IV. The Types and Estimated Numbers of Vaccine-Related Injuries

Typically, adverse vaccine reactions are mild and self-limiting, for example, a sore arm or possibly a fever for a day or two. Less frequently, transient reactions occur that are more unpleasant and frightening; for example, some babies (1 in 12,000) display a pattern of abnormal screaming for several days following DTP vaccination. DTP vaccination may also be followed by convulsions (1 in 5,000); however, in the absence of other neurological symptoms, these are short-lived and leave no permanent brain damage. Similarly, children (but more commonly, adult women) occasionally suffer from temporary arthritis (less than two weeks) following vaccination against rubella (German measles).

For an exceedingly small number of vaccinees, adverse reactions take the form of serious illness that result in long-lasting or permanent disability or even in death. Among the least serious of such reactions are cases of encephalitis (inflammation of the brain) which require hospitalization but from which the patient does eventually recover fully. In some cases encephalitis or some other still rarer neurological disorder results in permanent brain damage. Brain damage may manifest itself via physical disability (e.g., loss of motor coordination) but more often takes the.form of mental retardation. Occasionally, encephalitis or other neurological disorders prove fatal.

Live oral polio vaccine carries a very slight risk of resultant polio disease (1 in 4,000,000). It is actually more common for polio to occur in adults who have close contact with young children who have been vaccinated with live oral polio vaccine. Typically, these adults were never vaccinated against polio or received less than the full series of live oral polio vaccine in the days when the three types were administered separately. Apparently, some individuals are more likely to express paralytic polio reactions to the continued very low level of virulence in a given virus.

Guillain Barre paralysis does not appear to be associated to any significant degree with vaccines other than A - New Jersey influenza vaccine (i.e., the swine flu vaccine). A special study carried out by CDC found that the relative risk of developing GBS within 8 weeks of influenza vaccination during the 1978 - 1979 flu season was 1.4 per million vaccinees as compared to a non-vaccine-related natural incidence of 1 per million. In contrast, the incidence rate associated with swine flu vaccination for the equivalent 8 week period was 6.2 per million. Similarly, while CDC'S adverse reaction monitoring system has received reports of GBS occurring within 4 weeks following almost all of the childhood vaccines, the evidence thus far suggests that these are probably naturally-occurring cases coincidental with vaccination. One of the difficult decisions that will have to be made if a compensation program is established is whether or not to extend the benefit of doubt to such cases and provide compensation. In 1978 - 1979, CDC received 22 reports of GBS occurring within 4 weeks of vaccination.

Finally, there is a slight risk (estimated at 1 in 10,000,000) that a person receiving a vaccine may go into anaphylactic shock (a very severe form of allergic reaction) and die. Almost all such deaths due to anaphylactic shock would be expected to occur within minutes of vaccination. Less severe anaphylactic reactions would not normally be expected to have lasting consequences.

No one really understands why these various adverse vaccine reactions occur. In many cases the biology of the individual vaccinee appears to play a role. Some injured vaccinees may have subtle immunological deficiencies; others may be particularly prone to allergic reactions. On the other hand, certain methods of culturing viruses for vaccine production seem to be associated with higher rates of adverse reactions; e.g., dog-kidney versus duck-embryo cultured rubella vaccines.

Also, it can take years of experience for scientists to determine the proper

degree of attenuation (weakening of the virus so that infection is inhibited but the immunological response is retained) for live viruses that will secure maximum immunity with a minimum risk of adverse reactions. However, over the years, continued research on improving vaccines as well as various immunization policies (such as focusing immunization campaigns on children, who tend to be less susceptible than adults to adverse vaccine reactions) have resulted in a lowering of the adverse vaccine reaction rates for most vaccines currently in wide use.

The major adverse vaccine reactions are described in the following pages (A.D. Little, 1979). Some of the adverse vaccine reactions described below in connection with a specific vaccine may occur in connection with other vaccines as well. Anaphylaxis is an example; it is believed to occur or to have a potential for occurrence with all vaccines, although it is expected to be more common in connection with DTP, due to the comparatively less-refined character of pertussis vaccine.

DTP (Diphtheria/Tetanus/Pertussis) Vaccine

Potential adverse reactions that have been linked to DTP vaccination include: anaphylaxis, convulsions, peripheral mononeuropathy, and encephalitis.

Most of the adverse vaccine reactions associated with DTP vaccine are attributed to the pertussis (whooping cough) component, as researchers have not yet succeeded in developing a pertussis vaccine that is as refined as most other vaccines currently in use.

Anaphylaxis: Anaphylaxis is a form of allergic reaction whose outcome can range from rapid death to benign local reactions that subside spontaneously. Most serious reactions occur within 12 hours of exposure; fatal reactions usually begin within minutes of exposure. Accordingly, a presumptive causal linkage between the vaccine and severe cases of anaphylaxis should not be too difficult

to establish. There is a possibility that in some cases death due to SIDS (Sudden Infant Death Syndrome) could be mistakenly attributed to DTP induced anaphylaxis or vice versa.

Anaphylactic reactions to DTP vaccines, and fatal ones in particular, are quite rare. The most frequently reported outcome is complete recovery.

From the perspective of a compensation system, the most costly potential outcome is a recovery with brain damage. Although theoretically possible, no such cases have actually been reported. It is hypothetically possible, however, that modern resuscitative techniques could result in an improved survival rate at the expense of brain damage among some percentage of those saved from death.

