

## REVIEW

### FETAL ALCOHOL SYNDROME: THE 'AMERICAN PARADOX'

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**Abstract** — Nearly all cases of fetal alcohol syndrome (FAS) identified in prospective epidemiological studies have been conducted in the United States of America. The very high incidence rate for FAS in the USA and the relatively low rate in other countries does not correspond to measures of alcohol consumption. By analogy with the 'French paradox', we have termed the high rate of FAS in the USA coupled with its relatively low level of alcohol consumption, the 'American paradox'.

#### INTRODUCTION

Drinking alcohol is common around the world and, except where prohibited by religion, is the norm, rather than the exception. In the United States of America, about two-thirds of the adult population drink alcohol to some extent (US Department of Health and Human Services, 1993). For the overwhelming majority of those who drink alcoholic beverages, this behaviour has no health, personal or social consequences. Damage to the individual and to society can occur, however, if drinking becomes excessive or uncontrollable (US Department of Health and Human Services, 1993).

Whereas countries that have the highest rates of *per capita* alcohol consumption also have high rates of alcohol-related problems, such as cirrhosis, these same countries may also have very low rates of other health-related disorders such as cardiovascular disease and stroke (Renaud and de Lorgeril, 1993; Criqui and Ringel, 1994; Burr, 1995). For example, France has the highest *per capita* alcohol consumption in the world (Pyorala, 1990) and a relatively high rate of liver cirrhosis. But France also has a relatively low rate of cardiovascular disease compared to countries like the USA, although the French consume more

saturated fats, have higher serum cholesterol levels and higher blood pressures. This latter phenomenon has been labelled the 'French paradox' (Renaud and de Lorgeril, 1993; Criqui and Ringel, 1994; Burr, 1995), and has been attributed to the greater consumption of alcohol in France.

#### THE 'FRENCH PARADOX'

The 'French paradox' is a paradox, however, only in the sense that the effects of alcohol are not linearly related to health. Whereas there are health benefits at low levels of consumption, e.g. increases in high density lipoproteins, and increased levels of antioxidants, at very high levels of consumption, there are no health benefits to cardiovascular or other bodily functions (US Department of Health and Human Services, 1993). Beyond awareness of the fact that alcohol consumption in and of itself is not a health risk, the 'French paradox' ought to guide investigations as to the aetiology of the paradox. Such studies may point the way to additional factors that may work in conjunction with alcohol to cause or prevent disease.

#### THE 'AMERICAN PARADOX' AS RELATED TO THE FETAL ALCOHOL SYNDROME

In studying the effects of maternal alcohol consumption on the fetus, we have identified

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Table 1. Alcohol consumption and estimated incidence of fetal alcohol syndrome (FAS) per 1000 births based on prospective studies

Country	<i>Per capita</i> consumption (l)	FAS cases/ sample size	Estimated incidence/ 1000	FAS/no. heavy drinkers	Estimated incidence/ 1000 heavy drinkers
Australia	10	0/31 713	0	0/240	0
Canada	7.8	0/600	0	0/21	0
Denmark	9.6	0/286	0		
France <sup>a</sup>	13.0	18/13 802	1.30	2/52	38
Germany	10.5	0/999	0	0/6	0
Italy	10.0	0/1516	0	0/25	0
Netherlands	8.3	0/3447	0	0/274	0
Portugal	10.5	0/430	0	0/22	0
Spain	13.0	0/2663	0	0/-	0
Sweden	5.4	2/1133	1.76	14/632	22
Switzerland	11.0	0/1537	0	-	-
UK	7.3	0/6063	0	0/392	0
USA	7.3	91/46 497	1.95	91/1843	49

Data are adapted from Pyorala (1990) and Abel (1995).

