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RISKS OF INFECTION
USING NON-STERILE EQUIPMENT OR CONTAMINATED VACCINE
IN THE EXPANDED PROGRAMME ON IMMUNIZATION

by

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Expanded Programme on Immunization

CONTENTS

1. INTRODUCTION

The Expanded Programme on Immunization (EPI) offers protection against six infectious diseases: diphtheria, pertussis, tetanus, polio, measles and tuberculosis. None of the vaccines is 100% effective in providing protection, nor are they entirely free from risk.

In industrialized countries, vaccines are most often administered using sterile equipment. The focus on risk from immunization, therefore, is centered on the qualities inherent in both the biological and non-biological constituents of the vaccines themselves, on the hazards resulting from not respecting contraindications to immunization and from improper injection technique (1, 2). The risks of adverse reactions associated with the vaccines and toxoids used in the EPI have been estimated by Halsey et al (3) and are summarized in Table 1. These estimates show that the risk of the natural disease is far higher than the risk of vaccine-induced complications, although this cannot be precisely quantified in every case.

In developing countries, shortages of equipment, poor equipment and handling techniques, inadequate training and suboptimal supervision may all lead to the use of non-sterile equipment. Contamination of vaccine after opening and before use may also lead to complications (4, 5, 6, 7, 8). This paper addresses the question of the magnitude of the health risks that might be expected to be associated with the use of non-sterile immunization equipment, particularly in developing countries.

2. TRANSMISSION OF INFECTIOUS DISEASES BY THE PROCESS OF IMMUNIZATION: GENERAL CONSIDERATIONS

There are several ways that the process of immunization may be implicated in transmission of infection. Cross infection from child to child may occur when an infectious child is brought close to others at a clinic. This facilitates person-to-person transmission by droplet infection, as with measles or pertussis, or transmission through the use of shared unsterilized immunization equipment. Similarly, infectious staff may be the agents to transfer infection.

2.1 Local factors

Diseases vary in their geographic distribution, and the level of risk of transmission during immunization programmes will relate to the specific epidemiology of the disease in question. It would not be meaningful to estimate a single risk level for a disease and apply it globally. Similarly, a given endemic disease may become epidemic from time to time. Risk of transmission will rise steeply during such periods.

2.2 Dilution factor

If blood left in a syringe is the means of transmitting a particular disease, the first injection given subsequently will flush out the majority of the infected blood and the following injection will contain less pathogen. Those diseases known to be transmitted by an extremely low dose, e.g. hepatitis B, must be considered likely to infect many more individuals, notwithstanding any dilutional factor.

Table 1.

Adverse reactions associated with vaccines and toxoids administered in the Expanded Programme on Immunization

Antigen	Adverse effect	Estimated rate associated with vaccination	Rate associated with natural disease	Relative risk: natural disease vaccine
DTP	Fever 39°C	1/25-1/16	+[a,b]	Positive[c]
	Local swelling	1/2.5	-	
	Sterile abcess	1/67,000-1/1,000	-	
	Schock	1/17,500-1/2,000	+ +[b]	Positive[c]
	Convulsions	1/25,000-1/1,500	1/100-1/30	20-800
	"Persistent screaming"	1/14,000-1/50	?	?
	Encephalopathy	1/750,000-1/30,000	1/125-1/50	800-2,000
	Neuropathy	rare ?	+	?
Attenuated poliovirus	Paralytic poliomyelitis		1/1,000-1/100	500-30,000
	based on doses of vaccines distributed	1/3,000,000		
	based on susceptible children vaccinated	1/500,000		
	based on susceptibles adults exposed to vaccinated children	1/100,000		
	convulsions	1/8,600	+ +	Positive[c]
Measles	Fever 39,4°C	1/16-1/6	1/2-1	3-16
	Rash	1/100-1/5	1	5-15
	Febrile convulsions	1/2,500-1/100	1/200-1/100	1.0-25
	Encephalitis/ Encephalopathy (and other neurologique disorders)	1/1,000,000-1/17,600	1/1,000	17.6-1,000
	Subacute sclerosing panecephalitis (SSPE)	1/1,000,000[d]	1/200,000-1/50,000	5-20
	Thrombocytopenia	Common	Common	?
	Thrombocytopenic purpura	Very rare	+	Positive[c]
BCG	Subcutaneous abcess	+	-	-
	Suppurative lymphadenitis	1/1,000-1/250	+ + +	Positive[c]
	Osteomyelitis and septic arthritis	1/1,000-1/50,000	+ +	Positive[c]