Medical costs in the event of mild to moderate anaphylaxis would be expected to be low because no or only brief (l-2 day) hospitalization would characteristically be required, and long-run effects requiring medical attention would not be expected. Medical costs associated with death would also be expected to be low because death, when it occurs, is usually an immediate reaction.

Convulsions: Convulsions occurring within 48 hours of immunization are considered most likely to be causally related to vaccination. The frequency of convulsions following DTP vaccination is uncertain. One set of estimates based on recent prospective studies gives a range of 1 per 1,000 to 1 per 2,200 vaccinations. Other estimates range from 1 per 3,200 to 1 per 50,000. The estimate by the Center for Disease Control is 1 in 5,000.

Patterns of convulsive episodes are apparently quite variable. There may be a single short convulsion, multiple short convulsions over a period of hours to several days, a prolonged 5-10 minute convulsion, or continued convulsive activity. Convulsions alone are rarely fatal.

In most cases the outcome is complete recovery with medical costs being primarily a matter of diagnostic tests and follow-up visits for monitoring purposes. In rare. instances patients may develop chronic epilepsy with or without mental retardation or become hyperactive and retarded. Should hyperactivity and/or retardation develop, the need for special education or long-term care would generate high medical costs.

Encephalitis, Encephalomyelitis and Aseptic Meningitis: These terms refer to various conditions involving abnormal necrologic function due to inflammation of the central nervous system. It is thought that such conditions, occurring within 48 hours of DTP vaccination, have a high probability of being vaccine related. Some encephalitic reactions are relatively short-lived (36 hours at most) and always end in complete recovery. These short-lived reactions include unusual and persistent crying and a syndrome known as “collapse” that is marked by decreased spontaneous activity, extremely poor fluid intake, lethargy and pallor. One prospective study of 2,298 children found the incidence of persistent crying to be 5.9% and of “collapse” to be 0.2%. Medical costs associated with these types of reactions would be low because patients appear always to recover without lasting effects and only in the case of the comparatively infrequent “collapse” syndrome is hospitalization (of about three days on average) considered warranted. .

There is a great deal of uncertainty surrounding the incidence of encephalopathic reactions following DTP immunization. At a 1977 PHS Immunization Conference, CDC officials cited an estimate of 0.009 cases of encephalopathy per 1,000 associated with pertussis vaccination and an incidence of 0.006 per 1,000 of retardation. In 1977, a British commission tentatively concluded that the risk of brain damage following DTP vaccination was probably about 1 in 300,000. Good data on the incidence of encephalopathy related to DTP does not appear to be available. In Britain, where adverse reactions related to pertussis vaccine

became a political issue due to the efforts of the Association of Parents of Vaccine Damaged Children, there has been more attention paid to the question of the incidence of encephalopathy or other neurological disorders following DTP vaccination than in the United States. The following quote from an article on the British controversy both summarizes the available data and the problems with the data:

> Encephalopathy or other serious neurological complications following whooping cough vaccination have been recorded by several individuals, but to establish an association between the event and the vaccine is again not easy. The problem is usually made more difficult because the evaluation of the illness and the evidence has usually been made in retrospect.... The available reported information on the frequency of serious neurological complications of all types following whooping cough vaccine are variable, and estimates of their frequency have varied from no cases of encephalopathy in about 19,000 children who were following up in the MRC trials of 1948 and 1957 in the United Kingdom to four or five serious neurological illnesses in 215,000 children inoculated in Sweden in 1955-58 (Malmgren et al., reviewing the data of Strom) which gives a rate of 1:50,000 and three cases of 'destructive encephalopathy' between 1959 and 1965 in 516,276 children in Strom's second series in Sweden. A guess of 1:10,000 to 1:50,000 which was based on unconfirmed data from various sources using vaccines which were available in the UK prior to 1968 was made by Dick. This guess is very similar to the estimates arrived at by Malmgren et al. and Strom for the vaccines used in Sweden in the 1960s. Hannik has recorded cases of encephalopathy associated with quadruple vaccine in the Netherlands, but it is not possible to calculate the frequency.
>
> No serious neurological complications have been reported in a study which began in January 1975 and is as yet incomplete and unpublished, in 80,000 children in the North West Thames Region who had recently received a primary dose of triple vaccine. The number so far studied is too small to make it possible to draw any sensible conclusion. All of the above studies except that of Pollock were essentially retrospective.
>
> From personal experience of trying to evaluate retrospectively neurological complications allegedly associated with the administration of whooping cough vaccine, perhaps less than 20% of them merit serious consideration because of inaccurate diagnosis (see also Stephenson and Ounsted) and of the onset of an event in time which could in no way be rationally associated with immunization (Dick, 1978).

Occasionally serious encephalitic reactions end in death, typically after a hospital stay of about 10 days. The medical costs associated with such deaths would tend to be high because of the lengthy hospitalization and intensive nursing and physician care during hospitalization. Survival with serious permanent neurological disability is, of course, costly, both in terms of the

lengthy and intensive hospital care involved but even more so because of the need for intensive rehabilitation therapy, special schooling, and sometimes long-term institutional care for retardation.

