice or more), otorrhea, or a severe respiratory infection (twice or more) in their first year of life were more likely to have impaired adult hearing function than those who did not have any infections in early life.

Conclusion: The occurrence of some, but not all, childhood infections appears to have an effect on adult hearing function across different frequencies. Reducing the incidence of infectious diseases in early life may reduce subsequent incidence of hearing impairment among adults. However, further research in modern cohorts is needed to clarify the links between infectious childhood diseases and adult hearing function.

Key words: Childhood, Epidemiology, Hearing, Infections.

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INTRODUCTION

Hearing loss is a major public health issue, the magnitude of which is often under recognized (Wilson et al. 1992). The World Health Organization (2010) estimated that there are 275 million people globally with an impaired hearing status and, within the United Kingdom, one in six adults has impaired hearing (Action on Hearing Loss 2011). Hearing loss has physical, emotional, and economic consequences for both individuals and society (Bess 1998; Mohr et al. 2000; Dalton et al. 2003). It can lead to high levels of social isolation and an increased risk of mental-health problems (Dalton et al. 2003).

Ninety percent of all acquired hearing loss is thought to be sensorineural, that is, as a result of permanent damage to the cochlea (Parmet et al. 2007). Although a number of causes of hearing loss are known, over half of all childhood hearing loss and three quarters of all adult hearing loss is associated with no known cause (Zahnert 2011). Identifying new plausible, preventable risk factors for hearing loss could inform future interventions aimed at alleviating this burden of disease nationally or globally.

Many infectious diseases remain common during childhood; some are self-limiting, while others have serious short-term or long-term implications. Analysis of UK general practice data has shown that children under 1 year of age will have an infectious disease episode, on average, three times a year and those aged 1 to 15 years, once a year (Fleming et al. 2002). Although the incidence of some infectious diseases such as pertussis has recently decreased, there has also been a resurgence of preventable infections like measles due, in part, to low vaccination uptake (Health Protection Agency 2013; Public Health England 2013).

One of the known risk factors for sensorineural hearing loss in childhood is incidence of common childhood infections such as intrauterine cytomegalovirus, rubella, postnatal otitis media, meningitis, measles, and mumps (which causes characteristically unilateral hearing loss) (McKenna 1997; Zahnert 2011). Whether the occurrence of any of the number of childhood infections up to 5 years is predictive of longer term impaired (adult) hearing function, or, if the predictive importance of childhood infections for hearing impairment diminishes across the life course, due to competing risk factors, is unknown.

The aim of this study was to assess infectious disease occurrence in early life as a plausible, preventable risk factor for adult hearing loss using data collected at age 61 to 63 years in the Newcastle Thousand Families birth cohort.

MATERIALS AND METHODS

The Newcastle Thousand Families study is a birth cohort of all 1142 children born in May and June 1947 to mothers resident in Newcastle upon Tyne, United Kingdom (Pearce et al. 2009, 2012). The health, growth, and development of the cohort were followed in great detail up to age 15 years. Throughout the first years of the children's lives, all families were visited, both on a routine (up to every 6 weeks during infancy and at least quarterly until age 5 years) and ad hoc basis, by the study team, which consisted of health visitors and pediatricians. Children

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were formally examined by a pediatrician at the end of the first, third, and fifth years.

The cohort underwent a major follow-up at age 49 to 51 years. Participants in the investigation were members of the cohort who were either traced through the National Health Service Central Register or contacted the study team in response to media publicity. A full-scale follow-up was repeated at age 61 to 63 years, including, for the first time in adulthood, a hearing assessment. Health and lifestyle questionnaires were sent out for completion and return, and study members were invited to attend the clinical examination, which took place over the same time period.

Early-life information was prospectively recorded for all study members. Information recorded throughout the first year of life included any occurrence and frequency of a respiratory infection, which were grouped into the following categories: bronchitis, colds/influenza, otorrhea, pertussis, pneumonia, tonsillitis, and the total number of the most severe respiratory infections recorded (occurrences of pneumonia, bronchitis, or both) within the first year. Overcrowding in the home was also assessed from health visits during the first year of life. Infection and illness details, collated up to the age of 5 years, consisted of the occurrence and frequency of upper respiratory tract infections (URTI; acute nasopharyngitis, acute pharyngitis, acute tonsillitis, acute laryngitis, acute URTI of multiple or unspecified sites, acute URTI of other multiple sites, chronic rhinitis, unspecified sinusitis chronic, unspecified chronic disease of tonsils and adenoids, other diseases of pharynx not elsewhere classified, other and unspecified diseases of upper respiratory tract, other diseases of respiratory system, other diseases of respiratory system, not elsewhere classified, cough), lower respiratory tract infections (LRTI; bronchopneumonia, pneumonia, bronchitis, chronic bronchitis, bronchiectasis or pleurisy), chicken pox, measles, mumps, rubella, scarlet fever, pertussis, tuberculosis, influenza, and ear infections.

