

Unfortunately, the morbidity and mortality associated with whooping cough have not been measured in today's circumstances, when most children are well nourished and hospital intensive care is readily available. General practitioners will, however, have seen enough whooping cough in the last few years to have formed their own assessment of its morbidity in their own communities. The massive National Childhood Encephalopathy Study investigation has shown that if all the 600 000 (normal) children born in Britain each year are immunised with pertussis vaccine two will have severe reactions with permanent disability. The balance between risks and benefits to the individual tips strongly in favour of the vaccine when acceptance rates are low and the disease is common; it tips the other way as vaccination rates climb and the disease declines.

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<sup>3</sup> Stewart GT. Vaccination against whooping cough. Efficacy versus risks. *Lancet* 1977;ii:234-7.

<sup>4</sup> Swansea Research Unit of the Royal College of General Practitioners. Effect of a low pertussis vaccination uptake on a large community. *Br Med J* 1981;**282**:23-6.

<sup>5</sup> Department of Health and Social Security. *Review of the evidence on whooping cough vaccination by the Joint Committee on Vaccination and Immunisation*. London: HMSO, 1977.

<sup>6</sup> Department of Health and Social Security. *Whooping cough: reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation*. London: HMSO, 1981.

## Late consequences of abortion

Early in the 1970s the effects of induced abortion on future fertility seemed likely to prove little short of disastrous. Gynaecologists feared that tubal damage might lead to infertility,<sup>1</sup> and there were reports that women becoming pregnant after a termination faced 10 times the normal risks of midtrimester abortion<sup>2</sup> and ectopic pregnancy,<sup>3</sup> as well as doubled rates of premature delivery<sup>1 5</sup> and stillbirth.<sup>5</sup> These early studies were quickly contradicted by others<sup>6-8</sup> finding no increased risks after termination, but in the mid-1970s more reports of adverse effects appeared, generating further controversy. Why is consensus so elusive?

One reason is that conditions vary so much in different countries. For example, induced abortion is illegal in Greece,<sup>9</sup> where its sequelae include infertility,<sup>9</sup> ectopic pregnancy,<sup>3</sup> premature delivery,<sup>4</sup> and stillbirth,<sup>5</sup> but countries with low rates of criminal abortion may be different. In Taiwan, where abortion is also illegal, a large study<sup>7</sup> found no effects on subsequent pregnancy, but there abortions—though illegal—are said to be commonly performed by doctors.<sup>7</sup> Another problem facing investigators is that women undergoing abortions tend to be smokers<sup>10-12</sup> and to come from lower socioeconomic groups<sup>10 13</sup>—factors which themselves jeopardise pregnancy. A further reason for confusion is that termination of a young girl's first pregnancy may have different effects from abortion in an older woman who has already had children.<sup>14</sup> Finally, the method of abortion and degree of cervical dilatation<sup>15</sup> are important but are difficult to determine retrospectively.<sup>16</sup> Dilatation of the cervix to more than 10 mm is now known to be harmful<sup>15</sup> and is avoided when possible—but this was not always the case 10 years ago.<sup>11 17</sup>

Many investigations did not eliminate the effects of other risk factors. In one of the few British studies<sup>18</sup> 211 pregnant women who had had their only previous pregnancy terminated in the early 1970s were compared with 147 women whose only pregnancy had miscarried spontaneously. The termination group had double or treble the rates of first-trimester abortion and premature delivery, and the rate of midtrimester abortion was increased sixfold to 8.5%. Eleven patients had suffered cervical laceration during their termination: six of these women lost their next baby and only one of the 11 pregnancies went beyond 36 weeks. A later Australian study<sup>19</sup> found no increase in first-trimester abortions, but late abortion and premature labour were appreciably increased—whether or not a woman had had a full-term pregnancy before her termination. Among 504 primiparae in Holland<sup>20</sup> there was a much smaller increase in midtrimester abortion and prematurity, perhaps because 95% of abortions in Holland are performed early with minimal cervical dilatation. In Norway<sup>21</sup> increased risks of late miscarriage and premature delivery became worse in the third and fourth pregnancies after a termination. A British follow-up<sup>22</sup> of prostaglandin-induced abortion showed a slightly increased risk of miscarriage but no increased prematurity.