Peripheral mononeuropathy: Peripheral mononeuropathy is a reaction that affects the peripheral nerves causing disorders of sensation, mobility or visceral function. Typically the symptoms begin 7-10 days after vaccination, but the onset of the reaction may range from a few hours to six weeks following injection.

Patients exhibit weakness in the tendons and often a decreased sense of touch in the area. The reaction reaches maximum severity within a few days. Maximum severity may range from a complete paralysis of the affected muscles to a mild paresis. Most patients make a complete recovery but in a few instances there may be residual weakness or impairment of movement. The most serious type of residual impairment that can be anticipated is a “winged scapula” that diminishes shoulder mobility for life.

Development of mononeuropathy following DTP vaccination seems to be mainly characteristic of adult males. Of the 21 cases ever reported, only four were children, the rest were adult males. The main population at risk appears to be men in military service who undergo strenuous exercise involving possible trauma to nerves, as well as mutiple immunizations.

Peripheral neuropathy can also be caused by physical trauma to the affected areas or by a toxic reaction to heavy metals. It may sometimes be mistaken for Guillain-Barre syndrome.

Medical costs can be anticipated to be fairly high because recovery is slow -- 2 to 3 weeks at best and may take up to a year -- and physical therapy is indicated. In the few instances of permanent disability, vocational counseling and/or retraining might be necessary.

Measles Vaccine

Adverse reactions associated with measles vaccine include: acute aseptic meningitis and acute encephalitis syndrome.

Acute Aseptic Meningitis and Acute Encephalitis Syndrome: There has been great difficulty in clearly associating live measles virus vaccine with acute central nervous system syndromes occurring soon after vaccination. The Center for Disease Control has, however, adopted the rule of reporting all such syndromes occurring within 30 days of vaccination as vaccine related. Over the years since live measles vaccine was introduced, reported rates of meningoencephalitis have varied between 0.92 and 1.16 cases per million doses of vaccine dispensed. The reported incidence of measles-vaccine meningoencephalitis is thus approximately 1,000 times less frequent than the rate associated with natural measles virus infection. Acording to one published research report (Landrigan & Witte, 1973), from 1963 through 1971, 84 cases of necrologic disorders with onset less than 30 days after vaccination were reported in the United States. 13 cases could be accounted for by causes other than vaccine, and another 11 were uncomplicated febrile convulsions probably related to vaccination. One case met the diagnostic criteria for subacute sclerosing panencephalitis. The remaining 59 showed clinical features of encephalitis or encephalopathy. The causes of these cases could not be established, but 45 had onset between 6 and,15 days after vaccination, which suggests a causal relationship with the vaccine. All 59 cases involved serious neurological disorders. Five cases were fatal. 26 recovered fully. 19 were left with residual disability: ataxia in two cases, retardation in 11, learning disability or hyperkinesis in another 3, seizure disorders in 9, and hemiparesis in 4.

Symptoms of encephalopathic disorders are quite variable and may include fever, vomiting and seizures, irritability and lethargy, possibly followed by coma or stupor. For this reason these disorders may readily be confused with a

host of other neurological problems or other diseases having similar symptoms.

The illness may last only a few days, followed by complete recovery, or may be prolonged and severe with residual neurological impairment including paralysis, epilepsy, and mental retardation. Death occasionally occurs.

In most cases of prolonged severe illness medical costs can be expected to be high both because of the lengthy hospitalization and the fact that those most severely afflicted often require intensive life maintenance measures during the period when cerebral inflammation is at the maximum. Similarly, in cases where the eventual outcome is death, lengthy hospitalization and heroic life support measures would lead to high medical costs. Recovery with residual impairment would also be expected to entail high costs because of special equipment, intensive physical therapy and, in the case of mental retardation, the long-term care that might be needed.

Mumps Vaccine

The adverse reaction associated with mumps vaccination is encephalitis.

Encephalitis: Encephalitis following natural mumps infection has been well documented; accordingly, it was expected that there would be some incidence of vaccine-induced encephalitis. The incidence of mumps vaccine related encephalitis has been calculated at 9 cases per million vaccinees, an incidence rate that might be too low because of underreporting and poor documentation. The reason for considering this estimate as too low is that the reported incidence of mumps vaccine related encephalitis contrasts strongly with the reported incidence of 2,600 cases of encephalitis per million cases of mumps.

Meningoencephalitis, with symptoms including headaches, photophobia, and stiff neck, appears to be more common than true encephalitis, with symptoms including confusion, loss of memory, weakness or paralysis and coma in severe

cases. Other reported conditions specifically known to have occurred with vaccine associated encephalitis include seizures, dizziness, deafness, cranial nerve palsies, diplopia, hemiparesis, and optic atrophy. The latency period between vaccination and onset of the disease appears to range from 1 to 55 days. Length of illness is expected to last from 4 days in mild cases to six weeks in severe cases.

In all reported cases of vaccine induced encephalitis in which the outcome is known, there was recovery. It is generally believed that recovery was complete, with no residual impairment, although lack of documentation makes this uncertain; however, wild virus induced encephalitis has not been known to leave residual effects and, typically, vaccine related side-effects are less severe than naturally occurring ones. The only lasting impairment that is hypothetically anticipated as potentially occurring is partial blindness.

Polio Vaccine

Vaccine associated adverse reactions include encephalitis, meningal encephalitis and encephalopathy without paralysis, and paralytic polio.

