ALCOHOL CONSUMPTION AND THE OUTCOMES OF PREGNANCY

This statement replaces green-top guideline No.9, Alcohol Consumption in Pregnancy, published in November 1996 and reviewed in December 1999.

1. Purpose and scope

Following a review of the available evidence, this statement has been designed to aid women and their care providers as they discuss the risks of alcohol consumption at the time of conception and during pregnancy. This statement addresses issues relating to fertility, early fetal development, growth and maturation and long-term neurodevelopmental and behavioural outcomes. Comparisons between published studies from different countries and settings are limited by differences in how alcohol consumption is reported and by the difficulties inherent with under-reporting of alcohol intake. Standardised units of alcohol are reported, where possible, to facilitate valid comparisons.

2. Identification and assessment of evidence

A complete literature search was performed in 1999. This was updated to 2005 including a search of EMBASE, the Cochrane Database of Systematic Reviews, published evidence-based guidelines and additional literature identified at specialist meetings.

3. Key points

- There is an increasing body of evidence suggesting harm to the fetus from alcohol consumption during pregnancy. While the safest approach may be to avoid any alcohol intake during pregnancy, it remains the case that there is no evidence of harm from low levels of alcohol consumption, defined as no more than one or two units of alcohol once or twice a week.

- Binge drinking in early pregnancy may be particularly harmful and specific advice to young men and women should make this clear. Advice on the risk of harm to an unplanned pregnancy, as well as the risk of sexually transmitted disease, should be widely available. Access to postcoital contraception and screening for sexually transmitted infection should be made available to those whose behaviour has put them at risk.

- In antenatal clinics, effort should be made to improve objective history taken about alcohol and other substance abuse, to attempt to identify the high-risk group of women with problem drinking or other behaviour that can be harmful to the fetus.
● Counselling and detoxification programmes should be made easily available to women.
● Continuing efforts should be made to identify a biochemical test that could be applied to give an objective assessment of chronic alcohol use in pregnant and nonpregnant women.
● It is quite likely that many cases of fetal alcohol spectrum disorder (FASD) are being missed and training in the recognition of this disorder and the availability of tertiary referral for confirmation of the diagnosis should be made more widespread in the UK through community and hospital based paediatric clinics.
● Long-term prospective cohort studies should be conducted to address the questions discussed in this statement. Existing longitudinal databases should be interrogated where maternal and paternal alcohol consumption in relation to pregnancy can be reported in relation to childhood outcomes.

4. Background

The consumption of alcohol offers no benefits in relation to the outcomes of pregnancy and alcohol is both teratogenic and fetotoxic in the human. Under reporting of alcohol consumption is thought to be widespread and the effects of alcohol consumption in the offspring may not always be recognised. It is important for GPs, obstetricians and midwives to devise ways of identifying women who may suffer from problem-drinking during or before any pregnancy, at a time when potentially beneficial interventions can be offered. On the other hand, there is considerable doubt as to whether infrequent and low levels of alcohol consumption during pregnancy convey any long-term harm – in other words, is there a safe upper limit for alcohol consumption in pregnancy?

Since 1981, the US Surgeon General’s Office has given consistent advice that, in the USA, women who are pregnant (or considering a pregnancy) are advised not to drink alcoholic beverages and alcohol-containing products carrying a health warning. UK agencies have not felt happy to endorse this advice based on assessment of the current literature. For instance, the Department of Health report, Sensible Drinking,1 made the following recommendation ‘to minimise the risk to the developing fetus women who are trying to become pregnant or are at any stage of pregnancy should not drink more than one or two units of alcohol once or twice a week and should avoid episodes of intoxication’. The Midwives Information and Resource Service (MIDIRS) in their evidence-based advice to women, updated in 2003,2 said that ‘pregnant women should be advised to keep to the guidelines of no more than one or two units once or twice a week. Women can be reassured that light infrequent drinking constitutes no risk to their baby’. The Medical Council on Alcohol, in their handbook, Alcohol and Health,3 state that ‘the most vulnerable period for the fetus is from 4–10 weeks of gestation but alcohol-related damage may occur throughout pregnancy. Thus, benefit to the infant can be obtained if alcohol is withdrawn at any stage of gestation. It is recommended that women avoid alcohol during the first trimester and then limit their intake to one to two units once or twice a week for the remainder of their pregnancy’. Most recently, in the National Institute for Health and Clinical Excellence clinical guideline on antenatal care,4 this statement was included: ‘Alcohol has an adverse effect on the fetus. Therefore it is suggested that women limit alcohol consumption to no more than one standard unit per day’.

