Most of the children admitted to a measles ward where a patient with pneumococcal disease had been nursed were later found to be carriers, and three developed pneumococcal bacteraemia. Attempts to eradicate carriage among the staff were complicated by the emergence of rifampicin resistance.

Epidemics of pneumococcal disease tend to occur in large closed communities.[22 23] Pneumococcal carriers have been firmly implicated in the spread of infection,[23] but there are well documented cases of transfer from patient to patient or patient to doctor.[24] More recently, simultaneous occult pneumococcal bacteraemia has been reported in twins,[25] and two sisters are reported to have developed pneumococcal disease within 48 hours of each other.[26] In large studies of pneumococcal bacteraemia several patients are usually found to have acquired their infection in hospital (p 1195).[4 6 21] If pneumococcal serotyping was carried out as frequently as in the 1930s more cases of cross infection would be reported.

Since man is the reservoir for *S pneumoniae*, and since pneumococcal carriage is so common, few measures to prevent cross infection, apart from sputum disposal, are justified outside an epidemic. In the past patients with pneumonia have sometimes been nursed in isolation,[27] but it is not common practice now, nor is it feasible in most hospitals.

Laboratory and clinical surveillance is needed, firstly, to detect any possible cases of cross infection and, secondly, to screen pneumococci for antibiotic resistance. Further measures such as serotyping, screening contacts, and isolation procedures should be instituted promptly as necessary. Antibiotic prophylaxis should be confined to serious epidemics. One hopeful prospect is that new developments in the pneumococcal vaccine may make it more immunogenic in children under 2—so more useful in curtailing potential epidemics.