Encephalitis, Meningal Encephalitis, and Encephalopathy: The medical literature on these conditions -- often referred to collectively as “nonparalytic polio” -- appears to be rather confusing. Cases have been reported of adverse reactions to both live and killed polio virus vaccines, but descriptions of such reactions tend to be sparse and lack precision of definition.

Thus, as well-defined clinical syndromes, descriptions of these reactions must be taken from the pre-vaccine poliomyelitis literature. On such a basis, these syndromes are described as typically beginning with an acute onset of fever, headaches, nausea and vomiting, which may be accompanied by pain in the legs and neck, cough, sore throat, backaches, nasal discharge, drowsiness, photophobia, convulsions, seizures, frothing at the mouth and constipation. The

course of the disease is quite variable and despite the label “nonparalytic polio” may include muscle weakness or even temporary paralysis as a component. Typically, the course of the disease is benign though prolonged; symptoms such as headache and stiff neck may last more than two weeks. Though total recovery is anticipated in most cases, death can occasionally occur (following about three weeks hospitalization and use of a respirator to sustain breathing artificially). In addition, permanent impairment in the form of serious behavioral disturbances, convulsions or mental retardation can occasionally result. Medical costs in these instances would be quite high due to the need for special education and vocational training. Lifetime placement in a residual facility for the emotionally/behaviorally disturbed or mentally retarded might be necessary.

Paralytic Polio: The occurrence of typical paralytic poliomyelitis following immunization with live virus vaccine has been documented in four clinical circumstances: (1) in vaccine recipients, (2) in contacts of vaccine recipients in the household, (3) in communities where live polio vaccine is being utilized but where clearcut contact by the afflicted person has not been demonstrated, and (4) in immunodeficient individuals in all the above categories.

Recent CDC estimates of risk for live polio vaccine induced paralytic polio in the U.S. are 10/193,000,000 doses of vaccine for recipients and 32/193,000,000 doses of vaccine for contacts. Taken together, these translate, rounded off, to the 1 in 4,000,000 estimate often cited. The risk for immunodeficient individuals is estimated at 10,000 times the above risk factors.

Recipient cases occur in children, since the risk of live polio vaccine for adults was recognized some time ago and its use in adults has been discontinued. Contact cases, however, are mainly adults in the household, exposed to vaccinated infants. Cases in adult contacts as well as among the immunodeficient are more likely to be lethal.

Typically, the disease is non-progressive with paralysis limited to the sites of original involvement. Residual weakness or paralysis of varying degree, rather than complete recovery, is the rule.

Generally speaking, vaccine association is readily accepted if polio occurs in a vaccine recipient within 3-60 days of vaccination. There is disagreement as to the earliest onset, with periods of 4-15 days having been cited. Most cases occurring before 4-12 days are thought to be due to natural polio, with vaccination being coincidental.

"Mild polio" is defined as illness requiring less than two weeks hospital stay, with the outcome being complete recovery or some residual paralysis in one limb only or a unilateral weakness. "Moderate" polio involves 2 to 3 weeks or more of hospitalization and permanent limb paralysis in one or multiple limbs. These cases typically require physical and occupational therapy for 3-6 months to a year, some home health care for several months, special equipment (wheelchairs, braces, home modification, etc.) and possibly a short stay (e.g., two months) in a rehabilitation facility. "Severe" paralytic polio requires a lengthy (2-3 months) acute care hospital stay and leaves a significant handicap, often affecting respiration. In some cases mechanical assistance to sustain breathing and other life support measures might be needed. Some of these cases would be expected to result in death after 2 to 3 months of intensive hospital care or as long as 2 years in a skilled nursing home. In cases of severe polio not resulting in death, extensive physical and occupational therapy, home health services over a period of months to a year or more, special equipment, and 2 to 6 months stay in a rehabilitation facility, would be required. Long-term institutionalization is, however, not expected to be necessary.

Rubella Vaccine

Adverse vaccine reactions associated with rubella vaccine include

arthritis/arthralgia, neuritis, and thrombocytopenic purpura.

Arthritis and Arthralgia: Arthritis/arthralgia following rubella vaccination may take either an acute or chronic form with the former much more common than the latter. Onset is expected to occur within 60 days of vaccination. Since the replacement of dog-kidney by duck-embryo vaccine, the probability of this reaction in children appears to have been all but eliminated. The population at risk is thus adult women of childbearing age who take the vaccine primarily in order to guard against birth defects that might be caused by having rubella during pregnancy. The incidence of rubella associated arthritis/arthralgia among adult women is rather high; 10% of women 15 to 17 years of age and 43% of women 22 to 41 years of age developed arthritis with the duck-embryo vaccine. The risk is greater for those individuals with a personal or family history of arthritis.

The prognosis is almost always excellent in rubella vaccine associated arthritis. In general there is no need for hospitalization and the period of disability lasts less than two weeks. Occasionally an acute case might need surgical intervention and an attendant short hospital stay. In the less frequent cases of chronic, recurrent disease there may be complete recovery or there may be a need for surgical intervention with residual impairment. Occasionally, severe permanent disability may result, necessitating extensive physical or occupational therapy and lifetime placement in an intermediate care facility. A more likely occurrence in the case of chronic arthritis would be mild to moderate recurrent disease in which there would be occasional loss of time from work or decreased productivity. These outcomes are rare, however, and would be far more likely to occur in adult women than in children, who are the main population affected in mass immunization programs.