Hearing function was assessed at age 61 to 63 years, by a trained research nurse, using a bilateral air conduction audiogram. Measurements were taken at eight frequencies between 250 Hz and 8 kHz, in octave steps, and at 3 and 6 kHz, following British Society of Audiology (1981) guidelines. MA25 portable audiometers were used along with Telephonics Dynamic Headphone (TDH) 49 earphones in audiocups (calibrated to the British Standard BS EN ISO 389-1). In line with British Society of Audiology guidelines, hearing levels better than 0 dB HL (i.e., negative values) were given a zero value. Individual hearing function was calculated as a weighted mean between the "best" and "worst" ear measurement in the ratio 4:1 (British Society of Audiology 1981; Welch & Dawes 2007). For example, if an individual had a hearing threshold of 10 dB HL at a frequency of 250 Hz for their left ear and of 25 dB HL for their right ear, the weighted mean would be calculated as follows $((4 \times 10) + 25)/5$.

At the time of hearing assessment, the use of hearing aids was noted and, if worn, removed during testing. The occurrence of any ear operation, past or present, was also noted at the time of hearing assessment. Participants returning the health and lifestyle questionnaire at age 61 to 63 years gave information on if they "had ever worked in a place that was so noisy you had to shout to be heard?", for which Yes or No responses were collated. Our theoretical framework for the analysis was based around the hypothesis that infections in childhood may have a long-term association with hearing function. To address whether such associations are real, it is also important to consider potential confounders. Some potential confounders in this study are likely to be driven by socioeconomic factors, hence the inclusion of childhood overcrowding and loud noise at work. It is also important to adjust for sex differences and differences induced by ear operations to ensure that potential confounding effects through these data are also accounted for.

Statistical Analysis

The representativeness of the analysis sample of the original cohort in terms of early life and childhood was tested using chi-squared, Mann–Whitney, and *t* tests with corresponding *p* values presented. Linear regression was used to assess the association between childhood infection and hearing function at each frequency. Associations found to be statistically significant ($p < 0.05$) were then assessed in multivariable regression models, adjusting for potential confounders. The total number of URTIs, LRTIs, and ear infections up to age 5 years were treated as continuous. The remaining infection variables, sex, overcrowding, loud noise at work, and ear operation were treated as categorical.

RESULTS

There were 333 study members who took part in audiometry testing at age 61 to 63 years and had data available from birth on infections during their first year of life. Of those 333 study members, 296 had data available from birth on infections up to their fifth year of life. There were no significant differences between the age 61 to 63 years hearing analysis sample and the available original cohort data for any respiratory illness during the first year of life (Table 1). There were, however, significantly more females, a higher proportion of individuals contracting influenza, URTI, measles, and chicken pox up to age 5 years, and a lower proportion of individuals living in overcrowded conditions in the first year of life among the study samples than in the available original cohort data (Table 1).

Hearing function ranged from 0 to 130 dB HL across all frequencies. There were significant differences between male and female hearing functions at 3, 4, 6, and 8 kHz ($p < 0.001$, all frequencies, results not shown). Females had hearing thresholds between 6 and 11 dB HL lower (indicative of better hearing function) than males, dependent on the frequency being tested. Of the study sample, 91 participants (75% of whom were male) had experienced working in a place that was so noisy you had to shout to be heard. Eighteen participants, within the study sample, reported having an ear operation either as a child or in adulthood.

In the first year of life, the most prevalent condition was common cold (24%; Table 1) followed by bronchitis (20%; Table 1). By the age of 5 years, 62% of the participants had contracted measles, 46% pertussis, and 29% chicken pox. The prevalence of the remaining illnesses was no higher than 14% (Table 1).

