MATTHEW HOTOPF, MB, BS, MRCPsych, MSC, RICHARD MAYOU, BM, BCH, MPHl, MSC, MA, FRCP, FRCPsych, MICHAEL WADSWORTH, BA, MPHl, PhD, Hon MFPHM, and SIMON WESSELY, MA, MSC, MD, FRCP, MRCPsych

Objective: The objective of this study was to assess the relationships among chest pain, psychiatric disorder, and early experience of ill health. Methods: The Medical Research Council National Survey of Health and Development is a population-based birth cohort study established in 1946 (N = 5362). During childhood, several informants (parents, teachers, and school physicians) were interviewed or completed questionnaires. Data were available on the subjects’ health, the health of their parents, and subjects’ personalities. At the age of 36 years, subjects were asked about chest pain using the Rose Angina Questionnaire and completed the Present State Examination, a semistructured psychiatric interview. Subjects were followed for another 7 years (to age 43 years) to determine the outcome of those with chest pain. Results: Chest pain was reported in 17.2% (95% CI = 15.9–18.5%) of respondents at 36 years. The prevalence of exertional chest pain was 1.0% (95% CI = 0.7–1.3%). There was little evidence of coronary heart disease in those with exertional pain at age 36 years when followed for 7 years. However, there was a powerful cross-sectional relationship between psychiatric disorder and chest pain (OR for psychiatric disorder and all chest pain = 3.55, 95% CI = 2.34–5.37; OR for psychiatric disorder and exertional chest pain = 29.08, 95% CI = 6.65–127.15). Childhood risk factors, including poor health reported in parents at age 15 years and fatigue during childhood, were also associated with chest pain. Conclusions: Chest pain (especially exertional chest pain) is strongly associated with psychiatric disorders in young adults. Childhood experiences, including illness in parents, are associated with subsequent chest pain. Key words: angina, atypical chest pain, psychiatric disorder, childhood risk factors.

INTRODUCTION

Chest pain is a common symptom in the general population, affecting approximately 10% of young adults according to some surveys (1). In clinical settings, the first priority in dealing with patients presenting with chest pain is to rule out defined organic diagnoses, such as ischemic heart disease. However, given the relative rarity of these conditions (especially in younger adults) compared with the high prevalence of the symptom, it is not surprising that for many patients, investigations yield no obvious cause of the pain (2). In a case series of patients presenting to a cardiologist with chest pain or palpitations, more than half had no evidence of cardiac disease (3).

Many hospital series of patients with chest pain and normal coronary arteries have found high rates of psychiatric disorder, in particular the common mental disorders anxiety and depression (3, 4). A number of possible physiological and psychological mechanisms, including hyperventilation, muscle tension, and increased perception of minor physiological change, may account for the relationship between such disorders and chest pain (5–7). Less is known about chest pain in the community. It may be that in the general population, there is no association between common mental disorders and chest pain and that anxiety and depression are responsible for the pattern of consultation behavior (presenting to primary care and being referred to cardiology) rather than the experience of pain itself. This pattern has been found for irritable bowel syndrome and fibromyalgia (8), in which the association with psychiatric disorder is strongest in clinical populations.

There has been growing interest in the role of previous experience in the etiology of medically unexplained symptoms. Several studies comparing patients with medically unexplained symptoms to those with either physical illness or overt psychiatric disorder have demonstrated that those with unexplained physical symptoms report high rates of physical illness during childhood. Patients with medically unexplained symptoms also have reported that their parents suffered from physical illness during their childhoods (9, 10). It is possible that individuals who have these experiences are more likely to attend to minor symptoms in adulthood. This may be due to the anxiety raised by physical illness or symptoms during childhood, leading to greater awareness of benign physical sensations in later life.
Prior experience of heart disease in the family may be especially important in the development of unexplained chest pain. Case series of children presenting to pediatric clinics with chest pain indicate relatively high rates of heart disease in the parents (11–13). Pediatricians have long known that children with innocent heart murmurs may have a poor psychosocial outcome (14). This is presumably due to the parents interpreting a benign sign as evidence of grave underlying disease. The discovery of an innocent murmur may lead to the child being protected and greater attention being paid to normal childhood symptoms. It is therefore possible that experience of heart disease in close family members or innocent murmurs may lead to a heightened sensitivity to minor physiological symptoms or symptoms arising from anxiety.