5. Alcohol consumption in pregnancy

5.1 Measuring consumption

Alcohol consumption is usually reported in units: the amount of alcohol found in many standard drinks (one small glass of wine, one measure of spirits, half pint of beer/lager) and is measured at 7.9 g or 10 ml of ethanol. International comparisons are difficult because of different alcohol contents of ‘units’ and uncertainties introduced by self-reporting of ‘drinks’.

RCOG Statement No. 5
The Table 1 gives a rough guide to the amount of alcohol found in standard measures of different drinks. These guidelines are approximate and may vary depending on the brand chosen and the size of measure. All alcohol sold in the UK above 1.2% alcohol by volume (ABV) should state how strong it is in a percentage. The higher the percentage, the more alcohol it contains. Pub measures are generally rather smaller than the amount poured at home. Drinking five or more drinks at one session for women is known as ‘binge drinking’.

5.2. Epidemiological studies

Despite the advice of the Surgeon General, regular surveys in the USA suggest that between 9% and 15% of women drink alcohol at least once a month during their pregnancy. There has been an upward trend of women reporting frequent drinking during pregnancy from a low of 0.9% in 1991 to 3.5% in 1999, the most recently published data. Anonymous surveys in Swedish women using the Alcohol Use Disorder Identification Test (AUDIT), in which a score of six or higher represents hazardous alcohol use, found that 185 out of 1101 women scored six or higher in terms of consumption prior to pregnancy. Fifty-eight per cent of these (185) consumed no alcohol once the diagnosis of pregnancy had been recognised, 27% drank alcohol not more than once a month and 15% reported alcohol consumption on two to four occasions a month during their pregnancy. Studies in the UK, such as that of James et al. in Bristol, reported alcohol consumption of 500 women between 28 and 32 weeks of gestation. Average consumption was less than one unit per day and the individual who reported the maximum intake in the survey was consuming just over two units a day. Anonymised screening of 233 unselected antenatal clinic attendees in Sheffield (unpublished data) revealed that 45% did not consume alcohol at all during their pregnancy and a further 44% reported consuming less than one unit per week. Ten percent

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Table 1. Guide to units of alcohol

(a) Beer, cider and ‘alcopops’

<table>
<thead>
<tr>
<th>Type of drink</th>
<th>Strength (ABV – %)</th>
<th>Measure (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Half Pint</td>
</tr>
<tr>
<td>Ordinary strength beer, lager or cider, e.g.</td>
<td>3–4</td>
<td>1.00</td>
</tr>
<tr>
<td>draught beer, Heineken, Woodpecker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Export’ strength beer, lager or cider, e.g.</td>
<td>5</td>
<td>1.25</td>
</tr>
<tr>
<td>Stella, Budweiser, Kronenbourg, Strongbow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extra strong beer, lager or cider, e.g.</td>
<td>8–9</td>
<td>2.50</td>
</tr>
<tr>
<td>Special Brew, Diamond White, Tennants Extra</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘Alcopops’, e.g. Bacardi Breezer, Smirnoff Ice,</td>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td>Reef, Archers, Hooch</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(b) Wines and spirits

<table>
<thead>
<tr>
<th>Type of drink</th>
<th>Strength (ABV – %)</th>
<th>Measure (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Small glass/pub measure</td>
</tr>
<tr>
<td>Table wine</td>
<td>10–12</td>
<td>–</td>
</tr>
<tr>
<td>Fortified wine (sherry, Martini, port)</td>
<td>15–20</td>
<td>0.8</td>
</tr>
<tr>
<td>Spirits (whisky, vodka, gin)</td>
<td>40</td>
<td>1.0</td>
</tr>
</tbody>
</table>

(Source: Reproduced with permission from the Royal College of Psychiatrists leaflet: Information for the Public: Alcohol and Depression, Help is at Hand, January 2004 (www.rcpsych.ac.uk/info/help/alcohol/AlcoholDepression.pdf)

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of women consumed up to one unit a day and 1% admitted to consuming more than one unit a day. It is important to bear in mind, when assessing the effects of alcohol consumption on pregnancy outcome, that most women who are suffering from problem drinking have other behaviours (such as smoking, drug abuse, poor nutrition) which may independently or synergistically contribute to an adverse outcome of pregnancy and defaulting from antenatal care. Women who have problem drinking during pregnancy should be treated with respect and compassion, as failure to do so may result in them ceasing to attend for antenatal care. There is evidence that interventions to reduce alcohol consumption in pregnancy are effective and where possible should be applied as a result of preconception counselling.