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[1] MacFarlane JT, Finch RG, Ward MJ, Macrae AD. Hospital study of adult community-acquired pneumonia. *Lancet* 1982;ii:255-8.
[2] Calder MA. The use of countercurrent immunoelectrophoresis (CIE) in the diagnosis of pneumococcal infections. In: Lambert HP, Caldwell ADS, eds. *Pneumonia and pneumococcal infections*. London: Royal Society of Medicine/Academic Press, 1980:39-46. (Royal Society of Medicine International Congress and Symposium Series, No 27.)
[3] Mufson MA. Pneumococcal infections. *JAMA* 1981;**246**:1942-8.
[4] Austrian R, Gold J. Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. *Ann Intern Med* 1964;**60**:759-76.
[5] Hook EW, Horton CA, Schaberg DR. Failure of intensive care unit support to influence mortality from pneumococcal bacteremia. *JAMA* 1983;**249**:1055-7.
[6] Bille J, Glauser MP, Freedman LR. Risk of death in adult pneumococcal bacteraemia. In: Lambert HP, Caldwell ADS, eds. *Pneumonia and pneumococcal infections*. London: Royal Society of Medicine/Academic Press, 1980:47-52. (Royal Society of Medicine International Congress and Symposium Series, No 27.)
[7] Finkelstein MS, Petkun WM, Freedman ML, Antopol SC. Pneumococcal bacteremia in adults: age-dependent differences in presentation and in outcome. *J Am Geriatr Soc* 1983;**31**:19-27.
[8] Tilghman RC, Finland M. Clinical significance of bacteremia in pneumococcic pneumonia. *Arch Intern Med* 1937;**59**:602-19.
[9] Goldacre MJ. Acute bacterial meningitis in childhood: incidence and mortality in a defined population. *Lancet* 1976;i:28-31.
[10] Pedersen FK, Henrichsen J. Pneumococcal meningitis and bacteraemia in Danish children 1969-1978, serotypes, incidence and outcome. *Acta Pathol Microbiol Scand* [B] 1983;**91**:129-34.
[11] McIntyre P, Kennedy R, Harris F. Occult pneumococcal bacteraemia and febrile convulsions. *Br Med J* 1983;**286**:203-6.
[12] Teele DW, Marshall R, Klein JO. Unsuspected bacteremia in young children; a common and important problem. *Pediatr Clin North Am* 1979;**26**:773-84.
[13] White PMB. Occult pneumococcal bacteraemia and febrile convulsions. *Br Med J* 1983;**286**:389.
[14] Hegarty MA, George RH. Occult pneumococcal bacteraemia and febrile convulsions. *Br Med J* 1983;**286**:473.
[15] Lewis HM, Valman HB. Occult pneumococcal bacteraemia and febrile convulsions. *Br Med J* 1983;**286**:473.
[16] Hendley JO, Sande MA, Stewart PM, Gwaltney HM Jr. Spread of Streptococcus pneumoniae in families. I. Carriage rates and distribution of types. *J Infect Dis* 1975;**132**:55-61.
[17] Bunim JJ, Trask JD. Familial studies on lobar pneumonia. Epidemiologic studies on families of children with pneumococcic lobar pneumonia. *Am J Dis Child* 1935;**50**:626-35.
[18] Gray BM, Converse GM III, Huhta N, *et al.* Epidemiologic studies of Streptococcus pneumoniae in infants: antibody response to nasopharyngeal carriage of types 3, 19, and 23. *J Infect Dis* 1981;**144**:312-8.
[19] Dowling JN, Sheehe PRL, Feldman HA. Pharyngeal pneumococcal acquisitions in "normal" families; a longitudinal study. *J Infect Dis* 1971;**124**:9-17.
[20] Radetsky MS, Istre GR, Johansen TL, *et al.* Multiply resistant pneumococcus causing meningitis: its epidemiology within a day-care centre. *Lancet* 1981;ii:771-3.
[21] Jacobs MR, Koornhof HJ, Robins-Browne RM, *et al.* Emergence of multiply resistant pneumococci. *N Engl J Med* 1978;**299**:735-40.
[22] Macleod CM, Hodges RG, Heidelberger M, Bernhard WG. Prevention of pneumococcal pneumonia by immunization with specific capsular polysaccharides. *J Exp Med* 1945;**82**:445-65.
[23] Smillie WG. A study of an outbreak of type II pneumococcus pneumonia in the Veterans' Administration Hospital at Bedford, Massachusetts. *American Journal of Hygiene* 1936;**24**:522-35.
[24] Tilghman RC, Finland M. Pneumococcic infection in families. *J Clin Invest* 1936;**15**:493-9.
[25] Singer JI, Berger OG. Simultaneous occult pneumococcal bacteremia in identical twins. *J Pediatr* 1981;**98**:250-1.
[26] Asmar BI, Dajani AS. Concurrent pneumococcal disease in two siblings. *Am J Dis Child* 1982;**136**:946-7.
[27] Cruikshank R. Pneumococcal infections. *Lancet* 1933;i:680-5.

# Wilson's disease

In 1911-2 S A K Wilson, a student of Babinski and of Pierre Marie, described a familial nervous disease associated with cirrhosis. It is found world wide, from Arabia to Japan, but is rare. Estimates of the incidence of Wilson's disease have, however, crept up steadily from five per million to 30 per million in the past decade—that is, from 250 to 1500 probable cases in Britain.[1-3] Of these, perhaps 1000 cases are unrecognised.[4] Scheinberg has estimated that the correct diagnosis is made in only a quarter of all patients with the disease.[5]

Untreated, Wilson's disease is always progressive and fatal. Treated, most patients have a normal life of normal length (unless terminally ill with liver or neurological damage when the diagnosis is made). This contrast is so dramatic, and the clinical picture so variable, that anyone between the ages of 5 and 50 with unexplained liver disease, enlarged liver and spleen, hypersplenism, or attacks of jaundice (the most frequent initial manifestations) should be considered to have Wilson's disease until otherwise proved. Similar suspicion should be aroused by signs of brain damage, tremor, clumsiness, ataxia, rigidity, failure at school, epilepsy, speech disorder, or dementia. Perhaps a fifth of patients present with a purely psychiatric illness,[1] and a few with renal or bone disease. All these are doomed to die in coma, bleeding, mute, immobile, or demented—unless the correct diagnosis is made and treatment given.