In this study, we used a population-based birth cohort to test a series of hypotheses related to the etiology of chest pain in young adults. The aim of the study was to describe the epidemiology of chest pain in a young adult population, including the importance of exertional chest pain as an indicator of cardiac disease. More specifically, we tested the following hypotheses: 1) In a community sample, chest pain is associated with common mental disorders and life events; and 2) Chest pain is associated with a range of indicators of ill health in childhood, including personal experiences of physical illness and the experience of physical illness in close family members.

METHODS

Medical Research Council National Survey of Health and Development

The Medical Research Council National Survey of Health and Development is a national birth cohort that was set up in 1946 (15). The survey was based on a social class-stratified sample of all single, legitimate births that occurred in England, Wales, and Scotland during 1 week of March 1946 (N = 5362). The sampling procedure and follow-up are described in detail elsewhere (15). The stratification was based on the father’s social class: All children born to farm laborers and nonmanual workers were surveyed, whereas those born to manual laborers were sampled at a ratio of 1:4. Since 1946, 19 waves of data collection have been performed; data collection consisted of gathering information from teachers, health visitors, parents, and school physicians during childhood and use of postal questionnaires and interviews with research nurses during adulthood.

Assessment of Chest Pain

Chest pain was assessed with use of the Rose Angina Questionnaire (16). This questionnaire has been widely used in epidemiological studies and asks the subject about the presence of chest pain and a series of additional questions about the pattern of pain. With use of this questionnaire, it is possible to derive three levels of severity of chest pain: nonexertional chest pain, probable angina, and definite angina. To determine the likelihood that responders with probable or definite angina had evidence of heart disease, additional information was gathered. Subjects were asked about a range of physical ailments, including heart and lung disease, at age 36. They were also asked about any hospitalizations. At age 43, they were again interviewed and administered the Rose Angina Questionnaire. At this point, subjects were again asked about any hospitalizations and physical ailments. Every time a subject reported a hospitalization, the hospital consultant was contacted and asked to complete a questionnaire soliciting information on the diagnosis and any investigations and treatment received based on case-note review. It was thus possible to determine whether survey members who reported probable or definite angina as defined on the questionnaire had received investigations or treatment for the condition up to the time of diagnosis and over a 7-year follow-up period. It was also possible to determine whether alternative noncardiac disease (eg, cancer or bronchitis) could have been responsible.

Assessment of Psychiatric Disorder

At age 36, subjects were administered a semistructured psychiatric interview (PSE) (17), a diagnostic assessment that asks about 48 psychological symptoms, including low mood, anxiety, and phobias. From the PSE, a validated ordered categorical variable, the “index of definition,” or ID, that corresponds to different levels of psychiatric disorder may be calculated with use of a computer program (17). An ID of 5 or more is considered evidence of psychiatric disorder, whereas an ID of 3 to 4 is considered evidence of subthreshold disorder. The PSE interviews were audiotaped and validated by a psychiatrist (18).

Assessment of Life Events and Parental Heart Disease at Age 36

At age 36, subjects were asked whether close friends or relatives had experienced hospitalization, separation or divorce, death, or injury or had been a source of any other concern in the past year. They were also asked if they had experienced burglary or robbery or disappointment at work. Thus, they could report a total of eight life events. Subjects were asked at this time whether either their mother or father had ever had heart disease.

Assessment of Childhood Risk Factors

A number of childhood risk factors were examined. These may be classified according to whether they refer to ill health in other family members or in the subject himself or herself.

Ill health in other family members. When the child was 6 years old, the mother was asked whether she thought family members were susceptible to continual or repeated colds or sore throats. When the child was 15, the mother was asked to rate her and the father’s health on a five-point scale from “excellent” to “bad.” At this time, the mother was also asked to report whether she or her husband had heart disease.