Univariate significant associations were present between hearing thresholds at 61 to 63 years and tonsillitis (250 Hz, 500 Hz, 1 kHz, 6 kHz, and 8 kHz), otorrhea (3, 4, 6, and 8 kHz), two or more episodes of bronchitis (2, 3, 4, 6, and 8 kHz), and two or more severe respiratory infections (2, 3, 4, 6, and 8 kHz) during the first year of life (results not shown). There were no unadjusted associations between hearing thresholds at any frequency and cold, influenza, pertussis, pneumonia, chicken pox,

TABLE 1. Childhood infection and hearing function summary statistics of the Newcastle Thousand Families study

	Study Sample		Original Cohort		
Variable	*n*	%	*n*	%	*p*
Sex	Total *n* = 333		Total *n* = 1142		
Male	151	45	583	51	0.013
Female	182	55	559	49	
Episode/s during first year of life					
Bronchitis	Total *n* = 333		Total *n* = 1010		
0	265	80	791	78	0.725
1	54	16	170	16	
2+	14	4	49	5	
Cold					
0	253	76	778	77	0.783
1	69	21	203	20	
2+	11	3	29	3	
Severe respiratory infections					
0	256	77	757	75	0.566
1	60	18	193	19	
2+	17	5	60	5	
Overcrowding					
No	245	74	666	67	0.002
Yes	88	26	326	33	
Otorrhea					
No	313	94	946	94	0.762
Yes	20	6	64	6	
Pertussis					
No	296	89	906	90	0.550
Yes	37	11	104	10	
Pneumonia					
No	321	96	964	95	0.309
Yes	12	4	46	5	
Tonsillitis					
No	321	96	978	97	0.580
Yes	12	4	32	3	
Episode/s up to age 5 years	Total *n* = 296		Total *n* = 992		
Chicken pox					
No	211	71	750	76	0.039
Yes	85	29	242	24	
Influenza					
No	283	96	966	97	0.023
Yes	13	4	26	3	
Measles					
No	113	38	451	45	0.003
Yes	183	62	541	55	
Mumps					
No	259	88	875	88	0.653
Yes	37	12	117	12	
Rubella					
No	254	86	874	88	0.146
Yes	42	14	118	12	
Scarlet fever					
No	185	96	967	97	0.117
Yes	11	4	25	3	
Pertussis					
No	160	54	577	58	0.087
Yes	136	46	415	42	
Tuberculosis					
No	281	95	925	93	0.167
Yes	15	5	67	7	
	Median	Range	Median	Range	
Number of URTI	5	(0–23)	5	(0–26)	0.002
Number of LRTI	0	(0–10)	0	(0–15)	0.558
Number of ear infections	0	(0–7)	0	(0–8)	0.611

LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.

measles, mumps, rubella, scarlet fever, tuberculosis, URTI, or LRTI. The only significant associations with hearing thresholds and childhood illnesses up to the age of 5 years was for the number of ear infections at frequencies 250 Hz, 500 Hz, 1 kHz, and 6 kHz (results not shown). However, this association did not remain significant after adjustment for ever having had an ear operation.

After adjustment for sex, overcrowding in first year, ever having worked in a noisy environment, and ever having had an ear operation, the majority of univariate significant associations between early-life infections and hearing thresholds at 61 to 63 years remained (Table 2). Having tonsillitis in the first year of life resulted in higher hearing thresholds at 250 Hz, 1 kHz, 6 kHz, and 8 kHz at age 61 to 63 years (Table 2). For example, at a frequency of 6 kHz, having a tonsillitis infection resulted in a 12.91 (95% confidence intervals 2.90–22.90) dB HL increase in hearing threshold, with higher hearing thresholds indicative of worse hearing function. Having otorrhea in the first year of life resulted in higher hearing thresholds at 4 kHz, 6 kHz, and 8 kHz at 61 to 63 years (Table 2). Contracting bronchitis twice or more and having two or more severe respiratory infections resulted in higher hearing thresholds at 2, 4, 6, and 8 kHz at 61 to 63 years. However, the associations between otorrhea with 3 kHz and tonsillitis with 500 Hz (which bordered on significance [$p = 0.056$]) became nonsignificant.

DISCUSSION

In this prospective study relating hearing data in the seventh decade of life to infections in the first 5 years of life, we have shown associations with a number of childhood infections and hearing thresholds across different frequencies at age 61 to 63 years. Individuals who had tonsillitis, otorrhea, two or more severe respiratory infections in their first year of life, or two or more episodes of bronchitis up to 5 years were more likely to have impaired hearing status in adulthood compared to those who did not have these infections. Associations were independent of a number of potential confounding factors, including early socioeconomic disadvantage (as measured by household overcrowding) and occupational noise exposure as adults.

