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CONTRAINDICATIONS TO VACCINATION IN  
ENDEMIC AREAS

by

Dr. J. D. Millar \*  
WHO Temporary Adviser

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\* Chief, Smallpox Eradication Programme, National  
Communicable Disease Center, Atlanta, Georgia, USA

additional de facto contraindications: (6) life-threatening disease of any sort, (7) malnutrition, (8) concomitant acute febrile disease. The usual practice is to withhold vaccination until resolution of the acute problem. The National Communicable Disease Center survey suggests that careful observance of these contraindications in the United States would halve the incidence of serious complications.

These accepted contraindications in non-endemic areas where the risk of infection is dependent on importation may be viewed as the contraindications "ceiling". The present problem is to define acceptable contraindications, if any, for areas where risk of smallpox infection is higher.

#### THEORETICAL CONSIDERATIONS

Adequate data do not exist permitting a confident analysis of the relative risks of smallpox infection and smallpox vaccination in the endemic areas. Endemic countries generally lack data sufficient to define smallpox incidence with precision; none have data on complications sufficient to measure even grossly this risk. One must therefore compare the apparent risk of infection in endemic areas with the risk of complications observed in non-endemic areas; obviously the degree of error in such a conjunction may be vast.

However, one boldly attempts a specific example. Nigeria has a relatively high incidence of smallpox (8.3 cases per 100,000 population in 1966).<sup>10</sup> In excess of six million vaccinations have been done in Nigeria in the past decade,<sup>11</sup> so probably no more than one quarter (including previous cases) of the population are presently immune to the disease. With cases occurring among the susceptibles only, the attack rate therefore approximates 100 cases per million susceptibles per year. Present case fatality ratios in Nigeria approximate 25 per cent; thus the probability of dying from smallpox in a given year in Nigeria is approximately 25 in a million for the unvaccinated individual.

The United States figures indicate an expected mortality of about one death per million primary vaccinations. If one extrapolates the United States data to the Nigerian situation, the probability of an unvaccinated person's dying from smallpox in a given year is twenty-five times the probability of dying from a primary vaccination. If any conclusion is warranted from so gross a conjecture, it is that any contraindications to vaccination in endemic areas are difficult to justify.

The major drawback to this reasoning is that persons with one of the conditions enumerated bear higher risks of a complication than the overall rate suggests. While risks of death from smallpox vaccination might be one per million primary vaccinations for the general population, they are undoubtedly substantially higher for such persons. An attempt to derive comparative risks for eczema will be presented.

#### GENERAL CONSIDERATIONS

The delineation of contraindications to vaccination in endemic areas must be done in the light of two basic considerations,

1. The world is embarked on a smallpox eradication campaign, the success of which would permanently remove the need for vaccination and,
2. The establishment of any contraindications presupposes a sufficient clinical resource to permit screening for the contraindicating condition.

One hears the view expressed that expeditious prosecution of smallpox eradication is of such importance as to militate against the establishment of any contraindications in endemic areas. While this position may be technically defensible, it abrogates the moral responsibility inherent in performing a medical procedure on a mass basis. One should not simply resolve the issue of contraindications by saying that the "end justifies any means." The only morally acceptable solution is to define as clearly as possible those conditions carrying

a high risk of post vaccinal mortality and make some serious effort to avoid vaccinating such persons.

It is also frequently stated that in most endemic countries, screening for contraindicating conditions is impossible. This is not the case. Among the sixteen countries now executing a regional smallpox eradication programme in West Africa, all have some mechanism currently functioning for excluding certain persons from vaccination. In general terms, persons excluded include those so acutely ill as to appear moribund, those with grossly extensive skin disease, and in some areas, pregnancy. The screen, whether indicated or not, and of whatever effectiveness, is in fact functioning.

#### FORMULATING SPECIFIC CONTRAINDICATIONS

Each of the accepted contraindications to vaccination in non-endemic areas is examined below as to applicability to endemic areas in the light of (a) the possibility of screening for the condition, (b) available information on the risks, and (c) the epidemiologic impact of excluding affected persons from vaccination.

##### 1. Immunologic Disorders

Diagnosis of these conditions requires elaborate clinical and laboratory procedures; in virtually all instances diagnosis is impossible under field conditions. This contraindication to vaccination cannot be supported as feasible in endemic areas.

##### 2. Neoplastic Disorders of the Reticuloendothelial System

Except in situations where patients have been hospitalized with this diagnosis, persons will not be identifiable. There is one possible African exception; children with Burkitt's tumor may be identified. The risks of vaccinating these children are totally unknown. However, the limited numbers of such cases would make it entirely possible to exclude such children from vaccination with no numerical effect on the mass vaccination campaign.

### 3. Immunosuppressant Therapy

Due to the level of medical development in most smallpox endemic countries, it is highly unlikely that persons receiving these treatments will be found outside the hospital environment. The consideration of such therapy as a contraindication is probably irrelevant in all endemic areas.

### 4. Eczema

Vaccinia in the eczematous child may be extremely severe and frequently fatal. Kempe<sup>12</sup> estimated the case fatality ratio for eczema vaccinatum at 30 to 40 per cent in the absence of treatment with vaccinia immune globulin. The National Communicable Disease Center survey identified 111 United States cases in 1963 with two deaths. (All patients were treated with vaccinia immune globulin).