Ill health in the child. A variable for severe physical illness throughout childhood (0–15 years) was available. This was defined as physical illness during childhood that had led to 1 months’ hospitalization or a prolonged period of school absence. Other variables were the teacher’s rating of energy levels and school absence when the child was 13 years old. Finally, the school physician examined the child at four time points (at 6, 7, 11, and 15 years) and noted the presence of heart murmurs. At the same time, the physician was asked to note any evidence of rheumatic or congenital heart
disease. “Innocent” heart murmurs were defined as murmurs detected at any point in childhood that were not thought to be due to rheumatic or congenital heart disease.

Potential Confounders

Potential confounders were subdivided into those present before the age of 15 years (sex and father’s social class) and those present after age 15 (highest educational level attained, smoking status, and marital status at the age 36). Educational level was coded as “O” level status or above; “O” levels are a general examination taken by students at age 16 that is required for many nonmanual occupations.

Statistical Analyses

All analyses were performed using Stata computer software (19). This study was a nested case-control study with two outcomes. The first outcome was “all chest pain” at age 36 years, and subjects with this outcome were compared with subjects who reported no chest pain. The second outcome was “exertional chest pain” at age 36 years (ie, definite and probable angina on the questionnaire), and subjects with this outcome were again compared with individuals with no chest pain. For the second outcome, those who reported nonexertional chest pain were excluded from analysis. After univariate analyses assessing the strength of relationships between risk factors and outcome, logistic regression analysis, weighted for sampling fractions, was performed. This analysis controlled for demographic variables and smoking. Because chest pain was strongly associated with psychiatric disorder, and because many of the childhood exposures of interest could have been nonspecific risk factors for psychiatric disorder, score on the PSE was entered into models assessing the relationship between chest pain and childhood risk factors. For binary data, likelihood ratio tests of heterogeneity were assessed. For the second outcome, those who reported no chest pain were compared with individuals with no chest pain.

RESULTS

Follow-Up and Representativeness of Sample

In 1982 (subjects aged 36 years), 3322 (62%) of survey subjects were interviewed. When subjects who had died or moved abroad were excluded, this proportion rose to 83%. The survey’s representativeness of the original sample has been described elsewhere (15). There is a modest difference in contact according to sex, with a slightly higher proportion of women than men being traced, but this is mainly accounted for by higher death rates and more emigration by men. Subjects who had suffered a physical illness in childhood were less likely to be interviewed at age 43 years ($\chi^2 = 53.6$, 1 df, $p < .001$), which was accounted for by their higher death rates (15). Low energy in childhood also predicted not being interviewed ($\chi^2 = 8.4$, 2 df, $p = .02$). This was accounted for by permanent refusal to participate or failure to contact the subject. There were no associations between parental perceived health, childhood abdominal pain, or maternal neuroticism and follow-up status at age 36 years.

Prevalence of Chest Pain, Probable Angina, and Definite Angina at Age 36 Years

Of the sample, 17.2% (95% CI = 15.9–18.5) reported experiencing any chest pain. Thirteen of 3322 individuals met criteria for definite angina (0.4%, 95% CI = 0.2–0.6%), and another 21 met criteria for probable angina (0.6%, 95% CI = 0.4–0.9%). Because of the small numbers of patients with definite and probable angina, these two categories were combined into an “exertional chest pain” category for additional analyses. Table 1 shows the sociodemographic associations of chest pain. Chest pain as a whole was reported slightly more often by men, those from nonmanual backgrounds, and heavy smokers, with no obvious relationships according to educational status or marital status. For the exertional chest pain category, the sociodemographic relationships are somewhat different, with considerably higher rates in those from nonmanual backgrounds, with lower levels of educational attainment, and who were single or divorced. Exertional chest pain was equally prevalent in men and women and was again associated with heavy smoking.