Though the Dutch investigators used age-matched controls, none of these studies controlled for other factors. A more elaborate investigation<sup>13</sup> in the United States matched 571 cases with controls for six variables including age, religion, and socioeconomic state and concluded that termination had no adverse effect whatever on subsequent pregnancy—a result which the same authors had shown in Taiwan.<sup>7</sup> Nevertheless, a later American study<sup>11</sup> of 3500 cases and 28 000 controls painted a less straightforward picture. After allowing for other risk factors among parous women there was no increase in miscarriage, but among nulliparous women late miscarriage was increased: termination performed before 1973—generally by dilatation and curettage—trebled the rate of midtrimester abortion. After 1973 the gentler technique of suction evacuation after laminaria dilatation had been used, and the risk of midtrimester abortion was increased only 1.4 times. Nulliparous women who have two or more terminations treble their chances of late miscarriage.<sup>11 23</sup> Congenital deformities are no commoner after termination.<sup>13 24 25</sup>

In Europe, controlled studies have produced similar results. A multicentre investigation<sup>12</sup> found increased rates of late miscarriage and prematurity where termination was by dilatation and curettage but not after vacuum aspiration. Carefully controlled Danish studies showed no effect on early or late miscarriage,<sup>26</sup> placental function values,<sup>27</sup> or birth weight<sup>28</sup> in subsequent pregnancy, but threatened abortion and retained placenta were commoner<sup>28</sup>: cervical dilatation to more than 12 mm was associated with low birth weight and recurettage with retained placenta.<sup>29</sup> There was no increase in secondary infertility<sup>30</sup> unless the termination had been complicated by infection: a similar conclusion has been reached in America.<sup>31</sup>

Early predictions have proved inaccurate partly because they were based on uncontrolled investigations and partly because techniques of termination have improved. Uncomplicated early vacuum aspiration has little effect on subsequent fertility, but infection, excessive cervical dilatation, and repeated terminations are dangerous, especially to nulliparae. Unfortunately women still too often present late to gynaecologists and termination is too often followed by another unwanted pregnancy.<sup>18 22</sup>

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## Regular Review

### Timolol after myocardial infarction: an answer or a new set of questions?

J R A MITCHELL

*"How long halt ye between two opinions? . . . Let them therefore give us two bullocks and let them choose one bullock for themselves and cut it in pieces and lay it on wood and put no fire under, and I will dress the other bullock and lay it on wood and put no fire under. And call ye on the name of your gods and I will call on the name of the Lord. And the God that answereth by fire let him be God. And all the people answered and said, it is well spoken."*

I KINGS XVIII, 21-24

This early controlled trial illustrates very vividly the advantages and problems of our main tool for investigating the effect of treatment. The end point chosen by Elijah was immediate and clearcut so it could be observed by everyone. It resembled early trials of treatment in previously fatal conditions such as diabetes, pernicious anaemia, and tuberculous meningitis, where the first survivals showed that insulin, liver, and streptomycin respectively worked. This contrasts sharply with trials in chronic diseases, where end points such as death or disability

accumulate slowly over many years, leaving ample scope for many variables to influence outcome. Elijah attempted a contemporaneous comparison of like with like, so that the only factor which should have influenced outcome was a difference between the regimens under scrutiny. Purists will immediately see that by allowing the trialists to choose their own bullocks he introduced potential bias. Random allocation would have prevented him from selecting a readily combustible animal for himself whereas his enemies were given a less flammable beast. In our clinical trials we must be sure that the groups used are comparable in all respects other than the variable under scrutiny. An ideal trial thus has a clear and objective end point and is conducted so that the presence or absence of the treatment being tested is the only difference between the groups. Such perfection is unattainable in the real world, especially in chronic conditions with a variable and unpredictable natural history, such as myocardial infarction, stroke, and cancer, where trials are difficult to mount but easy to criticise.