<sup>a</sup> Includes study by Dehaene *et al.* (1991) not included in previous survey.

another paradoxical relationship between alcohol consumption and health. This relationship is the mirror image of the French version, viz. the USA has a relatively low rate of *per capita* alcohol consumption but has the highest incidence of fetal alcohol syndrome (FAS) in the world. By analogy, we call this latter relationship the 'American paradox'. In a previous publication, we also found a definite influence of country on the prevalence of alcohol-related spontaneous abortions (Abel, 1997). In that survey, we found that 'epidemiological studies reporting increases in spontaneous abortion rates associated with very low levels of drinking during pregnancy are singular in that virtually every study reporting such a relationship was conducted in the United States or Canada whereas those which did not find a significant link between the two were conducted in Europe or Australia' (Abel, 1997). It would appear, therefore, that we are dealing with a general phenomenon related to alcohol.

The 'American paradox' for FAS is reflected in Table 1, where incidence data are presented for FAS along with *per capita* alcohol consumption for those countries in which FAS incidence data have been obtained from prospective epidemiological studies (Pyorala, 1990; Abel, 1995). The reason why only prospective studies were relied

upon is that this strategy involves examining every newborn, rather than selectively examining children, which means that there is less bias associated with identifying children with FAS than would be the case with a retrospective strategy (Abel, 1989).

As indicated in Table 1, the USA has the world's highest incidence of FAS, but has a relatively low *per capita* rate of alcohol consumption. Annual *per capita* alcohol consumption in the USA is about 7.3 l of absolute alcohol, which is considerably less than countries like Spain, Switzerland, Germany, Italy, and Australia. The high rate of FAS in the USA is thus a paradox, given that countries with considerably higher *per capita* consumption rates have incidence rates of 0 cases per 1000. The UK, which has an annual *per capita* consumption very similar to the USA, likewise has 0 cases per 1000 births.

An analysis of all the prospective studies of the worldwide incidence of FAS indicated that, out of the 95 cases of FAS observed in these studies, 91 cases were diagnosed in the USA (Abel, 1995). Although there were far more studies conducted in the USA, the total number of children examined in the USA was less (46 497) than the number of children examined in other countries (51 079). In other words, whereas fewer children were examined in the USA compared to the rest of the world,

the incidence of FAS in the USA is about 20 times higher than it is for all of the rest of the world combined (Abel, 1995).

Although the worldwide incidence of FAS is 0.97 cases/1000 (Abel, 1995), this estimate is based almost entirely on the USA, since nearly all of the FAS cases observed systematically for the disorder were diagnosed in the USA. If, instead of estimating the incidence for FAS on the basis of dividing the total number of cases by the total number of children examined, we average the incidence rate among each of the 29 prospective studies in which these 97576 children were examined, the worldwide incidence rate is 0.5 cases/1000, and both the median and the mode for all study sites are 0 cases/1000 (Abel, 1995). In other words, the 'American paradox' seems to account for the entire world incidence of FAS! It is important to emphasize, however, that these estimates are based entirely on prospective studies. If the mothers of children with FAS do not participate in such studies, these estimates may be invalid. The extent to which the prospective estimates underestimate or overestimate the actual incidence has not yet been determined. However, since prospective designs are generally accepted as producing the most accurate assessments of incidence (Abel, 1989), these estimates should be accepted as valid until proven otherwise.

### PREVALENCE OF DRINKING DURING PREGNANCY

*Per capita* alcohol consumption, however, may be misleading in terms of its relation to FAS, since *per capita* data are based on the total adult population in a country and include men and women. Men, however, are not only more likely to be alcohol consumers than women, they also typically drink more than women, and have a higher prevalence of alcohol abuse and dependence (US Department of Health and Human Services, 1993). Since *per capita* consumption data do not differentiate between men and women, comparisons between the incidence of FAS and *per capita* consumption data may be misleading, if the proportion of male to female drinkers is not the same in each country.

An alternative way of exploring the 'American paradox' is to compare rates of drinking among

women in various countries and especially the number of women who drink during pregnancy. The latter, however, is more complicated than the former, since drinking tends to decrease during pregnancy (Little *et al.*, 1976; Sokol *et al.*, 1980), and the decrease in consumption is usually proportional to pre-pregnancy levels (Little *et al.*, 1976). Unless rates of drinking during pregnancy are determined during the same trimester, cross-cultural comparisons may be distorted as a result of the time at which drinking histories were obtained.

