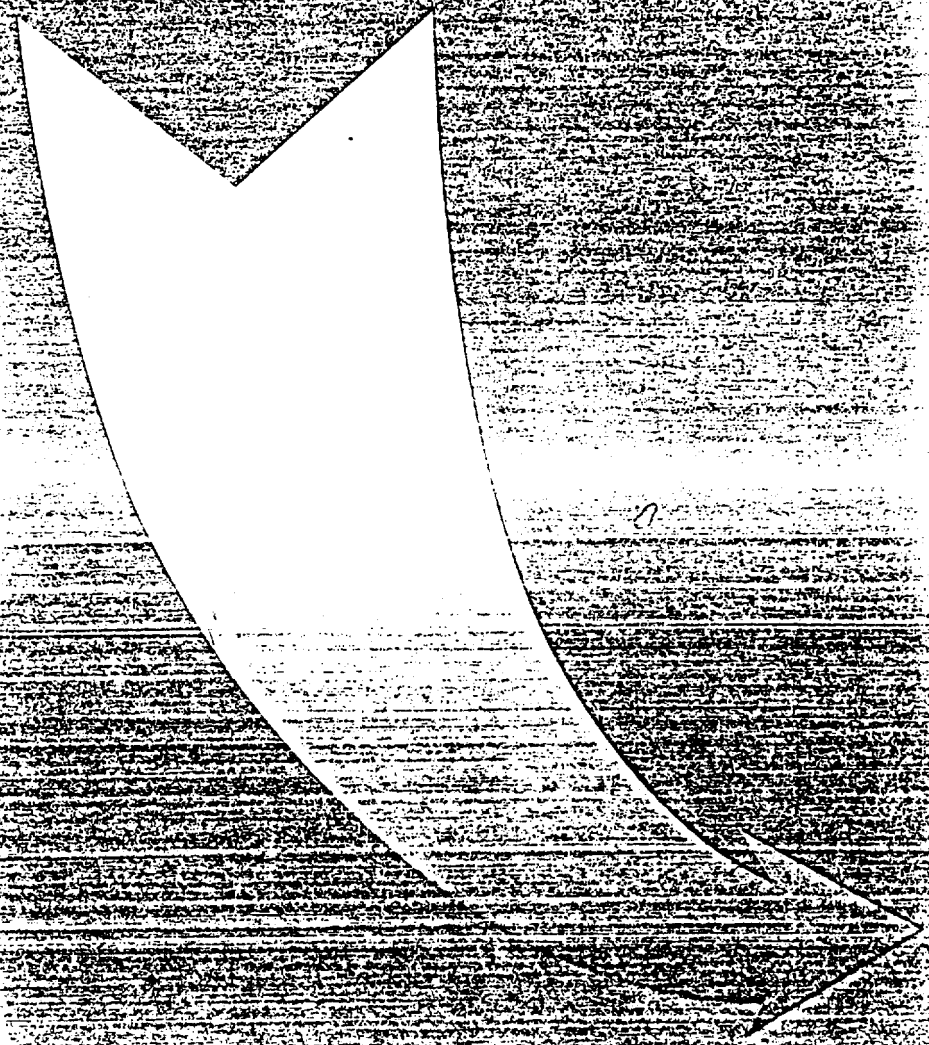


EPIDEMIOLOGY IN MEDICINE

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number in such a small population during the time period studied was clearly in excess of what was expected and led to the formulation of the hypothesis that occupational exposure to vinyl chloride caused hepatic angiosarcoma. Later the same year, this hypothesis was substantiated by data from two analytic studies [57, 69]. A single case report from that plant might not have been sufficient to allow formulation and subsequent testing of this hypothesis.

The usefulness of case reports and case series in the recognition of new diseases and the formulation of hypotheses concerning possible risk factors can be illustrated by the early epidemiology of acquired immunodeficiency syndrome (AIDS) [61]. Between October 1980 and May 1981, 5 cases of *Pneumocystis carinii* pneumonia were reported among young, previously healthy, homosexual men in Los Angeles [10]. This case series was unusual in that this type of pneumonia had previously occurred only in older cancer patients whose immune systems were suppressed, usually as a result of chemotherapy [75]. Similarly, in early 1981, an unprecedented number of cases of Kaposi's sarcoma were diagnosed in young homosexual men. Again, this was noteworthy because previously this malignancy had been seen almost exclusively in the elderly and affected men and women equally [11]. As a result of these case series, the Centers for Disease Control immediately initiated a surveillance program to quantitate the magnitude of this problem and to develop diagnostic criteria for what appeared to be a new disease. This program quickly identified that homosexual men were at high risk of developing this syndrome. Subsequent case reports and case series suggested that AIDS also resulted from blood-borne transmission among intravenous drug abusers as well as recipients of transfusions [2] and hemophiliacs receiving blood products [12]. These descriptive data provided clues used in the design and conduct of analytic studies, which subsequently led to the identification of a number of specific risk factors for the development of AIDS. The availability of sera from these cases and comparable controls also has contributed to the identification of human immunodeficiency virus (HIV) as the transmissible agent [61].

While case reports and case series are very useful for hypothesis formulation, they cannot be used to test for the presence of a valid statistical association. One fundamental limitation of the case report is that it is based on the experience of only one person. The presence of any risk factor, however suggestive, may simply be coincidental. Although case series are frequently sufficiently large to permit quantification of frequency of an exposure, the interpretability of such information is severely limited by the lack of an appropriate comparison group. This lack can either obscure a relationship or suggest an association where none actually exists. For example, in an attempt to explore the possible association between the use of OCs and hepatocellular carcinoma in women,