[a] From + to + + + = relative frequency.
[b] Variable rate depending upon complications.
[c] The rate following natural disease is higher than that following vaccination, but the ratio is unknown.
[d] No cases of SSPE have been proven to be caused by measles vaccine.

From Halsey, N. et al. (3).

2.3 Vial contamination

Not only may a syringe and needle become contaminated, but by the same process a multidose vial, into which the needle is dipped to draw up the next dose, may also become contaminated. One of two events may then take place:

(a) the additives in the vaccine, e.g. preservatives or antibiotics, may progressively reduce the contaminating organism,(6); or

(b) the vaccine medium will be a suitable place for the contaminating organism to grow and multiply (6, 7, 8).

In the case of (b), even if a sterile syringe and needle are used for subsequent injections, the vial has been contaminated and will be a potential source of infection for the remainder of the doses. A reconstituted vial of BCG vaccine is a potential problem as it is an excellent medium and contains no preservatives.

2.4 Transmission from adults

Children usually attend special immunization or MCH clinics for immunization, but there are instances where adult polyclinics will operate from the same premises and may even run concurrently. In these instances, injection equipment may be shared. The opportunity then arises for adult-to-child cross infection in addition to child-to-child infection.

2.5 Period of viability of microorganisms

The period of time that the infectious agents of a given disease may remain in the blood is highly variable. Hepatitis B in neonates is very likely to produce a carrier state with high levels of HBeAg being excreted for years (9). Some organisms are extremely fragile outside the human body, others more robust. It is known, for example, that the Hepatitis B virus can successfully withstand drying (10). It would therefore be likely to remain pathogenic if left in dried blood on the inside of a contaminated syringe. It is doubtful, on the other hand, if the malaria parasite would survive many seconds outside the human body.

2.6 Incrimination of Syringes

Serious disease has been shown to be transmitted by contaminated syringes. Although it did not involve children receiving immunization, the outbreak of Ebola Fever in 1976 clearly demonstrates the potential for the spread of disease (11). In this outbreak 280 deaths occurred as a direct result of using a syringe which was infectious for Ebola virus for administration of various medicines. Outbreaks of hepatitis B have been well documented in drug abusers where transmission was by contaminated syringes.

2.7 Age of recipients

Newborn infants carry some level of passive immunity to many of the organisms they meet during their first six months of life. As the child grows older, he will lose maternal antibodies to some diseases such as measles, but over the same period will acquire antigenic stimulation through natural exposure to some diseases and through immunization to others. A child's risk of transmitting infection to others directly or through contaminating equipment will, therefore, vary somewhat with age.

2.8 Polio droppers

Droppers used to administer oral polio vaccine to infants are not designed to protect against oral disease transmission. During proper use, the vaccine dropper should not touch any part of the oral mucosae. However, in the process of giving the vaccine in a busy clinic, droppers may come into contact with the oral mucosa and saliva, and may be implicated in the spread of diseases which are transmitted by droplet or saliva. Pathogens such as hepatitis B and the AIDS virus have been demonstrated in saliva, but transmission as a result of an immunization procedure has not been documented.

3. DISEASES OF GLOBAL CONCERN

3.1 Viral Hepatitis

Three main types of viral hepatitis have now been recognized: hepatitis A (HAV), hepatitis B (HBV) and hepatitis non A non B (HNANB). Another type of infection called delta agent is also known to "piggy back" on HBV infection. All types of viral hepatitis may be transmitted by blood, with HBV notable for the minute dose needed to effect transmission of the disease.