Abel (1998) conducted an analysis comparable to that shown in Table 1, except that, instead of *per capita* consumption, the percentages of women of reproductive age who drink prior to or during pregnancy in various countries were compared. An almost identical percentage of US women drink prior to, and during pregnancy (68 and 49% respectively), compared to those in European countries and Australia/New Zealand (69 and 49%, respectively). The similarity implies that the incidence of FAS is not higher in the US because more American women drink during pregnancy compared to elsewhere.

Since FAS only occurs in individuals whose mothers are alcohol abusers, surveys of drinking during pregnancy, like surveys of *per capita* consumption, may not reflect any meaningful relationship with FAS. This is because there are so few alcohol abusers and alcoholics relative to the overwhelming number of women who drink during pregnancy and who never experience any problems as a result of their drinking. The 20-fold difference in incidence between the USA and other countries may, therefore, reflect differences in the percentage of women characterized as alcohol abusers or alcoholics in different countries. However, this kind of analysis is currently impossible to perform, since there is no international consensus about the operational definitions of these terms. Instead, the closest approximation is that of 'heavy' drinking, which is defined as consumption of an average of two or more drinks a day, 45 drinks or more per month, or a positive MAST (Michigan Alcoholism Screening Test) score.

Table 1 contains data with respect to the incidence of FAS among these 'heavy' drinkers. These data indicate that the incidence of FAS increases to 4% when we focus on women who are

selected on the basis of 'heavy' drinking during pregnancy. However, the incidence is still relatively low, given that this is a subpopulation most at risk for FAS. The inference from this percentage is that the criterion for 'heavy' drinking is too low to isolate those women who put their children at risk for FAS because of their drinking.

Although misclassification of drinkers as 'heavy' is widely recognized because of 'denial', and the tendency to lie about drinking increases proportionately to the amount of drinking (Ernhart *et al.*, 1988), misclassification has a relatively minor impact on incidence rate. For example, if 10% of a group of 50 'heavy' drinkers (women drinking five or more drinks per day) claim to be drinking only an average of two drinks a day, then the total number of 'heavy' drinkers in this category would be 45. The number of FAS children in the entire study population, however, would be the same. If there were five FAS children, the incidence of FAS among 'heavy' drinkers would then be 11% instead of 10%. If 20% of the women consuming five or more drinks were placed in the two or more drinks category, then the incidence for the 'heavy' drinking group remains relatively unchanged at 12%. These rates would change if the children with FAS were born to the 'heavy' drinkers who were misclassified, and these children were removed from the population of FAS children, but the birth of a child with FAS to a 'moderate' drinker should alert any researcher to the likelihood of misclassification.

A different kind of misclassification possibly contributing to the disparity in incidence rates of FAS among 'heavy' drinkers involves the formidable problem of comparing 'drinks' as if this were a standardized amount of absolute alcohol. The amount of absolute alcohol in a 'drink' can vary greatly from country to country. A 'drink' in the UK, for instance, contains about 75% less absolute alcohol than a 'drink' in the USA (8 vs 13 g) (Plant, 1985; Abel and Kruger, 1995). This means that international studies that use a criterion of a number of drinks to define 'heavy' drinking may be comparing drinking levels that vary by more than 50%. The number of drinks may be the same, but the amount ingested will differ. This difference will not be apparent, but could obfuscate any attempt to correlate drinking level with a particular outcome.

## EXPLANATIONS OF THE 'AMERICAN PARADOX'

International comparisons require certain concessions. The practitioner has to digest many primary sources and find some common ground in terms of methodology and criteria. Since these concessions are often arbitrary, scientists from each country may question details abstracted from their studies. Even if the details are correct, they may still debate the glosses often resorted to in these analyses and question the generalizations derived from these studies. If constructive, however, such debate can result in better refinements and analyses.