Neuritis: The incidence of rubella induced neuritis appears to have been markedly reduced following the replacement of dog-kidney by duck-embryo vaccine.

Onset of symptoms has occurred between 7 and 99 days, with the mean interval in connection with the duck-embryo vaccine being 2 weeks. No cases involving adults have ever been reported.

There are two distinct syndromes: (1) brachial radiculoneuritis or the so-called "arm syndrome" in which the patient awakens at night with pain in the forearm, wrist and hand that lasts 30 to 60 minutes, abating, then recurring a short time later during the night; and (2) lumbosacral radiculoneuritis or so-called "catcher's crouch syndrome" in which the patient has pain in the knees and walks on the toes with a characteristic crouching gait. Typically the gait disturbance is worse in the morning and may disappear by noon. In a prospective study of 32 patients with rubella associated neuropathy, there were 8 children with the "arm syndrome," 19 with "catcher's crouch syndrome," and 5 mixed cases. Only 2 cases of "catcher's crouch syndrome" qualified as severe and recurrent.

Complete recovery is the anticipated outcome in all instances, typically within 1 to 6 weeks, though in chronic recurrent cases complete recovery may require as long as 6 months. Hospitalization is not anticipated with the exception of rare instances of chronic recurrent "arm syndrome" with immobility of thumb and index finger, in which a brief hospital stay for neurological testing might be required.

Thrombocytopenic Purpura: Thrombocytopenic purpura refers to a low platelet count in the blood, which, as a naturally occurring complication of rubella, has been known to lead to gastrointestinal hemorrhages or cerebral hemorrhages, the latter leading in turn to brain damage. Although these are theorized to be possible outcomes of a rubella vaccine induced low platelet count, no such case has ever been documented. Although low platelet count per is thought to be a fairly common occurrence following rubella vaccination, the actual incidence is not known, because the condition has no clinical manifestion that would cause the patient to be given the blood test necessary for detection. The only clinical

manifestations associated with rubella vaccination are red spots, indicating slight bleeding under the skin. No medical care other than two office visits to a pediatrician has been required in actual known cases.

Influenza Vaccine

The association between influenza vaccine and Guillain-Barre syndrome came to light during the 1976 mass immunization campaign against swine flu. It is not currently known whether Guillain-Barre syndrome is associated with other influenza vaccines as well.

The latency period is typically 1 to 3 weeks. The first symptom of Guillain-Barre is muscle weakness followed by progressive paralysis (often ascending up the torso). Typically the progression of paralysis takes two weeks but can occur gradually over a period of up to 2 months. Facial weakness and involvement of cranial nerves takes place in 50 to 80% of cases, especially vaccine associated cases. Urinary incontinence or retention occurs in 20% of cases but is transient. From 10% to 25% of patients may have paralysis of breathing and require artificial respiratory support. Pulmonary complications, seizures, and residual necrologic defects may occur but, typically> complete recovery is gradually achieved in one year. Mortality, usually from respiratory involvement, is approximately 5%. Residual paralysis occurs in 10 to 30% of cases.

Generally speaking, it is expected that 50 to 60% of Guillain-Barre victims can return to their normal routine within one year. Approximately 15% will be completely disabled permanently. Relapses can occur weeks or even years following the original attack.

The relative risk in swine flu vaccinated persons was found to be 12 times greater than in unvaccinated persons. All ages were at risk, though the risk was higher among adults, especially young adults (25-44) and those over 65. The most

recent calculation of comparative risk is 6.29 per million among those vaccinated against swine flu versus 0.58 per million for the unvaccinated poulation (DHEW, 1980).

Even a mild case is estimated to require a minimum of 3 weeks hospitalization and 3 months of frequent physical therapy following hospital discharge. Severe cases could require a two month hospital stay on average, up to six months in a rehabilitation facility, physical and occupational therapy, nursing care at home, and considerable need for special equipment and home modifications.

It is important to note, however, that DHHS has agreed to provide compensation in substantiated cases of GBS following swine flu vaccination and is in the process of settling these claims. Swine flu vaccine is not now in use and it appers highly unlikely that it will be in use again in the future.

The significant quesiton is thus whether there is a similar risk of Guillain-Barre syndrome associated with influenza vaccines currently in use. A study carried out by CDC in concert with state epidemiologists and the American Academy of Neurologists has calculated the risk of Guillain-Barre to be 1.4 per million population with the vaccine used during the 1978-79 influenza season (DHEW, 1980).

The natural incidence rate of GBS -- that is, non-vaccinated related -- is about 1 case per 1,000,000. The rate of association between Guillain-Barre syndrome and influenza vaccines currently in use is quite close to the normal background incidence, and it is much lower (1.4 per million vs. 6.2 per million) than the rate of incidence associated with the swine flu mass immunization campaign.

summary

Estimating the number of serious adverse vaccine reactions that occur

annually in the United States cannot be accomplished with absolute certainty. There are conflicting incidence estimates for the various adverse reactions, and no one really knows how many doses of vaccine are actually administered (versus distributed) annually, particularly by private physicians. An often-used conservative rule of thumb is to estimte one-fourth wastage,

However, OTA has compiled what we believe are reasonable “ballpark” estimates. Our best estimate of the number of instances of long-lasting disability due to vaccination of children (diphtheria, pertussis, tetanus, polio, mumps, measles, and rubella) is that there are unlikely to be more than 200 or so such cases occurring annually. Also, we suspect that this estimate is likely to be in error on the high rather than on the low side. The main source of uncertainty is the incidence rate of brain damage caused by adverse neurological reactions to the pertussis vaccine or the pertussis component of the DTP vaccine (See Table 4). In addition, we estimate that there might possibly be as many as 100 - 250 cases of vaccine related illnesses requiring hospitalization but where the outcome would be full recovery.