6. Adverse outcomes of alcohol consumption on the reproductive process

6.1 Fertility

Alcohol may be exerting toxic effects throughout the reproductive process from infertility through miscarriage, aneuploidy, structural congenital anomaly, disordered fetal growth, perinatal death, developmental delay and indeed susceptibility to disease in adult life. Grodstein et al.\textsuperscript{10} reported a dose response effect of weekly alcohol consumption on anovulatory infertility with an odds ratio (OR) of 1.3 (95% CI 1.0–1.7) in women consuming less than 100 g of alcohol a week compared to nondrinkers and an OR of 1.6 (1.1–2.3) in those consuming more than 100 g of alcohol a week. Infertility associated with endometriosis was also more common in those who drank but there was no dose-related effect. There was no excess of infertility associated with tubal disease or ‘unexplained infertility’ in their case series.

The suggestion of delayed ovulation was not confirmed amongst fertile women in the Danish birth cohort. Juhl et al.\textsuperscript{11} reported no prolongation of waiting time to pregnancy by amounts of weekly alcohol consumption and, in fact, both light and moderate drinkers had shorter waiting times to conception than women who did not consume alcohol. (OR 1.18 95% CI 1.12–1.25).

There is less information about male fertility but postmortem studies based on testicular biopsies showed normal spermatogenesis of men consuming less than 40 g of alcohol a day compared with nondrinkers.\textsuperscript{12} There was a dose response reduction in spermatogenesis at consumption levels higher than this, with a significant number of aspermic men among a group consuming more than 80 g of alcohol a day.

Another effect of alcohol on reproductive health is the relationship between binge drinking and unprotected sexual activity. Studies on female college students in the USA suggested that infrequent binge drinkers were three times more likely and frequent binge drinkers seven times more likely to risk sexually transmitted disease and unplanned pregnancy than nondrinkers or women who while consuming alcohol did not indulge in bingeing, here defined as five or more drinks at one session.\textsuperscript{13}

6.2 Miscarriage and structural congenital malformations

Alcohol consumption is associated with an increased rate of miscarriage. One study reports an increase in first-trimester miscarriage with alcohol consumption of more than five units a week, although no increase in second-trimester losses.\textsuperscript{14} Earlier studies by Harlap,\textsuperscript{15} however, showed no dose-related excess of first-trimester miscarriage but a clear dose-related increase in second-trimester loss. First-trimester miscarriage is where aneuploidy or major structural malformations might be expected to predominate. Animal experiments in the mouse suggest that preovulatory exposure to alcohol leads to aneuploidy via nondisjunction exclusively confined to the oocyte-derived chromosome set.\textsuperscript{16} In continuing pregnancies, major structural malformations are seen about three times more commonly in women drinking more than 35 g a day compared with those
consuming less or none at all. In the years since this publication, the ability to recognise structural malformations, particularly in terms of brain development, has been enhanced by the availability of techniques such as magnetic resonance imaging (MRI). It may be that alcohol-induced structural brain malformations have been underestimated in the past.

6.3 Preterm labour

The Danish birth cohort revealed a relationship between alcohol consumption both in early pregnancy and in late pregnancy and preterm birth but only at levels of consumption in excess of 10 drinks a week. A survey from Mexico suggested that, while absolute amounts and the pattern of drinking, including bingeing, were associated with a dose response effect in terms of low birth weight, there was no significant effect of either the amount or pattern of drinking on preterm delivery rates.

6.4 Fetal growth and development

There is a clear dose response relationship between alcohol consumption in the second half of pregnancy and fetal growth. The OR of producing infants below the tenth centile of weight for gestational age compared with nondrinkers for women consuming less than one unit per day is 1.1 (95% CI 1.00–1.13), one to two units a day 1.62 (1.26–2.09) and three to five units a day 1.96 (1.16–3.31). Tolo et al. compared short-term outcomes of pregnancy in women whose usual pattern of drinking was binge drinking either before or during pregnancy and women who continued to consume alcohol during pregnancy but at a rate of less than two units a day. No differences in birth length, weight, head circumference, gestational age or Apgar scores were reported. There is more concern about the longer-term effects of binge drinking. The primate studies of Clarren et al. used a model based on cognitive behavioural and motor assessments in offspring of animals exposed to weekly ‘binges’ for 3, 6 or 24 weeks (full gestation). The 3-week cohort were ‘equivocally normal’ but the 6 and 24 week cohorts were uniformly abnormal compared with controls and with each other. There was an excess of spontaneous abortions in the three alcohol-exposed groups.