The generalization arrived at in this analysis is that there is a wide international disparity in the reported incidence of FAS, such that nearly all the reported cases have been found in the USA. Since drinking levels in the USA are not greater than those in many countries which have no prospectively identified cases of FAS, we have labelled this incongruity the 'American paradox'. The 'American paradox' is easier to identify than explain. In the remaining part of this article, some of the possible factors contributing to this paradox are outlined. Since international comparisons are being made, these explanations will focus primarily on broad, rather than individual, differences.

As pointed out previously, national *per capita* alcohol consumption rates do not reflect national rates of FAS. However, analyses based on *per capita* rates may not be as heuristic as focusing on either the type of alcoholic beverage consumed in a particular country or the pattern of consumption. In Mediterranean countries such as Italy, France and Spain, and also in Portugal, for instance, the main alcoholic beverage is wine, whereas in northern European countries like Germany, Denmark and the UK and also the USA, the main alcoholic beverage is beer (Pyorala, 1990). Although total consumption in Mediterranean countries is higher than in other parts of the world, many studies, including those conducted in France, have found that alcohol-related reproductive problems occur primarily among women who drink beer (Kaminski *et al.*, 1981; Kline *et al.*, 1987; Kuzma and Sokol, 1987; Walpole *et al.*, 1989). *Per capita* beer consumption may thus be a better correlate of FAS than total *per capita* beverage consumption. Although there may be

something unique to beer, it is also noteworthy that beer is consumed by a relatively small minority of women, many of whom are characterized by low socioeconomic status (SES). It may be that the consumption of beer by these women is a reflection of their SES and it is this factor, rather than beer consumption, that contributes to FAS. The combination of beer consumption and low SES may be another important factor. The role of SES in FAS is considered further later in this Review.

Not only do countries differ in the type of alcoholic beverage most commonly consumed, they also differ in the patterns with which it is consumed. In Mediterranean countries, wine is consumed daily, primarily with meals, and drunkenness is not tolerated socially (Bennett and Ames, 1986). In northern European countries, and in the UK and the USA, drinking does not occur on a daily basis, typically occurs outside meals, and usually during leisure time (Hupkens *et al.*, 1993). In the Scandinavian countries, drinking also occurs outside of meals and at leisure times, usually during the weekends, resulting in a 'binge' pattern of consumption (Zeeman-Polderman, 1994). In both northern European and Scandinavian countries, drunkenness is socially tolerated more than it is in the Mediterranean countries (Bennett and Ames, 1986). If international comparisons are to shed light on the 'American paradox', information regarding beverage type and patterns of consumption will have to be reported more systematically than is presently the case.

An altogether different set of factors contributing to the disparity between countries in the reported incidence of FAS may lie in either those making the diagnosis, or the populations being diagnosed. One of the reasons FAS was not recognized clinically until recently is that the disorder is subtle and relatively uncommon. In this regard, it is noteworthy that the syndrome was not discovered at the time of birth, but rather when children were several years of age (Jones and Smith, 1973). In other words, diagnosis at the time of birth is very difficult, yet incidence data are based on diagnosis at the time of birth. One artifactual explanation for the paradox may be that American physicians are more astute at recognizing FAS than physicians in other countries. This chauvinistic hypothesis has no evidence support-

ing or controverting it. A related possibility that likewise lacks evidence but cannot be dismissed outright is that physicians in different countries differ in the assiduity with which they are willing to identify cases (Austin *et al.*, 1994; Lasky and Stolley, 1994). Since American clinicians tend to be 'more aggressive' in making many other diagnoses than clinicians in other countries because American medicine places a greater emphasis on identification and clinical management of high-risk individuals (Payer, 1989), incidence rates may be higher in the USA because American clinicians are more inclined than physicians elsewhere to characterize anomalies as FAS. It is also noteworthy that, alternatively, American physicians may be more inclined to render a diagnosis of FAS so that families can obtain medical reimbursement for services (Stratton *et al.*, 1996).