Since almost all known adverse reactions to the major childhood vaccines are extremely rare as naturally occurring, non-vaccine-related illnesses, it would be feasible to draw up a schedule of adverse reactions (and time periods following vaccinations) for which the causal role of the vaccine would be assumed and compensation provided. Proof could be limited to documentation of vaccination within the alloted time period and diagnosis of the particular illness in question.

Tables 1-4 summarize the information on vaccine-related injuries.

TABLE 1

REPORTED REACTIONS TO COMMONLY USED LIVE VACCINES
(IN IMMUNOLOGICALLY NORMAL RECIPIENTS)

	Known	Probable	Possible
Measles	Fever Rash Convulsions (Primarily Febrile)	Encephalitis Encephalopathy Subacute Sclerosing Panencephalitis (SSPE) Reye's Syndrome	Other Necrologic Disorders -Guillain-Barre Syndrome -Transverse Myelitis -Atixia -Cranial Nerve Paralysis -Teratogenesis
Mumps		Parotitis	Encephalitis, Aseptic Meningitis Unilateral Nerve Deafness Allergic Reactions Rash, Pruritis, Purpura Reye's Syndrome Deafness and Other Necrologic Disorder: -Teratogenesis
Rubella	Lymphadenopathy Fever Rash Arthralgia Arthritis Peripheral Nueitis	Teratogenesis	Thrombocytopenia Encephalitis, Aseptic Meningitis Other Necrologic Disorder -Transverse Myelitis -Guillain-Barre Syndrome -Hemiparesis -Ataxia -Convulsions
Polio	Paralytic Polio	Teratogenesis	Reye's Syndrome
Smallpox	Local Infection (Pustule) Regional Lymphadenopathy Fever "Toxic" Eruption Dissemination and Eczema Vaccinatum	Encephalitis, Encephalopathy	Transverse Myelitis Hemiplegia Reye's Sydnrome Guillain-Barre Syndrome Teratogeneiss
Diphtheria and Tetanus Toxoids and Pertussis Vaccine (DTP)	Local Swelling Sterile abscesses Fever Convulsions	Encephalopathy encephalitis Persistent Screaming	Reye's Syndrome Guillain-Barre Syndrome Peripheral Neuritis

TABLE 1 continued

	Known	Probable	Possible
Tetanus Toxoid and Tetanus-Diphtheria Toxoids (T,DT, & Td) Adult	Hypersensitivity Local Reactions Fever Convulsions (Febrile)		Encephalitis, Aseptic Meningitis Other Necrologic Disorders -Peripheral Neuropathy -Cranial Nerve Palsy (Neuritis)
Polio Vaccine Inactivated (IPV)			Allergic reactions Guillain-Barre Syndrome Teratogenesis (Neurogenic Tumors)
Influenza	Local Reactions Fever, Malaise Guillain-Barre Syndrome Allergic Reactions		Peripheral Neuropathy -Neuritis

Source: Center for Disease Control.

TABLE 2

RATES OF COMPLICATION (Per 1000)* FOLLOWING VACCINES AND NATURAL DISEASES

Disease or Vaccine Complications	Natural Disease	Vaccine	Background Rate (Unknown Cause)	Ratio:Disease/Vaccine
Measles				
Fever >103°F	900-1000	60-350	50	2.6-16.7
Rash	900-1000	30-100	0-20	9-33.3
Otitis Media	25.2-90		(?)	
Pneumonia (and other resp)	38-73		(?)	
Febrile Convulsions	6.9	1.9	0.3	3.6
Encephalitis (and other necrologic disorders)	1-4	.001	.001-.003	1000-4000
SSPE*(l)	.006-.022	.0004-.001	+	6-55
Death	0.1-1.0	.0002		300-5000
Mumps				
Fever ≥103°f	100-200(?)	0-0.2	.001	500-1000(?)
Parotitis	500-660	?	?	
Orchitis	100-250(Males)	?	?	
Oophoritis	+		?	
Pancreatitis	+		?	
Meningoencephalitis (& other necrologic complications)	10-150	.001	.001-.003	10000-150000
Deafness	.005-.07	(1 case)	?	
Death	0.18			

*I_n the 30 day period following vaccination or onset of natural disease

(1) Occurs 1 month-20 years after measles or vaccine.