Evidence of Physical Disease in Exertional Chest Pain

Over the period of follow-up, one subject with exertional chest pain died of cancer, but there were no cardiovascular deaths. At age 43, 80.6% of those with exertional chest pain were interviewed. In 11 (44%), no chest pain was reported. None of these subjects had been treated for heart disease. Between the ages of 36 and 43 years, only four subjects with exertional chest pain had been evaluated for heart disease, and in only

<table>
<thead>
<tr>
<th>TABLE 1. Sociodemographic Associations of Chest Pain and Exertional Chest Pain*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Manual social class</td>
</tr>
<tr>
<td>Marital status</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Single</td>
</tr>
<tr>
<td>Divorced/widowed/separated</td>
</tr>
<tr>
<td>Educational attainment below O level</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Nonsmoker</td>
</tr>
<tr>
<td>1–10 cigarettes/day</td>
</tr>
<tr>
<td>11–20 cigarettes/day</td>
</tr>
</tbody>
</table>

*Uncorrected odds ratios derived from logistic regression analysis with sampling weights included.
one case were any of the results abnormal. Eight cases (25%) of exertional chest pain had been investigated or treated for respiratory diseases (asthma, bronchiectasis, and bronchitis).

Evidence of Psychiatric Disorder in Chest Pain

Table 2 shows the relationship between increasing severity of psychiatric disorder and the two categories of chest pain. For both outcomes, there was a strong cross-sectional relationship with a dose-response gradient: With increasing severity of psychiatric disorder, the odds of reporting chest pain increased. Assuming that there was a direct causal relationship between psychiatric disorder and all chest pain, the population-attributable fraction for above-threshold psychiatric disorders (ID = 5+) was 7.6%. When subthreshold disorders (ID = 3–4) were included, this increased to 24.2%. The relationship was more dramatic with exertional chest pain, and the population-attributable fraction for above-threshold psychiatric disorder was 30.2%, rising to 59.0% when subthreshold disorders were included.

Is the psychiatric disorder responsible for chest pain or vice versa? Table 2 shows the odds ratios of reporting new onset of chest pain at age 43 years according to the severity of psychiatric disorder 7 years earlier. There is again a strong, albeit less powerful, relationship between previous psychiatric disorder and future chest pain. For new onset of exertional chest pain, the relationship is somewhat weaker but still present.

Table 3 shows the relationship between the number of reported life events and the two outcomes. The analysis shown here controls for psychiatric disorder and thus is showing the independent effect of life events on the outcomes. There was a weakly significant relationship between increasing life events and all chest pain. There was also a statistically insignificant effect of increasing life events on exertional chest pain.

Relationship Between Childhood Exposures and Chest Pain

Table 4 shows the relationship between various childhood exposures and future chest pain and exertional chest pain. Taking all chest pain first, children.
with a history of severe physical illness were at no greater risk. However, other measures of childhood ill health were associated: Children who were frequently absent from school or who were viewed as having decreased levels of energy by their teachers were at higher risk for both outcomes. Measures of ill health in the family were also associated with poorer outcome. For example, subjects whose parents were rated as having poor health had a higher risk of reporting the symptom of chest pain. There was also a very slightly increased risk of reported chest pain in children from families with frequent colds and coughs. Surprisingly, innocent murmurs were associated with a decreased risk of chest pain at age 36.

Some similar relationships are present for exertional chest pain. However, because of the small number of subjects with exertional chest pain, the confidence intervals are wider, and some of the exposures could not be estimated because of empty cells. Overall, the exertional chest pain group also had increased fatigue and more school absences as children and were likely to come from families that reported frequent colds. The relationship with parental ill health was less clear, probably as a result of low statistical power. Finally, there was an association between history of heart disease in the father reported when subjects were 36 years old and both outcomes.

**DISCUSSION**

The main findings of this study are, first, that chest pain is relatively common and exertional chest pain (ie, probable and definite angina defined by the Rose questionnaire) is uncommon in young adults. Second, young adults with exertional chest pain probably have very low rates of heart disease, and respiratory illness is a more important cause. Third, there is a powerful cross-sectional and prospective relationship between reported chest pain and psychiatric disorder and between exertional chest pain and psychiatric disorder. Fourth, defined diseases in childhood are not associated with any increased risk of chest pain later in life; however, children who are rated as being fatigued and frequently absent from school are more likely to develop chest pain. Fifth, chest pain in adulthood is associated with poor perceived health in other close family members during childhood. Finally, although there were no statistically significant associations between the outcomes and family history of heart disease in childhood, there was an association between heart disease in the father reported by the subject at age 36 and both chest pain and exertional chest pain.

