to counterbalance Th2 cell-induced airway hyperreactivity but cause severe airway inflammation. *J Clin Invest* 1999; **103:** 175–83.

5 Randolph DA, Carruthers CJ, Szabo SJ, Murphy KM, Chaplin DD. Modulation of airway inflammation by passive transfer of allergen-specific Th1 and Th2 cells in a mouse model of asthma. *J Immunol* 1999; **162:** 2375–83.

6 Jonuleit H, Schmitt E, Schuler G, Knop J, Enk AH. Induction of interleukin 10-producing, nonproliferating CD4(+) T cells with regulatory properties by repetitive stimulation with allogeneic immature human dendritic cells. *J Exp Med* 2000; **192:** 1213–22.

7 Akbari O, DeKruyff RH, Umetsu DT. Pulmonary dendritic cells secreting IL-10 mediate T cell tolerance induced by respiratory exposure to antigen. *Nat Immunol* 2001; **2:** 725–31.

8 Akdis CA, Blesken T, Akdis M, Wuthrich B, Blaser K. Role of interleukin 10 in specific immunotherapy. *J Clin Invest* 1998; **102:** 98–106.

9 Robinson DS, Hamid Q, Ying S, et al. Predominant Th2-like bronchoalveolar T-lymphocyte population in atopic asthma. *N Engl J Med* 1992; **326:** 298–304.

10 Takahashi T, Tagami T, Yamazaki S, et al. Immunologic self-tolerance maintained by CD25(+)CD4(+) regulatory T cells constitutively expressing cytotoxic T lymphocyte-associated antigen 4. *J Exp Med* 2000; **192:** 303–10.

11 Akbari O, Stock P, Meyer E, et al. Essential role of NKT cells producing IL-4 and IL-13 in the development of allergen-induced airway hyperreactivity. *Nat Med* 2003; **9:** 582–88.

# Measles surveillance: the importance of finding the tip of the iceberg

Chantal van Isterdael and colleagues recently published a study of completeness of reporting of cases of measles by general practitioners during an outbreak of measles in a community with low vaccination coverage in the Netherlands.[1] By surveying all families with children under 13 years of age served by a large general-practice group, they estimated a rate of measles attack of 10% (164 cases in 1654 children) according to parental diagnosis. The researchers noted that families sought health care for only 50 (30%) children with measles symptoms and that the perceived seriousness of illness, self-reported complications, and parental opinions that medical care should be sought for respiratory infections, were all significant factors in predicting which cases were brought to medical attention. The investigators also showed that of the 50 patients with measles seen or diagnosed in the clinic, only 15 (30%) were reported to the municipal health service. Combining these two proportions, van Isterdael and colleagues estimated that only 9% of all cases of measles in the population were reported by general practitioners to the municipal health service. We congratulate the authors for this addition to the sparse literature on sensitivity and completeness of measles surveillance (ie, the proportion of all cases of measles in the community that get reported).

Although many readers might be concerned that only 9% of patients with symptoms consistent with measles cases were reported to the public-health system, this result accords with previous studies. Harpaz recently published a review of studies of completeness of measles case reporting in the USA, in which he outlined the steps required for case detection and reporting: patient seeks health care, provider considers diagnosis of measles, and provider reports to public-health authorities.[2] Confirming the diagnosis is another critical step that might occur before or after the provider reports the case. Completion rates for each step can be assessed and the product of all of these rates is the overall reporting rate. The community-based reporting rates were 26% in Maryland in 1922–23,[3,4] 10% in the USA in the decade before vaccine licensure in 1963,[5] 7% in St Louis in 1970–71,[6] and 29% in Los Angeles in 1990–91.[7] In the Los Angeles study, researchers noted an 80% rate of consultation, compared with 30% in the van Isterdael study. Other studies have assessed notification rates in patients who had been seen and diagnosed by health-care practitioners. Compared with the 30% notification by general practitioners in the van Isterdael study, 48% of patients seen and diagnosed with measles were reported to the health department in Los Angeles in 1990–91. In studies of people in hospital with measles, researchers found higher reporting rates: 58% in 1986 and 51% in 1989 in Los Angeles and 45% in New York in 1991.[8,9] In general, the more severe the case of measles, the more likely it is to be reported, as was documented in the van Isterdael study.

Van Isterdael and colleagues rightly conclude that estimates of measles incidence, would be less than optimum on the basis of the less than 10% of measles cases diagnosed by parents that were reported by general practitioners in their study. Their study is an important reminder that passively reported measles cases are the tip of the iceberg of measles incidence. Most measles cases are unreported. However, even an insensitive passive surveillance system


Science Photo Library

**Measles virus (red envelope, blue nucleocapsid) budding off infected cell**

can fulfil some major purposes of measles surveillance: detect transmission of measles virus, determine age groups at risk, identify causes of transmission (ie, vaccine failure or failure to vaccinate), guide public-health action, and monitor trends in transmission. The measles surveillance system in the Netherlands, although it detected only a fraction of cases, adequately achieved all of these tasks and, most importantly, was able to guide activities to control outbreaks.

