

Section 100⁵ criteria for use of combination therapy with interferon alfa 2b and ribavirin

Patients with chronic hepatitis C who satisfy the following criteria are eligible for interferon alfa 2b and ribavirin:

- On liver biopsy, are staged as METAVIR stage 2 or greater, or METAVIR stage 1 with grade A2 or A3 inflammation (except patients with coagulation disorders);
- Have abnormal alanine aminotransferase levels in conjunction with demonstration of viral infection (HCV RNA positive);*
- Do not have other liver disease;*
- Are not pregnant, not lactating, and are using two reliable methods of contraception;*
- Have no history of significant psychiatric illness;
- Would be likely to attend regularly for treatment and follow-up; and
- Take no more than seven standard alcoholic drinks a week.

Genotype of virus should be assessed before treatment

Treatment course is 24 weeks except:

- With Genotype 1 and patients with cirrhosis or bridging fibrosis (regardless of genotype), where treatment course is 48 weeks; and
- Treatment will be continued for 48 weeks only if HCV RNA qualitative assay is negative at 24 weeks.

OR

- Patients who have relapsed after treatment with interferon 2a/2b monotherapy supplied as a Section 100 medication. This course is limited to 24 weeks.

Section 100⁵ criteria for use of monotherapy with interferon alfa 2b

Patients with chronic hepatitis C confirmed on liver biopsy (except patients with coagulation disorders) are eligible for interferon alfa 2b monotherapy if they satisfy the criteria marked with asterisks above. (*When monotherapy fails, patients become eligible for combination therapy.*)

Treatment is to cease if plasma HCV RNA remains detectable by HCV RNA qualitative assay after 12 weeks of treatment.

The course must be continuous and excludes retreatment of non-responders or patients who relapse.

most chronic liver diseases can be diagnosed before biopsy. Biopsy remains an important tool for histological diagnosis of cirrhosis. However, as unexpected findings are uncommon and some patients will be treated irrespective of liver histology, there is an emerging argument not to perform liver biopsy routinely. This argument will strengthen if valid biochemical markers of fibrosis are confirmed.⁶ We believe each patient should be assessed individually, and treatment could be offered without biopsy to patients who:

- meet all criteria for treatment under current guidelines other than known liver histology;
- have no alternative or additional diagnoses after thorough work-up;
- strongly desire treatment regardless of histology, and there is sound indication for treatment (eg, extrahepatic symptoms, concerns of vertical or occupational transmission);
- have a high chance of sustained viral response (eg, favourable genotype);
- have no clinical, biochemical or haematological suggestion of cirrhosis; and
- with the physician, accept the implications of treatment without biopsy.

An alternative strategy could be to consider a biopsy in patients who do not have a sustained virological response, to allow prognostication. Clearly, such

changes would greatly affect biopsy practices in Australia.

1. Law MG. Modeling the hepatitis C virus epidemic in Australia. *J Gastroenterol Hepatol* 1999; 14: 1100-1107.
2. Janes CH, Lindor KD. Outcome of patients hospitalized for complications after outpatient liver biopsy. *Ann Intern Med* 1993; 118: 96-98.
3. Saadeh S, Cammell G, Carey WD, et al. The role of liver biopsy in chronic hepatitis C. *Hepatology* 2001; 33: 196-200.
4. Poynard T, Ratziu V, Benmanov, et al. Fibrosis in patients with chronic hepatitis C: detection and significance. *Semin Liver Dis* 2000; 20: 47-55.
5. *National Health Act 1953* (Cwlth), s 100.
6. Imbert-Bismut F, Ratziu V, Pieroni L, et al. Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. *Lancet* 2000; 357: 1069-1075. □

Changes in serum folate concentrations following voluntary food fortification in Australia

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TO THE EDITOR: With the recognition that supplements of folate given early in pregnancy can reduce the incidence of neural tube defects,^{1,2} Australian manufacturers were allowed voluntary food fortification with folate from 1995, and these foods subsequently became available from August 1996. We assessed the impact of this fortification by comparing the results of assays of serum folate, a sensitive index of folate intake, before and after the introduction of folate-fortified foods.

Data were available for serum folate samples assayed by the chemiluminescence method (Chiron Healthcare Pty Ltd, Scoresby, Victoria) at our laboratory in Melbourne. Quality assurance data indicated no analytical drift, and external proficiency testing yielded satisfactory results throughout the period under study.

A total of 20 506 samples from women aged 14–45 years, the target group for supplementation, and 5528 samples from men of the same age group were assayed during 1993–2000. The results for the years 1993–1996, before fortification, where sample numbers were relatively small, were pooled. The results were analysed by Bhattacharya plot, eliminating the effect of outlier values,³ mindful of the limitations of extrapolating data derived from clinical

Serum folate concentrations in Victorian women and men aged 15–45 years before (1993–1996) and after (1997–2000) the introduction of voluntary food folate fortification

	Year				
	1993 to 1996	1997	1998	1999	2000
Women					
Number	3865	2989	4168	4385	5099
Mean folate concentration (nmol/L)*	14.0	14.5	15.3	16.4	16.7
95% confidence limits	6.7–28.3	5.0–38.6	5.7–38.1	5.7–41.0	5.6–45.5
% Low values†	8.5	7.1	5.7	4.3	4.1
Men					
Number	1077	849	1130	1117	1355
Mean folate concentration (nmol/L)*	14.0	14.9	15.7	16.5	16.2
95% confidence limits	6.4–28.7	4.7–31.0	5.5–35.6	6.2–41.6	5.9–42.1
% Low values†	7.9	8.1	6.5	4.1	5.1

* Derived from log normal distribution of community values by Bhattacharya method. † 8.0 nmol/L.

material to the community. The mean values are shown in the Box. In both groups there was a small incremental rise in mean serum folate concentrations, and a fall in the prevalence of low values, after the introduction of fortification. The mean value of 14.0 nmol/L for women in 1993–1996 increased by about 19% to 16.7 nmol/L in 2000. The percentage of low values decreased from 8.5% to 4.1% over that period. Although it is possible that the increase in serum folate concentration reflects dietary education and use of folate supplements in women of reproductive age rather than food fortification specifically, parallel changes were also observed in men.