Hearing function among this subsample of the Newcastle Thousand Families cohort was measured using pure-tone audiometry, and, as such, we are unable to determine whether any hearing loss measured was conductive or sensorineural. However, because of the age of participants, it is likely that the majority of hearing loss is sensorineural (Parmet et al. 2007). As analyses used a weighted mean of the "best ear" to "worst ear," hearing threshold at each frequency was tested to portray a unified measure of overall hearing function for each participant.

The longitudinal data collated within the Newcastle Thousand Families cohort, in particular, the prospective ascertainment of a number of childhood infections, make this study possible. Indeed, we are unaware of any other study that has looked prospectively at the effect of childhood infections on adult hearing function among a representative population-based sample in this manner. As such, comparisons to our study findings have been made with findings from studies of single infectious disease exposures and their effect on hearing outcomes.

We found, consistent with other hearing studies, that males have higher hearing thresholds across the majority of frequencies (3, 4, 6, and 8 kHz [$p < 0.001$]) than females. It was thought that this known sex effect may have been exaggerated in our study because 33% of participants, 75% of whom were men, had worked in a noisy environment where you had to shout to be heard, which is also a known risk factor for adult hearing loss (Centers for Disease Control and Prevention/NIOSH 1998). However, females had only slightly better average hearing when compared to males, with thresholds better by between 6 and 11 dB, dependent on the frequencies being tested.

No associations were seen between hearing thresholds and a number of infectious and congenital diseases previously linked to hearing loss, including rubella (Borton & Stark 1970), measles (McKenna 1997), mumps (McKenna 1997), tuberculosis (Khoza-Shangase et al. 2009), pneumonia (Swanson et al. 1992), and scarlet fever. These null associations likely reflect a lack of power to detect small effects within our study as the subsample within which hearing data were available at 61 to 63 years of age is relatively small. Further, with such a high incidence of now-vaccine preventable diseases (such as measles, mumps, and rubella) in this cohort, it is important to note that the limited numbers without these infections means that we cannot use our null findings to disagree with previous associations with these, predominantly, childhood infections that we had little statistical power to investigate.

It was not possible to test hearing under sound-proofed conditions because of embedding the hearing assessment within the wider clinical assessments used for the Newcastle Thousand Families study. However, the use of standardized conditions ensures that no bias should have been introduced into the study, although this does preclude comparing hearing levels with data from sound-proofed conditions.

In a previous study involving a subsample of the Newcastle Thousand Families cohort, for whom we have childhood hearing measurements, we reported that an increasing number of ear infections from birth to age 13 years predicted poorer hearing thresholds at age 14 years (250 Hz [$p = 0.04$] and 500 Hz [$p = 0.03$]). This remained true for females, but not males in sex-specific analysis (Pearson et al. 2013). Associations were also identified between the occurrence of scarlet fever or bronchitis (up to the 13th year of life) and hearing thresholds at 8 kHz when aged 14 years (Pearson et al. 2013). Our current study has found that an association also exists between the occurrence of bronchitis (twice or more before age 5 years) and adult hearing function at age 61 to 63 years. However, unlike for childhood hearing, no association between adult hearing thresholds and the occurrence of ear infections (after adjustment) or scarlet fever was found. We cannot say if the effects of bronchitis on hearing at different ages are related and, thus, whether the effect of bronchitis on hearing during childhood tracks through to adulthood, or, whether the timing of ear infection and scarlet fever onset is important to their effects on hearing.

We have identified a number of studies that have investigated the long-term effect of ear infections on hearing. Although the present study found no association between ear infections and adult hearing at ages 61 to 63 years, a Norwegian study completed by Tambs et al. (2004) found an association between ear infections and hearing status during early adulthood (ages 20–44 years). Tambs et al. (2004) found that ear infections were associated with impaired hearing function at frequencies from 250 Hz to 8 kHz and that this effect was stronger among women and those who had an earlier onset of ear infections. The findings of

TABLE 2. Associations of hearing function at age 61 to 63 years with infection from the first year of life

