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## Pertussis vaccine

Vaccination against whooping cough was the medical topic most in the public eye in the mid 1970s. The story began with journalistic comment on a report<sup>1</sup> from the Hospital for Sick Children in Great Ormond Street, London, of 36 children with brain damage attributed to pertussis vaccine; public anxiety was fuelled by warnings from medical experts<sup>2 3</sup> that the risk of an adverse reaction causing neurological damage might be as high as one in every 10 000 vaccinations. It was little wonder, then, that between 1974 and 1978 vaccine acceptance rates for pertussis fell from around 80% to 31%, with figures as low as 9%, in some parts of the country.<sup>4</sup>

This calamitous decline in public confidence in the vaccine was not stemmed by reassurances from the Joint Committee on Vaccination and Immunisation,<sup>5</sup> and one obvious reason was the lack of reliable data on the incidence of vaccine-related damage. The National Childhood Encephalopathy Study was set up in 1976 to assess the risks of neurological disorders associated with immunisation in childhood. This week the DHSS has published a report<sup>6</sup> from the study giving details of 1000 cases, and a shorter version has been prepared for the *BMJ* by the authors (p 1595). The main conclusions are that most neurological illness in early childhood is attributable to causes other than immunisation, but that such illnesses occur more frequently than would be expected by chance within seven days and particularly within 72 hours after triple (DPT) vaccine and within seven to 14 days after measles vaccine. Most affected children make a complete recovery; and, by taking alternative explanations into account, "it seems likely that permanent damage as a result of pertussis immunisation is a very rare event and attribution of a cause in individual cases is precarious."

Much of the uncertainty about pertussis vaccination that persisted in the 1970s in the minds of doctors and their patients was due to three separate issues having become intermingled and confused. Firstly, does pertussis vaccine cause brain damage and, if so, how often? Secondly, does pertussis vaccination protect against whooping cough? And, thirdly, should children who develop signs of brain damage after vaccination (and whose parents attribute their handicap to the vaccine) be compensated by the State irrespective of any question of negligence? Campaigning on behalf of children said to be vaccine-damaged was effective and received wide

publicity and must have played a large part in discouraging parents from agreeing to vaccination of their children.

The National Childhood Encephalopathy Study was designed to answer the first question by examining every admission to hospitals in Britain between June 1976 and July 1979 of children aged between 2 and 36 months with neurological disorders; the report is concerned with the first 1000 of the 1180 children admitted in the three-year period. Almost all the children had neurological illnesses unconnected with immunisation or infectious fevers, but 17 (previously normal) had recently had whooping cough: one died, one was left with major neurological sequelae, and one had mild speech delay. Twenty five (previously normal) children had had measles in the four weeks before admission; one died, two had minor developmental delay, and three others had recurrence of fits.

Of the 1000 cases, 35 children had been vaccinated with DTP vaccine within seven days; three had been previously abnormal. Twenty-one of the 32 previously normal children recovered completely; eight of the 11 damaged children (three with minor defects and five with serious neurological damage) had no other explanation for their defects. Comparison of these cases with controls led to a calculated attributable risk of a serious neurological reaction to DTP vaccine of 1 in 110 000; the risk of persisting neurological damage one year later is calculated at 1 in 310 000 immunisations.

This study should, then, provide a final answer to the first issue in the public mind. Pertussis vaccine does carry a risk of neurological damage but that risk is substantially smaller than had been claimed by some of its critics.

The drop in acceptance rates of pertussis vaccination has, as it happens, helped provide information on the second issue. Experience in the most recent pertussis epidemic has shown, says the report,<sup>6</sup> that vaccination provides satisfactory protection, either preventing the disease or substantially reducing its severity. Nevertheless, immunisation against pertussis remains less convincingly effective than immunisation against diphtheria or poliomyelitis. In an ideal world the manufacturers might be encouraged to try to improve the vaccine further; in reality no pharmaceutical company could view such a project with any enthusiasm in the present state of public opinion.

So what advice should doctors now give their patients?

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.

<sup>1</sup> Kulenkampff M, Schwartzman JS, Wilson J. Neurological complications of pertussis inoculation. *Arch Dis Child* 1974;**49**:46-9.

<sup>2</sup> Dick G. Reactions to routine immunisation in childhood. *Proc R Soc Med* 1974;**67**:371-2.

<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>

<sup>1</sup> Stallworthy JA, Moolgaoker AS, Walsh JJ. Legal abortion: a critical assessment of its risks. *Lancet* 1971;ii:1245-9.