3.1.1 Hepatitis A

In the tropics, most infections are probably acquired in childhood and the majority are subclinical. By adulthood, 80% or more of individuals in some countries will have evidence of past infection as denoted by the presence of anti-HAV antibody. In temperate climates, it is more a disease of adulthood and less than a quarter of the population may develop anti-HAV (12). The risk of a child being infectious in temperate climates is likely to be low.

Infectivity is maximal during the latter half of the incubation period, which varies from 15 to 50 days but on average is 28-30 days. There is no carrier state after infection. The threat to an immunization programme from HAV is extremely slight.

3.1.2 Hepatitis B

This disease is a major public health problem in many parts of the world. The prevalence of infection varies from country to country, depending on behavioural, environmental, and host factors. In general, it is lowest in countries or areas with high standards of living and highest in countries or areas where the socioeconomic level is lower.

Enormous differences exist in the frequency of persistent infection with hepatitis B virus. In most industrialized countries the carrier rate is under 1%, while in some areas of Africa and South-East Asia, it is higher than 15% (12). Intrapartum transmission from carrier mothers to their babies appears to be the most important factor in the high prevalence of infection in some areas, particularly China and South-East Asia.

While for adults the risk of becoming a carrier after infection is between 5% and 15%, for infants it may exceed 50%. It has been estimated that there are at least 200 million persistent carriers of hepatitis B virus in the world (13). The risk of primary hepatocellular carcinoma is increased in these individuals.

Especially where there is high endemnicity of the disease, notably in tropical climates, HBV represents a threat to immunization programmes if non-sterile apparatus is used. But the additional risk above that posed by the natural disease may be marginal (see Section 7).

3.1.3 Hepatitis non A non B

As more becomes known about this disease or group of diseases, it becomes clear that in some areas of the world it represents up to 25% of all cases of viral hepatitis. Insufficient data are available to estimate its prevalence in the childhood population. It does appear there is a carrier state (14).

3.2 Acquired Immune Deficiency Syndrome (AIDS)

This is a recently recognized viral infection with a high mortality rate. That children can acquire infection has been well documented (15), and AIDS virus transmission occurred in 12 out of 72 children in one series through receiving infected blood or blood products (16). The total number of cases of children infected with the AIDS virus is still very small and the risk of transmission is presently slight in most countries. However, the situation in some parts of Africa is unclear but may be significantly different. Also the number of adult cases is still rising exponentially and it is to be anticipated that increasing numbers of children will be born having been infected with the AIDS virus around the time of birth. Such children may be indistinguishable from non-infected children at immunization.

Inadequate data are available to describe the situation in all parts of the world. Reports suggest that AIDS may have been present in Africa before the emergence of the epidemic, first noted in the United States in 1980 (17, 18). Indications are that it is much more a disease of both sexes in Africa and there may be more infant infections there than elsewhere.

The EPI Global Advisory Group (GAG) noted that to date (November 1985) no demonstrated transmission of the AIDS virus had occured as a result of immunization (19). It also made recommendations to encourage member nations to achieve the highest possible levels of EPI coverage and to promote the concept of one sterile syringe and one sterile needle for every injection.

Because the situation and available data on AIDS are changing so fast, it is unrealistic in a paper such as this to do more than draw attention to important points and note trends. Any definitive statement is in danger of being out of date before it is printed.

3.3 Staphylococcus

The staphylococcus produces a number of diseases of variable severity. These range from skin abscesses to septicaemia and death. 30-40% of the general population carry coagulase-positive staphylococci in their anterior nares. Thus, the staphylococcus represents a continual and widespread potential threat to immunization programmes. An outbreak of pyogenic staphylococcal abcesses was reported following DPT (20) with an attack rate of 86%. Such events may be commoner than might be supposed from the literature, but go unreported. (Sterile abcesses have been recognized as a complication of DPT and measles immunization and are considered to represent an Arthus-type of hypersensitivity reaction (4, 20)).