The completeness of reporting of measles cases can and should be enhanced to increase the usefulness of the surveillance information for guiding and evaluating activities to control measles. Methods for doing this include: educating practitioners about the importance of surveillance; encouraging reporting of suspected measles cases from alternative sources, such as schools and laboratories; using electronic databases that have diagnostic information to trigger reporting; and carefully investigating reported cases to identify other cases in the chain of transmission.

Systems of measles surveillance that report only the tip of the iceberg of all cases are less than optimum for showing the true incidence of disease. However, they have been highly effective tools for achieving measles elimination in the USA, the Netherlands, and elsewhere.

*Mark J Papania, Peter M Strebel*
Measles, Rubella, Mumps Elimination Team (MJP), and Global Immunization Division (PMS), National Immunization Program, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA
mpapania@cdc.gov

We declare we have no conflict of interest.

1 van Isterdael CED, van Essen GA, Kuyvenhoven MM, Hoes AW, Stalman WA, de Wit NJ. Measles incidence estimations based on the notification by general practitioners were suboptimal. *J Clin Epidemiol* 2004; **57:** 633–37.
2 Harpaz R. Completeness of measles case reporting: review of estimates for the United States. *J Infect Dis* 2004; **189** (suppl 1)**:** S185–90.
3 Sydenstricker E. A study of illness in a general population group. Hagerstown morbidity studies no. I: the method of study and general results. *Public Health Rep* 1926; **41:** 2069–88.
4 Sydenstricker E. The reporting of notifiable diseases in a typical small city: Hagerstown morbidity studies no. II. *Public Health Rep* 1926; **41:** 2186–91.
5 Hinman AR, Brandling-Bennett AD, Bernier RH, Kirby CD, Eddins DL. Current features of measles in the United States; feasibility of elimination. *Epidemiol Rev* 1980; **2:** 153–70.
6 Cherry JD, Feigin RD, Lobes LA Jr, et al. Urban measles in the vaccine era: a clinical, epidemiologic, and serologic study. *J Pediatr* 1972; **81:** 217–30.
7 Ewert DP, Westman S, Frederick PD, Waterman SH. Measles reporting completeness during a community-wide epidemic in inner-city Los Angeles. *Public Health Rep* 1995; **110:** 161–65.
8 Ewert DP, Frederick PD, Run GH, Mascola L. The reporting efficiency of measles by hospitals in Los Angeles County, 1986 and 1989. *Am J Public Health* 1994; **84:** 868–69.
9 Davis SF, Strebel PM, Atkinson WL, et al. Reporting efficiency during a measles outbreak in New York City, 1991. *Am J Public Health* 1993; **83:** 1011–15.

# Epidemiology of ovarian cancer: a status report

In a recent study, Freddie Bray and colleagues[1] report that ovarian cancer incidence and mortality have decreased slightly over the past decade in much of northern and western Europe. Unfortunately, these improvements have been accompanied by substantial increases in incidence in southern, central, and eastern Europe. This evaluation provides a good opportunity to reflect on current knowledge about risk factors for ovarian cancer and to identify important directions for prevention research in the coming years.

Despite decades of research, there remain only a handful of well-established risk factors for epithelial ovarian cancer. Incidence increases with age and is higher in women with a family history of ovarian or breast cancer, largely attributed to the role of *BRCA1* and *BRCA2*.[2] Tubal sterilisation has consistently been associated with 20–80% reductions in risk, with longitudinal studies suggesting that protection lasts for 10 or more years and is not merely a benefit of screening of the ovaries during surgery.[3] The number of full-term pregnancies and the use of oral contraceptives are both inversely associated with risk,[4] presumably because they reduce the number of times a woman ovulates in her life and thus the chance for mutation to occur during the repair of ruptured epithelial tissue. In their report, Bray and colleagues cite increases in the prevalence of use of oral contraceptives in northern and western Europe and decreases in women's average number of full-term pregnancies in southern and eastern Europe as major contributors to recent changes in incidence.

Many prospective studies now have sufficient numbers of cases of ovarian cancer available for statistically powerful analyses and provide excellent opportunities to evaluate the effects of reproductive, lifestyle, and dietary factors at many periods in women's lives. These studies tend to be less influenced by the biases that are problematic in case-control studies, and allow for reassessment of factors for which previous results have been inconsistent. For example, hormone-replacement therapy has been associated with significantly increased risk in several prospective studies,[4,5] with incidence influenced by duration of use and perhaps by the timing of progesterone supplementation.[5] Other reproductive factors, such as late age at menarche, early age at menopause, and breastfeeding, probably contribute modestly to reductions in risk.[4] Although the effect of fertility treatment remains unclear, most studies show that treatments involving ovarian hyperstimulation do not substantially increase risk.[6] Several analyses suggest that obesity in young adulthood might increase the incidence of premenopausal ovarian tumours by about 50%, although the role of obesity in later life and the effect of body composition on postmenopausal disease remain unclear.[7] Uncertainty also persists about physical activity, which has been inversely associated with ovarian tumours in many