TABLE 2 Continued

Disease or Vaccine Complications

Rubella	Natural Disease	Vaccine	(Background Rate (Unknown Cause)	Ratio:Disease/Vaccine
Lymphadenopathy	500-1000	110-440	?	1-9
Rash	360-1000	10-120		3-1oo
Fever ≥100oF	600(est)	10-40	10-40	15-60
Arthralgia	250-500	30-300	40	1-17
Arthritis	10-300	1-1oo	2	0.1-300
Peripheral neuritis	+	.1	?	
Thrombocytopenic purpura	0.3(?)	+		
Encephalitis (& other necrologic disorders)	0.2	0.0005	1.0-3.0	400
Death	0.8	+(2 cases)		
Polio (live vaccine)				
Paralytic polio	1-1o	0.0002		5000-50000
Death	0.6-0.8	.00001		60000-80000
Smallpox				
Fever ≥101oF	1000	20-40(?)		25-50(?)
Toxic eruption	?	+		
Dissemination	1000	.03		33,333
Vaccinia necrosum	?	.001		
Encephalitis, encephalopathy	1.0	.002-.006		167-500
Death	10-300	.001		10000-300000

TABLE 2 Continued

Disease or Vaccine Complication	Natural Disease	Vaccine	Background Rate (Unknown Cause)	Ratio:Disease/Vaccine
Diphtheria				
(Pharyngeal) Fever ≥101o	500-800(?)			
Airway obstruction	100(?)			
Myocarditis	i-t			
Motor paralysis	20-750			
Anaphylaxis		+(very rare)		
Other allergic reactions		+(rare)		
Convulsions	+	0.014(DT)		
Death	18-100			
Tetanus				
Pneumonia	+++			
Peripheral or cranial neuropathy	++	+(5 cases)		
Myopathy	+			
Fever		70)		
Hives or rash		20)		
Swollen arm (severe)		10) jTd		
Abscess or infection		7)		
Death	500	+(rare)		

TABLE 2 Continued

Disease or Vaccine Complication	Natural Disease	Vaccine	Background Rate (Unknown Cause)	Ratio:Disease/Vaccine
Pertussis				
Pneumonia	+++			
Convulsions	-1+	0.03-0.45	0.9-2.0	-tl-
Encephalopathy	8-140	.009		890-15500
Retardation	+	.006		
Persistent screaming				
Hypersensitivity		+(very rare)		
Death	1-1o	+(very rare)		
Influenza A				
Fever ≥1O1o	>800	1-100		
Rash	+	.005		
Pneumonia	30-200			
Myocarditis	+			
Myopathy	+	+		
Guillain-Barre Syndrome	+	.01	.OO1	
Death	1.0	?		
Influenza B				
Fever ≥1O1o	>700	1-100		
Pneumonia	30-200			
Reye's Syndrome	.3-.6	–		
Death	+	?		

Source: Center for Disease Control

Center for Disease Control Notes to Table 1 and 2

Introduction

Reactions following the administration of vaccines have received increased attention in both the scientific and lay press in recent years. It is important that vaccine recipients be informed of the possible side effects from vaccines. Decisions regarding the use of vaccines must take into account several factors in order to balance the risks associated with the vaccines against the risks of remaining unvaccinated. If reasonably accurate information regarding the rates of complications following the vaccine and natural disease, and the risk of acquiring the natural disease are known, then it is relatively easy to "balance the risks." Therefore, we have attempted to compile a tabulation of the rates of complications occurring after vaccinations and the natural diseases that the vaccines protect against. We have not attempted to include the important factors of vaccine efficacy and the risks of acquiring the natural diseases.

Although toxoids (tetanus and diphtheria) are not technically vaccines, we have included them in this report.

Data Sources

The data in the attached tables have been derived primarily from reports published in the medical literature. These reports are of 3 general types:

1. Individual case reports of specific disorders noted following the receipt of a vaccine.

2. Field trials and other studies where vaccinees were actively followed to determine the rates of disorders.

3. Retrospective studies of specific disorders where a higher rate of vaccination was noted in persons with the disorder as compared to a control group.

In addition, we have utilized reports from vaccine manufacturers, practicing physicians, state and local health departments and other interested parties.

The background rates of disease have been obtained from several different sources and therefore the numbers vary considerably. Where possible, we have used the data collected from a control (or placebo) population. Therefore the age of the population and the case ascertainment were the same for the vaccinated and unvaccinated populations (for an example see Measles: rash and fever). In some cases, Particularly with rare disorders, we have had to use other sources such as community surveys or cases of the disorder reported to CDC that were not associated with known cases (e.g., encephalitis). Many of the background rates have been left blank. This does not mean that the disorders do not occur. We elected to leave blank those disorders where we did not have reliable data and the rates varied considerably depending upon the factors discussed in the next section.

Important Qualifications

The rates are not meant to be interpreted (or quoted) as absolute and firmly established numbers. We are merely trying to provide you with data to help in balancing the relative risks associated with vaccines and natural diseases. There are many variables that have been shown to affect the rates of vaccine reactions:

Vaccinees: age, sex, previous doses of vaccine, allergies, immune competence

Vaccine: culture media, type or strain of organisms, number of organisms, inactivation process, purification processes, adjuvants, stabilizers and preservatives

Administration: jet gun vs. needle and syringe, site of injection, tissue injected (ID, SC, IM or oral)

With regard to most reported reactions, a causal relationship between the vaccine and the disorder cannot be established with certainty. Most "reactions" also occur at some low but finite rate in an unvaccinated population and are usually of unknown cause. Limitations of the individual case investigation or of our scientific knowledge usually prohibit firm conclusions, often leaving us with a temporal relationship only. We must decide whether or not the temporal relationship suggests something other than a coincidental association. With live vaccines, most reactions occur when the vaccine virus or bacteria has had time to multiply within the body. This is usually 7-21 days after vaccination. With killed (inactivated) vaccines, the most common reactions usually occur early, within the first 24-72 hours.