3.4 Streptococcal disease

A variety of diseases, including rheumatic fever, may be produced by introducing Group A (beta haemolytic) streptococcus into the body. The organism is commonly found on the skin and even more frequently in the nasopharynx where carriers may harbour the organism for long periods of time. As with the staphylococcus, isolated clusters have been reported of abcesses following immunization (6, 7, 8). It is likely that this is a commoner problem than is reported, especially in areas where impetigo in children is frequent.

Streptococcal and staphylococcal abcesses do sometimes occur in clusters, even in clinics which attempt the best possible levels of sterility. It is reasonable, therefore, to assume that such abcesses occur at least as frequently, and probably more so, in less well equipped clinics in developing countries, as they do elsewhere. One study in the USA (9) estimated 0.7 per cent of those immunized developed an abcess or infection.

3.5 Malaria

The four human malarias have a wide distribution over warmer parts of the world. Falciparum malaria is particularly important in this context with a mortality in untreated children in excess of 10% in some circumstances, depending on the age of the child and the frequency of infection. The other malarias, although not as serious for adults, may nonetheless constitute a serious threat to young children. Parasites are known to have been transmitted in blood transfusion and therefore the possibility of infection by syringe must be taken as real. Because as many as 500 million people in the world suffer from the disease, the numbers involved makes malaria an important disease to consider with respect to transmission in EPI programmes. However, children in areas of high risk are much more likely to be bitten by infectious mosquitos several times a month; even though the risk of malaria being transmitted by syringe appears high in these circumstances, it nonetheless represents only a marginal additional risk over that posed by the environment and by natural disease. Additionally, maternal antibodies afford some protection in the early months of life.

4. DISEASES OF REGIONAL CONCERN

There are a number of other infections which theoretically could be involved in transmission via infected needles, syringes and vials. These include both haemorrhagic and non-haemorrhagic arbo viruses, bacterial diseases such as plague and relpasing fevers, rickettsias, eg typhus fevers and protozoal infections such as trypanosomiasis.

5. THE RISK OF CONTRACTING A MAJOR DISEASE THROUGH IMMUNIZATION

EPI estimated that the vaccine requirements for developing countries during 1985 would be 254 million doses of injectable vaccine and 100 million doses of oral polio vaccine.

In a hypothetical country with 1 600 000 newborns a year who were fully immunized (variable 'a'), the estimated consumption would have been 8 million injectable doses of vaccine. In one such country, 20 cases of arthropod-borne haemorrhagic fever were reported in those under 1 year of age population in one year (variable 'b'). A gross assumption would therefore be that one child in every 80 000 who presents for immunization here would have an attack of arthropod-borne haemorrhagic fever during the year. Patients are usually only infectious (i.e. with a viraemia) for about one week. The risk each of the 20 children represents, therefore, must be further divided by a factor of 50 (variable 'c').To make a generalization, then, the risk of a syringe becoming contaminated (which is far greater than the risk of a child becoming infected) can be stated as

$$\frac{B}{A} \times \frac{1}{C}$$

In the above example relating to arthropod-borne haemorrhagic fever, it works out as one event per 4 million injections.

A second example can be made of malaria in the same country where:

a = 1 600 000 children per year
b = 1 200 cases per year in the population under one year
c = 1 (because parasitaemia might extend throughout the year)

So the risk is

$$\frac{1,200}{1,600,000}$$

or one in 1 333 events.

As has been pointed in paragraph 3.4, the child in endemic areas is continually being exposed to natural malaria and an additional risk of one event in 1 333 is negligible. This is further reduced when it is taken into account that maternal antibodies are likely to give protection for the first few months of life.

A third example of hepatitis B in a country of high endemnicity is as follows:

a = 6,000 000 children a year
b = 1 500 cases per year in the population under one year
c = 1 (because once infectious, children stay so for years)

So the risk is:

$$\frac{1,500}{6,000,000}$$

or 1 in 4,000 events.