In the United States, folate fortification of all enriched cereal grain products was mandated from January 1998. This led to a dramatic increase of 250% in mean folate levels in women aged 15–44 years,⁴ and an increase of 50% in the median values (uncorrected for outliers) for men, women and children of all ages submitted for clinical evaluation.⁵ By comparison, the increase in folate levels in Australia has been very small. We conclude that to obtain a significant increase in folate intake in the community by food fortification, a policy of mandatory rather than voluntary fortification is required.

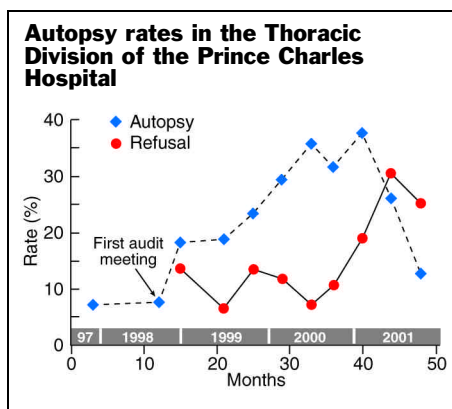
1. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 1991; 388: 131-137.
2. Czeizel AE, Dudás I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med* 1992; 327: 1832-1835.
3. Bhattacharya CG. A simple method of resolution of a distribution into Gaussian components. *Biometrics* 1967; 23: 115-135.
4. Folate status in women of child bearing age – United States, 1999. *MMWR Morb Mortal Wkly Rep* 2000; 49: 962-965.
5. Lawrence JM, Petitti DB, Watkins M, Umekubo MA. Trends in serum folate after food fortification. *Lancet* 1999; 354: 915-916. □

The decline in hospital autopsy rates in 2001

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TO THE EDITOR: In late 1998, a clinical audit in the Thoracic Division of the Prince Charles Hospital found the autopsy rate was 7% of all patients who died in the Division (excluding Palliative Care) for the 12 months to September 1998. Following discussions and acknowledgement of the importance of hospital autopsy as a clinical audit tool, the Division's policy to consider an autopsy in all patients who died was



reinforced. Registrars were educated in seeking approval and in counselling relatives.

As a result of these interventions and ongoing audit, a decision in relation to autopsy is now recorded in more than 90% of charts following a patient's death, compared with 40% initially. The autopsy rate progressively increased, and, from March 2000 to January 2001, it was 35%, five times the baseline rate, and the refusal rate was 11% (Box). The rate of limited autopsies (generally only excluding the brain) increased from 20% to 50%.

However, from early 2001, coinciding with the ongoing negative Australian press coverage related to aspects of autopsies, there has been a marked decrease in relatives' agreement to allow autopsy and extent of autopsy. The refusal rate for autopsy increased to 30% for the four months to May 2001, and was 25% to September 2001. The autopsy rate fell dramatically to 27% and 13% for the same periods. Nine of the 10 autopsies were limited, usually to a single organ or body cavity.

Data from death certificates are vital for education, research and public health purposes.^{1,2} Autopsies remain the only way to audit the accuracy of death certificates. A review found that the rate of clinical diagnostic inaccuracy for major findings at autopsy is about a third, and this rate has not changed since 1912.³ This unavoidable baseline of diagnostic error⁴ does not

necessarily indicate incompetence or malpractice. It is essential that the public understand that medicine is not an exact science, that we do misdiagnose conditions, and that identification of these "errors" is of value to relatives, to future patients and to society.

Legislative changes are being proposed in Australia that will make obtaining consent for autopsies more complex and potentially distressing for relatives. Education of medical staff and the general public must accompany these changes if they are not to be the final "nail in the coffin" of the hospital autopsy and remove an important facet of continuing improvement of medical practice.

1. Australian Bureau of Statistics. Cause of death certification Australia — a booklet for the guidance of medical practitioners in completing medical certificates of cause of death. Canberra: ABS, 1999.
2. McKelvie PA. Medical certification of causes of death in an Australian metropolitan hospital. Comparison with autopsy findings and a critical review. *Med J Aust* 1993; 158: 816-821.
3. Kingsford DPW. A review of diagnostic inaccuracy. *Med Sci Law* 1995; 35: 347-351.
4. Hill RB, Anderson RE. An autopsy-based quality assessment program for improvement of diagnostic accuracy. *Qual Assur Health Care* 1993; 5: 351-359. □

How much alcohol is drunk in Australia in excess of the new Australian alcohol guidelines?

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TO THE EDITOR: The National Health and Medical Research Council has launched new Australian alcohol guidelines¹ to help reduce alcohol-caused deaths in Australia, estimated to have been 3290 in 1997.² Male drinkers are advised to drink no more than an average of 40 g alcohol per day and

Percentage of alcohol consumed at risk levels for acute and/or chronic harm, as specified in the new Australian alcohol guidelines,¹ by age and sex (n = 10 030, weighted data)

Age (years)	Females (%)	Males (%)	Total (%)
14-17	71.3	77.4	75.1
18-24	82.3	92.9	89.9
25-39	68.1	66.4	66.9
40-64	67.7	62.0	63.6
65+	46.5	39.5	41.4
All ages	68.4	66.5	67.0