The diagnosis of Wilson's disease is exact, though several tests may be needed. The condition is due to copper poisoning from the body's failure to synthesise caeruloplasmin, or to an intrahepatic defect in copper metabolism. Studies of fibroblasts, which share the genetic defect with hepatocytes,[6] and also of Bedlington terriers, which have a recessively transmitted condition very like Wilson's disease,[7] are helping to explain how the autosomal recessive inheritance of two

faulty copper genes (almost always the result of consanguineous marriage) causes Wilson's disease. Heterozygotes are clinically well but may show some of the biochemical abnormalities.

Excess copper damages first the liver and then as copper is released from the dying hepatocytes it affects the brain, eyes, kidneys, bones and joints, and possibly the parathyroid glands.[8] The definitive biochemical signs are, firstly, a low plasma concentration of caeruloplasmin, usually but not always below 200 mg l, with low serum concentrations of copper (less than 12·6 $\mu$mol l (80 $\mu$g 100 ml)).[9] Secondly, the urinary copper excretion is high. (A high urinary output of copper is also, however, seen in biliary cirrhosis.[10]) Thirdly, the copper content of the liver is raised and histological examination of biopsy specimens shows fine fat droplets, nuclear vacuoles, and a positive stain for copper. Fourthly, there is an overall diminution of copper incorporation into caeruloplasmin and a prolonged turnover of body copper. And, finally, rusty brown Kayser-Fleischer rings near the limbus of the eye are said to occur in all cases with neurological damage.[11]

Over the past 30 years treatments for Wilson's disease have been largely developed by Walshe.[12 13] He began with injections of the chelating agent BAL (British—as opposed to Russian—antilewisite; dimercaprol) and then in 1956-7 developed oral treatment with penicillamine—a metabolite of penicillin of no previous importance—and showed that this effectively "decoppered" six patients with Wilson's disease. More important, clinical improvement, though sometimes slow, was spectacular. Renal tubular defects, liver disease, and neurological problems—and the CT scan abnormalities—are all reversed.[14]

Treatment with pencillamine needs to be continued for life, and mild or severe sensitivity reactions are not uncommon. Patients who develop a rash, leucopenia, fever, a lupus-like syndrome, or the nephrotic syndrome may need to have the dose reduced, or treatment with cortisone, or the drug may have to be withdrawn. If penicillamine cannot be tolerated other effective treatments are fortunately available, the most satisfactory of which is triethylene tetramine dihydrochloride.[15] Large doses of zinc by mouth also result in a negative copper balance.[16]

Our advances in the understanding of Wilson's disease have been spectacular over the past 70 years: over 1000 publications on the topic have appeared.[1] All too often, however, we are missing the diagnosis or making it too late.