Human studies by Streissguth et al. reported binge exposure prior to pregnancy recognition led to children at 7 years of age having learning problems, low academic achievement and hyperkinetic and impulsive behaviour problems.

The importance of recognising women who are heavy alcohol consumers during pregnancy and providing them with help to reduce or discontinue their habit is certainly clear in terms of birth weight, although damage in terms of cerebral structure and function may have already taken place. Autti-Rämö and others have reported alcohol-related neurodevelopmental disorder (see below) in relation to binge drinking in early pregnancy only. Among women who continued to drink more than two units a day throughout the third trimester, 45% had an infant with a birth weight below the tenth centile for gestational age, whereas in those who successfully reduced or discontinued their alcohol consumption during the last 3 months of pregnancy there was no excess of low birthweight with only 8% falling below the tenth centile.

7. Fetal alcohol syndrome and fetal alcohol spectrum disorders

Following the original recognition of fetal alcohol syndrome, a considerable amount of work has gone into recognising the pattern of disorders which might be associated with lesser degrees of harm from maternal alcohol consumption and in the US Institute of Medicine Report of 1996 these were referred to as fetal alcohol spectrum disorders. As well as recognised fetal alcohol syndrome, these include fetal alcohol syndrome without a confirmed history of alcohol consumption, the partial fetal alcohol syndrome, where some but not all of the four usual features
are present, alcohol-related birth defects, where typical structural defects are seen without the pattern of neurodevelopmental disorder, and the opposite situation where there is apparent alcohol-related neurodevelopmental disorder with no obvious structural defects (Table 2). A more detailed four-digit scoring system introduced by Astley and Clarren gives rise to a diagnostic formulation including up to 256 possible combinations, which can be combined into 22 separate diagnostic categories.

**Table 2. Diagnostic criteria for fetal alcohol syndrome (Stratton et al.)**

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Confirmed maternal alcohol exposure</td>
</tr>
<tr>
<td>2</td>
<td>Evidence of a characteristic pattern of facial anomalies that includes features such as short palpebral fissures and abnormalities in the premaxillary zone (e.g. flat upper lip, flattened philtrum and flat midface)</td>
</tr>
</tbody>
</table>
| 3     | Evidence of growth restriction as in at least one of the following:  
  - low birth weight for gestational age  
  - decelerating weight over time not due to nutrition  
  - disproportionally low weight to height |
| 4     | Evidence of central nervous system neurodevelopmental abnormalities, as in at least one of the following:  
  - decreased cranial size at birth  
  - structural brain abnormalities (e.g. microcephaly, partial or complete agenesis of the corpus callosum, cerebellar hypoplasia)  
  - neurological hard or soft signs (as age appropriate) such as impaired fine motor skills, neurosensory hearing loss, poor tandem gait, poor eye–hand coordination |

Children exposed to alcohol *in utero* may suffer from serious cognitive effects and behavioural problems as well as alcohol-related changes in brain structure which can be identified by modern imaging techniques. Brain mapping based on MRI analysis suggests disproportionate reduction in white matter compared with grey matter in these individuals. Children with fetal alcohol syndrome have a much smaller brain size, with specific reductions in the size of the caudate nucleus, thinning or agenesis of the corpus callosum and reduced size of the hippocampus, and cerebellum. Electroencephalograph studies are compatible with reductions of power and strength of $\alpha$ frequencies – the predominant type of activity in the relaxed subject and modified responses to stimuli compatible with defects in information processing. Positron emission tomography studies show that subcortical brain regions may be especially susceptible to prenatal alcohol insult. Functional MRI is starting to be applied to study differences in cerebral function between alcohol-exposed and non-exposed individuals.

The estimated incidence of the full-blown fetal alcohol syndrome is 0.6/1000 live births, based on detailed studies performed in Canada and the incidence of fetal alcohol spectrum disorders is suggested to be 9/1000 live births in studies from the USA. Abel suggested that these North American prevalence rates were up to 20 times higher than those seen in Europe and that African-American or Native American background and low socio-economic status predict a ten-fold increase in fetal alcohol syndrome. An important note of caution in labelling children with this diagnosis comes from a recent review by Hoyne *et al.*, who pointed out that, in their clinical experience, fetal alcohol spectrum disorders must always be a diagnosis of exclusion. This is because ‘many genetic and malformation syndromes have some of the clinical characteristics of fetal alcohol syndrome and children with other genetic and dysmorphic syndromes are born as frequently to women who abuse alcohol as they are to other women in the general population. Therefore, a diagnosis of fetal alcohol spectrum disorder continuum should not automatically be assigned to a child with disabilities just because his or her mother drank alcohol during the pregnancy’.
8. Do low levels of alcohol consumption harm the fetus?