In endemic areas it is common for around 20% of children under one year of age to have positive markers (HBsAg) for past HBV infections (21). In such areas, an added risk of 0.025% from immunization is small (800 times less than the risk of natural infection), but certainly cannot be ignored.

The example of HBV in a highly endemic area represents an extreme. It is doubtful if any other of the diseases of primary concern approaches this level, although it is not possible to make a more precise statement as it is only for HBV for which prevalence data for the under one age group has been published (21). It may be possible to make an estimate for infection with the AIDS virus in the future when sufficient data has been assembled.

The above model is highly simplified and gives only the broadest estimate of the situation. In reality conditions are not uniform, many other factors altering the risk of a syringe becoming infected. A high infant mortality rate will reduce the risk as there are less children available to be infected by the end of the first year of life, as will a high drop out rate. An uneven effect will be produced by the presence of maternal antibodies in children's blood for only the early immunizations. Subsequently, the absence of these antibodies will increase the risk of infection. The above model assumes that reusable syringes are used for immunization. Clearly if all equipment is disposable and used only once, the model is irrelevant. In reality, programmes may use a mixture of equipment.

The risk of a syringe becoming infected is highest in those areas where the EPI diseases themselves have the highest rates. Case-fatality rates from pertussis are in the order of 0.5% to 1.2% (22,23), while those from measles range from 0.02% to 15% (24,25). In these circumstances, the added risk from HBV, malaria and other diseases potentially transmissible by syringe and needle is negligible, except perhaps where a widespread epidemic such as one of the arboviruses affecting children is in progress. Even under such circumstances, it should be realized that immunization may not be the only source of "injection infection" for children, and that many of these other injections, e.g. with penicillin, may carry a risk of contamination at least as great as those given for immunization. If these other injections are frequent (as they often are), withholding immunization may have only a small benefit in reducing the risk of injection-associated transmission.

6. REDUCING THE RISKS OF TRANSMITTING INFECTION THROUGH IMMUNIZATION

Transmissions of infection through immunization can be eliminated by strict attention to sterile technique. Training, supervision and updating of staff in proper technique is clearly essential. Reusable syringes and needles, one per individual, are used in many countries and is EPI policy, but in many developing countries this policy is not adhered to.

Other factors which will reduce the risk of transmitting infection include: (i) discarding all opened vials at the end of the day; and (ii) not leaving a common needle for withdrawing vaccine in the stopper of a multidose vial (26). Multidose vials are of questionable advantage if they become a significant source of infection.

The risk for different multidose vaccines relates to the vehicle and preservative additives used in various vaccines, to the temperature at which the opened vaccine is kept and to the length of time an open vial is used.

7. CONSIDERATIONS WITH RESPECT TO STERILIZATION PROCEDURES AND PRESERVATIVES

Despite the fact that needles and syringes may have been subject to a sterilization process before use, a number of factors operate which may reduce its effectiveness. Micro-organisms vary widely in their response to physical and chemical challenge. Favero (27) states that few organisms approach the resistance of bacterial endospores such as those of the tetanus bacillus. It is for this reason that bacterial spores are used as biological indicators for sterilization cycles. In a broad descending order of relative resistance, considerably below that of bacterial spores, are tubercle bacilli, fungal spores, small or non-lipid viruses, vegetative fungi, medium-sized or lipid viruses, and vegetative bacterial cells. The use of substances which can reduce the risk of contamination of a vial must be such that it does not reduce the efficacy of the vaccine. Streptococci have been cultured up to two weeks after being innoculated into a DTP vial (6).

Under usual circumstances, the higher the level of microbial contamination the longer must be the exposure to the inactivating agent. So the lack of good physical cleaning of an item prior to subjecting it to sterilization may cause the process to fall short of its intended goal.