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[1] Scheinberg IH. Investigating diseases no one's got. *N Engl J Med* 1983; **309**:918-9.
[2] United States National Center for Health Statistics. *Vital statistics of the United States*. Vol 2. *Part A mortality 1968-1978*. Hyattsville, Maryland: Public Health Service. Section 1, table 7.
[3] Saito T. An assessment of efficiency in potential screening for Wilson's disease. *J Epidemiol Community Health* 1981;**35**:274-80.
[4] Cartwright GE. Diagnosis of treatable Wilson's disease. *N Engl J Med* 1978;**298**:1347-50.
[5] Scheinberg IH. Penicillamine in Wilson's disease. *Lancet* 1982;i:1469.
[6] Chan W-Y, Cushing W, Coffman MA, Rennert OM. Genetic expression of Wilson's disease in cell culture: a diagnostic marker. *Science* 1980; **208**:299-30.
[7] Su L-C, Ravanshad S, Owen CA Jr, McCall JT, Zollman PE, Hardy RM. A comparison of copper-loading disease in Bedlington terriers and Wilson's disease in humans. *Am J Physiol* 1982;**243**:G226-30.
[8] Carpenter TO, Carnes DL Jr, Anast CS. Hypoparathyroidism in Wilson's disease. *N Engl J Med* 1983;**309**:873-7.
[9] Scheinberg IH, Gitlin D. Deficiency of ceruloplasmin in patients with hepatolenticular degeneration (Wilson's disease). *Science* 1952;**116**: 484-5.
[10] LaRusso NF, Summerskill WHJ, McCall JT. Abnormalities of chemical tests for copper metabolism in chronic active liver disease: differentiation from Wilson's disease. *Gastroenterology* 1976;**70**:653-5.
[11] Sternlieb I. Diagnosis of Wilson's disease. *Gastroenterology* 1978;**74**: 787-9.
[12] Walshe JM. Penicillamine, a new oral therapy for Wilson's disease. *Am J Med* 1956;**21**:487-95.
[13] Walshe JM. Wilson's disease, a review. In: Peisach J, Aisen P, Blumberg WE, eds. *The biochemistry of copper*. New York: Academic Press, 1966: 475-502.
[14] Danks DM. Hereditary disorders of copper metabolism in Wilson's disease and Menkes disease. In: Stanbury JV, Wyngaarden JB, Fredrickson DS, Goldstein JL, Brown MS, eds. *The metabolic basis of inherited disease*. 5th ed. New York: McGraw-Hill, 1983:1251-68.
[15] Walshe JM. Treatment of Wilson's disease with trientine (triethylene tetramine) dihydrochloride. *Lancet* 1982;i:643-7.
[16] Brewer GJ, Hill GM, Prasad AS, Cossack ZT, Rabbani P. Oral zinc therapy for Wilson's disease. *Ann Intern Med* 1983;**99**:314-20.

# Changes in compensation for occupationally induced bladder cancer

Concern expressed in the *BMJ*[1] and elsewhere has led the Industrial Injuries Advisory Council recently to review neoplasm of the bladder as a prescribed industrial disease (PD 39) under the industrial injuries provisions of the Social Security Act 1975. This advisory body made recommendations in July 1983, which were accepted by the Secretary of State for Social Services and which became law in October 1983.[2]

The review was mainly concerned with three questions: whether the description of industrial bladder cancer was still satisfactory; what additional substances and occupations, if any, could be added to the terms of prescription; and whether there was evidence that carcinoma in situ could cause disablement before overt evidence of malignancy.

The council—whose members include doctors, lawyers, and representatives of industry, the trade unions, and insurance—recommended that the description of the disease should be amended to include carcinoma in situ and invasive carcinoma: all forms of transitional cell carcinoma of the urothelium are now included. It added benzidine to paragraph (*a*)ii as many people did not understand the chemical description of benzidine and its related compounds. It clarified the problem regarding auramine and magenta: the handling of these substances is not thought to induce carcinogenesis but their actual manufacture may produce tumours.

Methylene-bis-orthochloroaniline has now been listed as a substance under paragraph (*a*)i. This recommendation has been derived mainly from studies on animals showing it to be carcinogenic, and in this respect Britain is falling into line with the United States. Research work on this substance will be kept under review. In Britain a few men have probably developed cancer of the bladder from exposure to methylene-bis-orthochloroaniline.

Several other chemical compounds were considered by the council, but since the evidence was not convincing they were not included in the provisions. Nevertheless, research into (and evidence on) the effects of these substances is to be kept under review. Some evidence is accumulating that additional industries may have a raised incidence of neoplasm of the bladder—for example, printing. Concern has been expressed by the trade unions and the council has recommended a continuing review of epidemiological research into the occupational incidence of neoplasm of the bladder in specific occupations.

The last recommendation is that "every effort should be