The suggestion has been made that the evidence of harm from low levels of alcohol consumption in pregnancy is such that UK guidelines should be revised to recommend complete abstinence, in line with the US Surgeon General’s longstanding advice.\textsuperscript{14}

8.1 Fetal behavioural studies

Studies of fetal behaviour patterns have been extended to the influence of maternal alcohol consumption on spontaneous movements, startle reaction and habituation of the fetus at 18, 27 and 36 weeks of gestation.\textsuperscript{35} Especially in late pregnancy, spontaneous and provoked fetal activity was reduced and the effects were also seen in faster habituation patterns in infants at 5 months of age. The significance of these preliminary studies is uncertain.

8.2 Neurodevelopmental studies

It is postulated that some mother–infant dyads might have a predisposition to harm from low levels of consumption and that these individuals cannot be recognised in our current state of knowledge.\textsuperscript{34} Alcohol-related neurodevelopmental disorder may be related to the timing of exposure, levels of consumption, genetic factors affecting maternal or fetal metabolism or individual susceptibility, as well as interaction with other harmful behaviours.\textsuperscript{26} It is also not clear whether these effects fit a threshold or a dose response model.

The literature is confusing and does not offer clear guidance, perhaps because of the aetiological uncertainties referred to above.

Sood\textsuperscript{et al.}\textsuperscript{36} followed up children aged 6–7 years whose mothers reported alcohol consumption of at least 15 g of alcohol per day, with a small control group derived from women consuming less or no alcohol during the pregnancy. OR for delinquent behaviour was 3.2 (95% CI 1.3–7.6) for all alcohol-exposed infants but not significantly higher in the subgroup with low alcohol exposure. Aggressive behaviour was, however, significantly more common in the offspring of mothers consuming low levels of alcohol compared with children who were not exposed to alcohol. The population studied was African-Americans from Detroit, USA, and high rates of other potentially harmful exposures, such as cocaine use (18.8% of the non alcohol using mothers), low rates of stable union and high rates of exposure to violence throughout the cohort were reported. In contrast, Jacobson\textsuperscript{et al.}\textsuperscript{37} report no relation between pregnancy drinking below 15 g per day and developmental outcomes, also in an African-American population in Detroit.

A child development study performed in 18-month and 42-month follow-up appointments in Denmark reporting child development indices concluded that maternal alcohol intake up to one drink (12 g alcohol) a day was unlikely to have an impact on child development.\textsuperscript{38} An earlier follow-up study of infants born in Dundee in 1985/86, assessed by Bayley scales of mental and motor development at 18 months of age, showed no effect of early pregnancy alcohol consumption of less than 50 g a week compared with the infants of non drinkers.\textsuperscript{39}

8.3 Childhood growth studies

The studies of Day\textsuperscript{et al.}\textsuperscript{40} of a cohort of 580 14 year olds in Pittsburgh, USA, (46% white, 54% African-American) relates to growth in relation to maternal reported alcohol consumption in pregnancy. Even low levels of consumption (more than 0.0 but less than 0.2 drinks a day) were associated with a body weight reduction of 1.5 kg at 14 years compared with the offspring of non-drinkers. A consistent dose response relationship was seen with increasing alcohol consumption in
the mother. In regression analysis, the effect was related to first- and second-trimester exposures but not third trimester. Height and head circumference were both negatively associated with first- but not second- or third-trimester maternal alcohol exposure.

9. Conclusions

The consumption of alcohol offers no benefits in relation to the outcomes of pregnancy. Under reporting of alcohol consumption is thought to be widespread, such that adverse effects in the offspring may not always be recognised. It is important for GPs, obstetricians and midwives to devise ways of identifying women who may suffer from problem drinking, during or before any pregnancy, at a time when potentially beneficial interventions can be offered. On the other hand, there is considerable doubt as to whether infrequent and low levels of alcohol consumption during pregnancy convey any long-term harm, in particular after the first trimester of pregnancy.

It is important that long-term prospective cohort studies be conducted to address the questions discussed in this statement.

References


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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG.

Valid until March 2009 unless otherwise indicated.