This study, with its longitudinal design and large sample size, has some important advantages over previous work. However, there were methodological lim-

---

**TABLE 4. Associations Between Childhood Factors and Chest Pain or Exertional Chest Pain at 36 Years of Age**

<table>
<thead>
<tr>
<th>Risk Factora</th>
<th>Any Chest Painb</th>
<th>Odds Ratio</th>
<th>Exertional Chest Painb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innocent murmur in childhood (age 6, 7, 11, or 15; school physician)</td>
<td>0.55 (0.33–0.90)</td>
<td>NAc</td>
<td></td>
</tr>
<tr>
<td>Family suffered frequent colds (age 6; mother)</td>
<td>1.27 (1.00–1.60)</td>
<td>2.68 (1.15–6.25)</td>
<td></td>
</tr>
<tr>
<td>Serious illness (age 0–15)</td>
<td>1.18 (0.88–1.60)</td>
<td>1.21 (0.39–3.70)</td>
<td></td>
</tr>
<tr>
<td>Health rating of father (age 15)</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1.19 (0.89–1.60)</td>
<td>0.50 (0.16–1.5)</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>1.32 (0.94–1.86)</td>
<td>0.62 (0.18–2.07)</td>
<td></td>
</tr>
<tr>
<td>Not very good/poor</td>
<td>1.42 (0.84–2.39)</td>
<td>0.41 (0.05–3.78)</td>
<td></td>
</tr>
<tr>
<td>Health rating of mother (age 15)</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>1.46 (1.07–2.00)</td>
<td>0.60 (0.18–2.01)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1.64 (1.16–2.30)</td>
<td>1.11 (0.36–3.46)</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>1.80 (1.04–3.12)</td>
<td>2.29 (0.47–11.13)</td>
<td></td>
</tr>
<tr>
<td>Not very good/poor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain in mother (age 15)</td>
<td>1.56 (0.77–3.15)</td>
<td>1.87 (0.25–13.94)</td>
<td></td>
</tr>
<tr>
<td>Tired and washed out (age 13; teacher)</td>
<td>1.56 (0.97–2.51)</td>
<td>3.62 (1.08–12.15)</td>
<td></td>
</tr>
<tr>
<td>Many school absences (age 13; teacher)</td>
<td>1.50 (1.14–2.00)</td>
<td>3.40 (1.44–8.04)</td>
<td></td>
</tr>
<tr>
<td>Heart disease in father (age 36; subject)</td>
<td>1.39 (1.07–1.80)</td>
<td>2.86 (1.20–6.81)</td>
<td></td>
</tr>
<tr>
<td>Heart disease in mother (age 36; subject)</td>
<td>1.29 (0.93–1.79)</td>
<td>1.17 (0.38–3.57)</td>
<td></td>
</tr>
</tbody>
</table>

---

*a* Age of subject when risk factor was assessed is given in parentheses.

*b* Controlled for social class, sex, adult psychiatric disorder, and smoking.

*c* Odds ratio not available because of empty cell.

*d* Likelihood ratio test for trend.
simply reflect increased consultation rates in patients suggests that the high rates observed in clinics do not these disorders in this community-based sample. This normal coronary arteries (3, 4). We found high rates of anxiety and depression in patients with chest pain and order. Clinical case series have revealed high rates of coronary heart disease in those with nonexertional severe symptoms also suggests that the prevalence of convincing coronary artery disease was conspicuously absent in the chest pain group with the most years later, suggesting that heart disease was unlikely to be a cause. Spontaneous resolution is not the rule in angina confirmed by treadmill testing (20). The fact that convincing coronary artery disease was conspicuously absent in the chest pain group with the most severe symptoms also suggests that the prevalence of coronary heart disease in those with nonexertional chest pain was negligible. Therefore, alternative explanations should be sought.