7.1 Minimum standards for sterilization

Direct exposure to saturated steam at 121°C for 15 minutes is a safe sterilization procedure. This time and temperature conform closely to the thermal death time of the most resistant bacterial spores.

Boiling water at ambient pressure (760 mmHG) is the sterilization method which is most commonly used in immunization programmes in developing countries. This procedure does not necessarily result in destruction of highly resistant bacterial spores, even after prolonged boiling although it does inactivate most bacteria, viruses and all protozoa. For practical purposes, it can be considered as an effective means of sterilization provided exposure time is not shorter than 20 minutes and the following precautions are taken:

- syringes and needles are dismantled and thoroughly clean before boiling. The prime importance of thorough mechanical cleaning and rinsing with tap water as soon as use is completed cannot be over-emphasized. This requirement should be stressed during any training and supervision of sterilization activities.
- trapped air is avoided.
- fresh syringes and needles are not added during boiling.
- continuous boiling and complete immersion are maintained for the entire 20 minutes.

8. RESEARCH NEEDED

The question of "what is the risk?" still remains. The answer is always likely to be that it depends on the disease and the country in question, and these risks will need to be continually re-evaluated.

More emphasis should be placed on determining what complications do occur following immunization procedures. There are five occasions scheduled for EPI immunization during the first year of life, which means there are at least four occasions when the infant should return to the clinic. On these occasions, staff can ask what complications, if any, occurred after the previous injection. Clusters of illness would be detectable in this way. Outbreaks of pyogenic abcess would be particularly important to note and follow up.

Little is known about various practical aspects of injecting. Who gives injections? Who receives how many injections, for what purpose, and with what risk of complications? Answers to such questions are useful in order to make rational decisions, such as who should have priority in receiving new equipment, in deciding upon numbers of syringes and needles to be procured, distributed and issued to certain sections of the health services and in deciding who needs training in sterilization techniques. Such information is also needed to assist reviewing policies regarding the length of time an opened vial may be used.

However, retrospective analyses are often difficult to interpret and it is necessary to perform ad hoc prospective surveys looking at infants who have recently been immunized. This might, for instance, require a team to do follow-up home visits, looking particularly at the injection site for evidence of abcesses.

New technology is likely to present new methods of sterilization. Controlled trials of such new methods need to be undertaken to evaluate ways of sterilizing equipment, continuing the work currently being done with steam sterilization in Kenya, Indonesia and Lesotho (28).

One subject about which more information is needed is the utility of swabbing the skin prior to providing an injection. It makes intuitive sense that clean skin is preferable to dirty skin. In industrialized countries, swabbing with some mild disinfectant is generally a routine preparation prior to injection. But the efficacy of this procedure in reducing the risks of infection is not clear. In developing countries, the EPI policy states that cleaning the skin before an injection is good, especially if the skin is dirty, but is not essential (29).

9 . RECOMMENDATIONS

The following actions are recommended:

1. Ensure that every programme has adequate supplies of appropriate syringes, needles and sterilising equipment.

2. Intensify training, re-training and supervision for EPI field staff to ensure that sterilization procedures are followed. Encourage similar training and supervision for other health staff who provide injections.

3. Include in the training of field staff routine questioning of parents as to whether complications occurred following previous immunizations.

4. Evaluate and introduce as appropriate new technology for sterilization of equipment.

5. Provide the active surveillance for immunization-related abcesses as part of EPI evaluations and support operational research to define the magnitude of the problem. Pyogenic abcesses appear at present to provide the most practical marker of sterilization problems. Although they may be difficult to distinguish clinically from sterile abcesses, this should generally be possible on epidemiological grounds as pyogenic abcesses are more likely to be highly clustered by time and origin of vaccine.

10. SUMMARY

The possibility of transmitting disease by EPI has been discussed. Is it a sufficiently serious proposition that the programme needs to be altered significantly? The risk appears to be very slight for transmission of any of the major diseases identified. And the risk is negligible if the recommendations already in place to ensure sterility are observed.

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