Some disorders, such as encephalitis following measles vaccine, occur at a rate that is less than the known background rate in unvaccinated persons. However, a definite temporal clustering of cases occurs in the 7-15 days after vaccination. This timing of the reaction, plus the findings noted on post mortem examination in fatal cases and the occasional isolation of vaccine-like virus from the cerebrospinal fluid imply that a causal relationship exists with the vaccine.

Other rare disorders, such as peripheral neuritis following rubella vaccine and Guillain-Barre' Syndrome following influenza vaccine, were not detected until mass vaccination programs led to a clustering of cases in localized areas. Therefore, it is possible that other, as yet unknown, disorders, following vaccination might be detected under similar circumstances.

Some vaccines were developed and licensed many years ago. For some, we do not have field trial data which include control groups. Therefore, the rate of common reactions such as fever following DTP and smallpox vaccines are based on estimates, and not actual studies.

The early studies on diphtheria toxoid and pertussis vaccines were carried out using different preparation techniques and potency than are currently in use. Therefore, those studies are not applicable to what one would expect with today's vaccines.

For all of the reasons outlined on the previous pages, we urge you to be very cautious in the interpretation and use of the data in the accompanying tables. These data are the best currently available but are rough estimates and are therefore not intended for publication in the mass media. They are for your use in anticipating reactions to vaccines and answering questions in a general manner.

TABLE 3

TOTAL NET DOSES DISTRIBUTED

UNITED STATES, 1974-1978

BIOLOGICS	1974	1975	1976	1977	1978
Influenza Virus Vaccine, Bivalent[2]***	21,142,461	[illegible]	36,426,235	21,749,[illegible]	19,892,960
Influenza Virus Vaccine, Monovalent	**	**	48,992,625	5,199,[illegible]	[illegible]18,020
Diphtheria Toxoid with Tetanus Toxoid (pediatric)	1,107,220	1,060,365	1,111,653	904,966	823,326
Diphtheria and Tetanus Toxoids [illegible] Pertussis Vaccine	[illegible]7,491,646	17,333,487	19,021,934	16,862,740	17,992,360
Tetanus Toxoid with Diphtheria Toxoid [illegible]Adult)	6,875,790	8,763,624	9,843,770	9,650,244	9,191,122
Diphtheria Toxoid	**	**	3,716	3,590	960
Tetanus Toxoid	15,253,744	13,343,429	17,721,235	12,942,190	10,971,238
Pertussis Vaccine	106,626	47,766	91,133	21,110	100,610
Poliomyelitis Vaccine. Live. Oral. Trivalent	25.[illegible] Immoolln	24,804,475	19,474,835	23,211,560	**
Measles Virus Vaccine, Live, Attenuated[1]	7	7,378,229	7,478,646	10,675,623	8,931,344
Mumps Virus Vaccine [illegible]Live[1]	3	4,811,000	4,417,000	4,092,773	4,648,810
[illegible]bella Virus Vaccine, Live[1]	7	7,809,057	6,398,353	7,698,639	7,552,861
Smallpox Vaccine	6	6,232,300	3,802,743	4,493,239	4,648,810
Rabies Vaccine		**	181,516	**	**
Immune Serum Globulin, Human (reported in cc's)	6,676,509	6,684,871	8,144,494	4,905,267	4,005,759
Tetanus Immune Globulin, Human (reported in cc's)	1,121,428	1,075,563	1,548,325	1,320,590	1,339,681

**Not shown since fewer than three distributors reported
***Includes [illegible] lent [illegible] biva[illegible] vacci[illegible]

[1]All products containing this vaccine
[2]June-December 1975 includes polyvalent and bivalent vaccines

Source: Center for Disease Control Biologics Surveillance Report No. 76 (USDHEW/PHS/CDC:1978 .

TABLE 4

Estimates of Serious Illness Associated With Immunization
Against the Seven Major Childhood Infectious Diseases

Cases Per Year

Illness or Injury	Incidence Estimate	Estimated Annual Doses Administered on Average 1974-1978 (very rough estimate)*	Estimate of Annual Cases
Encephalitis following DTP	9-20 per million	13.5 million	122-270
Brain damage	Low: 1 in 300,000 doses (British Royal Commission Estimate) High: 6 per million (CDC) estimate of retardation)		(45-81)
Peripheral Mononeuropathy following DTP Vaccine	very rare ?	13.5 million	? probably too rare for even 1 case annually
Polio contracted from Polio Vaccine	1 in 4,000 doses	18 million	5 (most would be adult contacts)
Encephalitis following Measles Vaccination	0.92-1.16 cases per million doses (based on doses distributed)	9 million doses distributed in 1978	8-11 (some of these would probably result in permanent brain damage)
Encephalitis following Mumps Vaccine	Lowest Estimate: 1 per million		3-4
	Highest Estimte: 9 per million (possibly too low)	3-4 million	27-36 (Note: none are expected to leave permanent brain damage)
Death Due to Anaphylactic Shock (All Vaccines Commonly Given To Children)	1 in 10 million doses	50-60 million	5-6

Abased on net doses distributed (Table 3) minus one-quarter wastage.