The first alternative explanation is psychiatric disorder. Clinical case series have revealed high rates of anxiety and depression in patients with chest pain and normal coronary arteries (3, 4). We found high rates of these disorders in this community-based sample. This suggests that the high rates observed in clinics do not simply reflect increased consultation rates in patients with psychiatric disorders. Our finding that new onset chest pain is associated with previous psychiatric disorder implies that anxiety and depression may have a causal role. For all cases of chest pain, psychiatric disorder could explain at most about one-quarter of cases. In the case of exertional chest pain, psychiatric disorder, including subthreshold disorder, could potentially explain nearly 60% of cases in the population.

We hypothesized that an additional contributory cause of chest pain might be the experience of illness in childhood. The pattern of findings is consistent with those of other studies using this cohort. Children with serious medical illness diagnosed before the age of 15 years have a relatively good psychosocial outcome (21), provided they live to adulthood. However, children who were described as tired at school and were frequently absent were at higher risk of developing chest pain. The same applied to subjects whose parents reported being unwell (at least for the all chest pain outcome). It was not possible to determine which aspects of illness in the parents were responsible for this relationship. Parental heart disease was infrequently reported during childhood; therefore, this study has insufficient power to detect any effect of this variable on later chest pain. However, there was an association between heart disease in the father and both outcomes.

The counterintuitive protective effect of innocent heart murmurs in childhood and chest pain in adulthood requires explanation. However, it was not clear from the childhood records whether the children or their parents were made aware of the murmur. We would anticipate that for the murmur to have any effect in leading to later unexplained symptoms, the child and his or her parents would have to be informed.

What are the implications of these findings? Clinically, the relationship between chest pain and psychiatric disorder should act as a reminder to clinicians that a high proportion of patients presenting with chest pain will have anxiety and depression that may require treatment.

The relationship is also important in cardiological epidemiology. A number of studies have used probable or definite angina as defined on the Rose Angina Questionnaire as an indication of coronary heart disease (22–24). In younger populations, in which coronary heart disease is rare, the Rose questionnaire will have a very low positive predictive value. Psychiatric disorder is considerably more common in young populations; therefore, researchers who describe the epidemiology of angina as defined on the Rose question-
ANTECEDENTS OF CHEST PAIN

naire believing this reflects coronary heart disease morbidity are more likely to be describing the epidemiology of psychiatric disorders. This would account for the higher prevalence of chest pain in women than in men (22) (which would be surprising if it was due to coronary heart disease). It would also account for the differing patterns by which coronary heart disease presents in women and men. Results from the Framingham study (25) indicate that among subjects with presumed coronary heart disease, angina is a much more common presenting feature in women than in men. Thus, men are more likely to present with myocardial infarction or sudden cardiac death. It would also explain the relatively benign outcome (in terms of cardiovascular mortality) for angina in women (25).

The finding is also pertinent to recent studies, which suggest that social class gradients in cardiovascular mortality may be due to psychological risk factors, such as low job control or job satisfaction (23, 24). These studies used new onset angina as defined on the Rose questionnaire as an outcome that was interpreted as a sign of coronary heart disease. Instead, it may be that previous psychiatric disorder was related both to low job satisfaction and to noncardiac chest pain.

The relationship between certain childhood exposures and chest pain fits a multifactorial model of unexplained symptoms (5, 7). It suggests that certain previous experiences, which may include having relatives with physical illnesses or suffering from fatigue as a child, may prime the individual to attend to normal physiological sensations in a different way. Thus, individuals from sick families may be more likely to notice and remember minor symptoms such as chest tightness. More importantly, such individuals may then enter a process whereby they seek medical investigation and reassurance for such symptoms.

Dr. Hotopf is funded by a Medical Research Council Clinical Training Fellowship. The Medical Research Council National Survey of Health and Development is funded by the Medical Research Council. The authors thank Warren Hilder for his help with data management.

REFERENCES

17. Wing JK, Cooper JE, Sartorius N. The measurement and classification of psychiatric symptoms. Cambridge, UK: Cambridge University Press; 1974.