Incidence estimates for FAS may also be influenced by the patient populations being examined. Although the diagnosis of FAS is based on a pattern of anomalies, it is unduly weighted by a reliance on facial anomalies such as a depressed nasal bridge and epicanthic folds (Abel, 1998). While all of the facial features associated with FAS can be considered a normal variant within a particular ethnic group, reliance on these characteristics could result in a higher rate of occurrence than warranted. Epicanthic folds and a spoon-shaped depression of the nasal bridge, for instance, are common among aboriginal North Americans. Low birth weight is also much more common among African-Americans than Caucasian-Americans. Since Native American and African-American populations are overrepresented in epidemiological studies of FAS in the USA, their presence contributes strongly to the incidence of FAS in the USA (Abel, 1998). Since FAS occurs at a relatively low frequency, an obstetrician or neonatologist will not encounter many cases of FAS in a year and so his or her experience in recognizing the disorder will be limited. A physician with limited experience who encountered an aboriginal child whose mother drank during pregnancy may simply assume that that child's facial features are indicative of FAS (J. Nanson, personal communication).

SES is closely related to race. In the USA, incidence rates for FAS vary widely, depending on study site, and are almost entirely a function of

SES (Abel, 1995; Abel and Hannigan, 1995). The fact that the mean and median estimates for the incidence of FAS vary considerably implies that FAS does not occur uniformly. Analysis of incidence rates in the USA supports this conclusion. In studies in which the population examined was primarily of middle SES and Caucasian, the incidence rate was 0.26/1000, which is very close to the incidence rate in Europe. By comparison, the incidence rate at sites where the patient population was primarily of low SES, and was African-American, the rate was 10 times higher, 2.29/1000 (Abel, 1995). Since FAS occurs in all racial groups (Abel, 1995), apart from the artefact previously mentioned, race is not a primary risk condition acting in conjunction with alcohol abuse. The most likely alternative is that FAS arises out of a combination of alcohol abuse and poverty (Abel, 1995; Abel and Hannigan, 1995).

In many countries, there is a well-known inverse relationship between SES and infant mortality, low birth weight, and morbidity (e.g. Lahelma and Valkonen, 1990; Diderichsen, 1990). It is therefore not unreasonable to suggest that FAS is likewise influenced by SES. Due to the absence of information relating to SES and FAS in other countries, comparable studies to those conducted in the USA are not yet possible. Comparisons will be intrinsically difficult, however, due to differences in characterizing SES, which is typically defined in terms of occupation, income, and/or education status for a particular country (Lahelma and Valkonen, 1990). Of these three, educational levels may be the best standard for comparison, but comparisons for FAS have not relied on this criterion. However, while we may not have the benefit of epidemiological studies assessing the role of SES in conjunction with FAS, we do have a number of general comments from researchers on the subject, nearly all of whom mention that FAS is seen almost entirely in populations characterized by low SES (Abel, 1995). The possibility of identifying SES as a contributing factor in FAS, however, is only a starting point. Whereas the general relationship between health and social inequalities is relatively clear, the conditions associated with low SES that contribute to FAS along with alcohol are only beginning to be identified (e.g. Abel and Hannigan, 1995). Until research illuminates these relationships, the 'American paradox' awaits clarification.

