## Epidemiology of Wilson's Disease in Ireland

Few epidemiological studies of Wilson's disease (WD) have been complete population-based assessments; estimates of prevalence range from 18 to 30 cases per million; however, confidence intervals are broad.[1-5] We described a cohort of patients with WD in the Republic of Ireland in an epidemiological study for the period 1970 to 1989.[5] Given advances in disease detection and treatment, the aim of this study was to extend the epidemiological study to the years 1990 through 2011.

Patients with a diagnosis of WD, or those who had died with this condition in the period 1990 through 2011, in Ireland were identified from numerous sources on the basis of classical clinical, biochemical, and pathological results.[5] Cases were subdivided as either symptomatic or asymptomatic (diagnosed by screening). True prevalence was calculated using Irish census years, the numerator being the number of patients alive with WD plus the number alive who were subsequently diagnosed with WD. Crude birth incidence and adjusted birth incidence for each census year were calculated as described previously.[5] The study was approved by the Ethics and Medical Research Committee of St Vincent's University Hospital, Dublin.

In the period 1970 to 2011, 50 patients (41 symptomatic, nine asymptomatic) were diagnosed with WD (26 in 1970 through 1989,[5] 24 in 1990 through 2011). True prevalences per million for census years were 1971: 6.7; 1979: 7.4; 1981: 9.9; 1986: 9.9; 1991: 10.8; 1996: 11.9; 2002: 10.5; 2006: 9.7, and 2011: 9.0. Crude and adjusted birth incidence figures per million population are noted in Table 1; the mean adjusted birth incidence for the period 1950 through 1989 was 18.7 per million births (95% confidence interval [CI]: 11.3-27.8). No significant difference was seen between the incidence rates in 1950 through 1969 and 1970 through 1989, although the rate did rise slightly.

The mean age of onset (of the 41 symptomatic presentations) was 16.5 years (median, 15.5; range, 10-40), and the mean age at diagnosis was 18.9 years (median, 16; range, 11-40); predominant presentations were hepatic (16, 39%), neurological (14, 34%), neuropsychiatric (4,10%), hepatic and neurological (3, 7%), and hepatic and psychiatric (3, 7%), with a pure psychiatric presentation in one patient. The mean times to diagnosis according to mode of presentation were: neurological, 22 months; mixed clinical symptoms, 34 months; hepatic, 14 months. A minimal nonsignificant improvement in time to diagnosis was seen over the 40 years (1970-1989: 23.4 months, 1990-2011: 20.6 months).

Adjusted birth incidence rates per million births increased nonsignificantly over the 40-year period to a maximum of 26.2/million (1:38,168 births). A recent UK study[6] of the frequency of individuals predicted to carry two genetic mutations in the *ATP7B* gene known to be pathogenic found a conservative prevalence of 1:7,026, which is considerably higher than our highest birth incidence (1:38,168) and the usually quoted prevalence of WD (1/30,000). The authors concluded that either the penetrance of *ATP7B* mutations was reduced or the disease was not being diagnosed clinically; given advances in disease detection in the United Kingdom and Ireland, the latter explanation seems highly unlikely. Thus, a markedly reduced penetrance of 20% of pathogenic *ATP7B* mutations seems probable in the United Kingdom and Ireland. ■

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**TABLE 1.** Crude and adjusted birth incidence rates for Wilson's disease in Ireland per million population in decades (1950-1969) and 5-year periods (1970-1989) over the 40 years 1950-1989

| Period (years) | 1950-59 | 1960-69 | 1970-74 | 1975-79 | 1980-84 | 1985-89 |
|---|---|---|---|---|---|---|
| Births with Wilson's disease | 10 | 9 | 8 | 6 | 6 | 6 |
| Number of births in the population | 619,468 | 620,620 | 338,080 | 346,626 | 348,244 | 289,059 |
| Crude birth incidence/million births | 16.1 | 14.5 | 23.7 | 17.3 | 17.2 | 20.8 |
| Age-specific probability of detection | 100% | 100% | 97.8% | 95.7% | 87.4% | 79.1% |
| Adjusted birth incidence/million (95% CI) | 16.1 (NA) | 14.5 (NA) | 24.2 (9.1-42.4) | 18.1 (6.0-33.2) | 19.7 (6.6-36.1) | 26.2 (8.7-48.1) |

CI, confidence intervals; NA, not applicable.