Variable	Frequency*		β Coefficient	95% CI		p
Tonsillitis during first year of life (No = –reference category)	250		6.32	1.33	11.30	0.013
	500		5.33	–0.13	10.80	0.056
	1000		6.70	1.16	12.24	0.018
	6000		12.89	2.90	22.90	0.012
	8000		12.91	1.06	24.78	0.033
Otorrhea during first year of life (No = reference category)	3000		4.10	–2.33	10.53	0.211
	4000		10.69	3.31	18.07	0.005
	6000		12.20	4.05	20.36	0.003
	8000		15.47	5.83	25.10	0.002
Bronchitis during first year of life (No = reference category)	2000	Once	–1.08	–4.32	2.17	0.001
		2 or more	10.59	4.66	16.53	
	3000	Once	–0.76	–4.79	3.26	0.005
		2 or more	11.98	4.61	19.35	
	4000	Once	0.84	–3.84	5.52	0.009
		2 or more	13.47	4.91	22.03	
	6000	Once	3.21	–1.85	8.27	<0.001
		2 or more	22.93	13.67	32.18	
	8000	Once	7.38	1.32	13.47	<0.001
		2 or more	19.70	7.70	31.71	
Severe respiratory infections during first year of life (None = reference category)	2000	1	0.14	–3.01	3.28	0.037
		2 or more	7.18	1.68	12.68	
	3000	1	–0.30	–4.20	3.59	0.049
		2 or more	8.39	1.59	15.19	
	4000	1	0.81	–3.70	5.32	0.030
		2 or more	10.69	2.81	18.56	
	6000	1	3.42	–1.48	8.32	<0.001
		2 or more	18.11	9.55	26.67	
	8000	1	6.63	0.76	12.50	0.006
		2 or more	14.31	3.40	25.22	

**Linear regression at each frequency adjusted for sex, overcrowding in first year, ever having an ear operation, and ever working in a place with loud noise.*
CI, confidence interval.

Tambs et al. (2004) are similar to those from an earlier study, within the cohort, assessing the effect of ear infections on hearing thresholds at age 14 years (Pearson et al. 2013). Perhaps, ear infections only affect hearing in childhood and early adulthood. It is of note that, unlike the present study, Tambs et al. was reliant upon self-report data to identify the main outcome of interest (ear infections) and had a poor response rate (Tambs et al. 2004). In this study, data were prospectively collected on early-life factors, including the occurrence of ear infections during childhood, decreasing the likelihood of misclassification and other potential biases that may be introduced when using recalled information. A further study by Bauer et al. (1991) also identified an association between ear infections and hearing loss (with findings comparative to those of Tambs et al. (2004) and Pearson et al. (2013)). The study by Bauer et al. (1991) used data from a "highly" noise-exposed population, suggesting that noise exposure and early-life infections are not competing risk factors for hearing loss.

There are also a number of studies that have looked at the long-term effect of otitis media, for which otorrhea is a sign, on hearing status. Indeed, a number of previous studies have shown an association between otitis media infection and long-term high-frequency hearing loss (Rahko et al. 1995; Hunter et al. 1996; Laitila et al. 1997; Park et al. 2013). These findings can be broadly compared to our own for the somewhat less "specifically" defined otorrhea, which was also found to be associated with impaired adult hearing at high frequencies.

How the results of the present study, obtained from an historical prevaccinated cohort living in different conditions to today's children, transfer to modern populations is unclear. Among this study sample, in the first year of life, one in five had contracted bronchitis and approximately one in six had contracted otorrhea, a severe respiratory infection or tonsillitis. It may seem likely that those who will go on to contribute to the future burden of hearing impairment, in particular from high-income countries, will not have experienced such high rates of infectious disease as living conditions have improved and childhood vaccination programmes have been instigated. However, UK data show that around half of all hospital admissions among children are due to infectious diseases (Saxena et al. 1997), with rates of scarlet fever within the United Kingdom currently at their highest for nearly 20 years (Department of Health 2002), recent pertussis epidemics (Health Protection Agency 2013), and rates of diseases such as measles and pertussis remaining endemic in many parts of the world, due, in part, to low vaccination uptake (Guiso et al. 2011; Kmietowicz 2012; Mulholland et al. 2012; Public Health England 2013).

Knowing more about infectious risk factors for hearing loss may allow us to instigate appropriate public health policy and action to reduce the burden of adult hearing loss, but it should be noted that any relationships are likely to be impacted by cohort effects. Further research is needed in this area to clarify the long-term effect between childhood infection and adult hearing status.

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The authors declare no other conflict of interest.

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