## REFERENCES

- Abel, E. L. (1989) *Behavioral Teratogenesis and Mutagenesis*. Plenum Press, New York.
- Abel, E. L. (1995) An update on incidence of FAS: FAS is not an equal opportunity birth defect. *Neurotoxicology and Teratology* **17**, 437-443.
- Abel, E. L. (1997) Maternal alcohol consumption and spontaneous abortion. *Alcohol and Alcoholism* **32**, 211-219.
- Abel, E. L. (1998) *Fetal Alcohol Abuse Syndrome Revisited*. Plenum Press, New York, in press.
- Abel, E. L. and Hannigan, J. H. (1995) Maternal risk factors in fetal alcohol syndrome: Provocative and permissive influences. *Neurotoxicology and Teratology* **17**, 445-462.
- Abel, E. L. and Kruger, M. L. (1995) Hon v. Stroh Brewery Co.: What do we mean by 'moderate' and 'heavy' drinking? *Alcoholism: Clinical and Experimental Research* **19**, 1024-1031.
- Austin, H., Hill, H. A., Flanders, D. and Greenberg, R. S. (1994) Limitations in the application of case-control methodology. *Epidemiology Review* **16**, 65-76.
- Bennett, L. A. and Ames, G. M. (1986) (eds) *The American Experience with Alcohol*. Plenum Press, New York.
- Burr, M. L. (1995) Explaining the French paradox. *Journal of the Royal Society of Health* **115**, 217-219.
- Criqui, M. H. and Ringel, B. L. (1994) Does diet or alcohol explain the French paradox? *Lancet* **344**, 1719-1723.
- Dehaene, P. H., Samaille-Villette, C., Forderger-Fasquelle, P., Subtel, D., Delahouse, G. et al. (1991) Diagnostic et prevalence du syndrome d'alcoolisme foetal en maternite. *La Presse Medicale* **20**, 1002.
- Diderichsen, F. (1990) Health and social inequities in Sweden. *Science and Medicine* **31**, 359-367.
- Ernhart, C. B., Morrow-Thucak, M., Sokol, R. J. and Martier, S. (1988) Underreporting of alcohol use in pregnancy. *Alcoholism: Clinical and Experimental Research* **12**, 506-511.
- Hupkens, C. L., Knibbe, R. A. and Drop, M. J. (1993) Alcohol consumption in the European community: uniformity and diversity in drinking patterns. *Addiction* **88**, 1391-1404.
- Jones, K. L. and Smith, D. W. (1973) Recognition of the fetal alcohol syndrome in early infancy. *Lancet* **ii**, 999-1001.
- Kaminski, M., Franc, M., Lebouvier, M., Du Mazubrun, D. and Rumeau-Rouquette, C. (1981) Moderate alcohol use and pregnancy outcome. *Neurobehavioral Toxicology and Teratology* **3**, 173-181.
- Kline, J., Stein, Z. and Hutzler, M. (1987) Cigarettes, alcohol and marijuana: Varying associations with birth weight. *International Journal of Epidemiology* **16**, 44-51.
- Kuzma, J. W. and Sokol, R. J. (1987) Maternal drinking behavior and decreased intrauterine growth. *Alcoholism: Clinical and Experimental Research* **6**, 396-402.

- Lahelma, E. and Valkonen, T. (1990) Health and social inequities in Finland and elsewhere. *Social Sciences and Medicine* **31**, 257–265.
- Lasky, T. and Stolley, P. D. (1994) Selection of cases and controls. *Epidemiology Review* **16**, 6–17.
- Little, R. E., Schultz, F. A. and Mandell, W. (1976) Drinking during pregnancy. *Journal of Studies on Alcohol* **37**, 375–379.
- Payer, L. (1989) *Medicine and Culture*. Penguin Books, New York.
- Plant, M. (1985) *Women, Drinking, and Pregnancy*. Tavistock Publications, London.
- Pyorala, E. (1990) Trends in alcohol consumption in Spain, Portugal, France and Italy from the 1950s until the 1980s. *British Journal of Addiction* **85**, 469–477.
- Renaud, S. and de Lorgeril, M. (1993) The French paradox: dietary factors and cigarette smoking-related health risks. *Annals of the New York Academy of Sciences* **686**, 299–309.
- Sokol, R. J., Miller, S. I. and Reed, G. (1980) Alcohol abuse during pregnancy: An epidemiologic study. *Alcoholism: Clinical and Experimental Research* **4**, 135–145.
- Stratton, K., Howe, C. and Battaglia, F. (1996) (eds) *Fetal Alcohol Syndrome*. National Academy Press, Washington, DC.
- US Department of Health and Human Services (1993) *Alcohol and Health*. US Department of Health and Human Services, Washington, DC.
- Walpole, I. R., Zubrick, S. and Pontre, J. (1989) Confounding variables in studying the effects of maternal alcohol consumption before and during pregnancy. *Journal of Epidemiology and Community Health* **43**, 153–161.
- Zeeman-Polderman, M. (1994) Drinking behavior of various population segments in western countries: Differences and trends. *Alcohol Digest* **13**, 1–3.