Very little is known of the incidence of eczema vaccinatum among eczematous patients exposed to vaccinia virus. The incidence of eczema itself is poorly documented. Worth<sup>13</sup> estimates that three to seven per cent of United States and British children developed conditions described as "eczema".<sup>13</sup> Less is known about the incidence of eczema among children in non-endemic areas. The condition is believed to be much less common in tropical Africa than in the United States or Europe. Morley<sup>14</sup> describes it as "extraordinarily uncommon" in West Africa. Trowell and Jelliffe<sup>15</sup> regard it as a rare disease among the lower socio-economic groups in the tropics.

In assessing the theoretical risks of vaccinating eczematous children, one can make only a gross estimate based on the data available in the United States. In 1963, Neff found seventy-nine cases of eczema vaccinatum in children under the age of five years. The population of the United States under five years of age in 1963 was 20,750,000. If three to seven per cent of these had eczema (or a history of eczema), and one assumes that all were susceptible and all

were exposed, the minimum incidence of eczema vaccinatum is 50 - 130 cases per million exposed eczematoid children. Since it is certain that all eczematoid children were not exposed, and also certain that all eczematoid children exposed were not susceptible, the true incidence is undoubtedly much higher than 50-130 per million.

In situations where vaccinia immune globulin is not available, one would expect 30 per cent of eczema vaccinatum patients to die, thus the probabilities of an exposed eczematous child's dying of eczema vaccinatum is at least 15-40 per million. It is apparent that the risk of fatality accompanying the exposure of such children to vaccinia is dramatically greater than the risk to the population at large. The decision to deliberately vaccinate an eczematoid child cannot be undertaken lightly even where smallpox endemicity is moderate.

Of course an eczematoid child need not be vaccinated to contract eczema vaccinatum; the virus can be acquired from a vaccinated sibling or playmate.

There is no easy solution to the problem posed by the eczematoid child in a mass vaccination programme where neither isolation nor the administration of protective vaccinia immune globulin are feasible. His risk of dying following vaccination is at least 15-40 times greater than the general risk of death from vaccination. If left unvaccinated, the child runs a distinct risk of infection via contact with other vaccinated children. However, on the basis of information at hand, deliberate vaccination of eczematous children cannot be justified. If the evidence suggesting a low incidence of eczema in tropical areas is valid, exclusion of individuals identified as eczematous will have no numerical or epidemiological consequence in mass vaccination efforts.

5. Pregnancy

The existence of a contraindication to vaccinated on grounds of pregnancy is based almost entirely on theoretical rather than practical considerations. Fetal vaccinia is extremely rare; only seventeen instances are recorded in the world literature. Results of studies dealing with vaccination and abortion, stillbirth and prematurity in all but two instances suggest no effect of vaccination. Two<sup>16,17</sup> indicate an increase in abortion rates when vaccination is done during the first trimester of pregnancy. These studies, however, are marred by lack of a control group or by use of non-comparable controls. No studies implicate vaccinia as a teratogen. In contrast to the very meager evidence suggesting danger to vaccination in pregnancy, there is overwhelming evidence that smallpox in the pregnant woman is devastating both for mother and fetus. In the data reported by Rao<sup>18</sup> (see table), the case fatality among unvaccinated pregnant women is fully three times that in non-pregnant women and in males. The stillbirth rate for pregnant women with smallpox was 43.9 per cent for births classed as premature and 10.7 per cent for full-term births ("normal" rates in this area for pregnant women without smallpox are not stated). The conclusion is obvious; there is no justification for considering pregnancy a contraindication in any endemic area. Pregnancy, if anything, should constitute a positive indication for vaccination in endemic areas.

SMALLPOX IN THE PREGNANT FEMALE AS COMPARED WITH NON-PREGNANT FEMALES AND ADULT MALES IN THE SAME AGE GROUP (15-45 YEARS), SEEN OVER A TWELVE-MONTH PERIOD IN MADRAS, INDIA \*

	<u>Pregnant Women (94)</u>	<u>Non-pregnant Women (348)</u>	<u>Adult males (502)</u>
Overall Case			
Fatality Rate	7.6%	8.3%	6.1%
a. Vaccinated	0.7%	4.2%	3.0%
b. Unvaccinated	5.0%	25.7%	24.0%

\*After Rao, A.R., et al, J. Indian Med. Assoc. 40 : 353, 1963.

#### 6. Life-threatening Disease of any Sort

Since persons moribund or severely ill are rarely vaccinated in non-endemic countries, there exists no data to measure the risk of vaccinating such persons. It is logical to assume that the inoculation of a life virus vaccine into a desperately ill person is likely to increase the probabilities of demise. There is another very important reason for avoiding vaccination of such persons. If death should occur shortly after vaccination, an adverse public reaction to vaccination may be the result jeopardizing further vaccination activities.

#### 7. Malnutrition

It is generally felt in Africa that vaccination should be withheld from children with frank Kwashiorkor or Marasmus because of a presumed general decreased ability of these children to control infections. Some limited evidence has been presented on this point by Brown and Katz,<sup>19</sup> who, observing primary smallpox vaccination in 57 malnourished children, did not observe any apparent adverse effects of the procedure. In view of the relatively large numbers of children malnourished to varying degrees in tropical areas, exclusion of children from vaccination on the basis of nutritional deficiencies would exclude significant numbers of persons in groups of great importance in smallpox transmission. Furthermore, the clinical diagnosis of nutritional deficiencies except in far advanced cases is a difficult one. As a general rule, nutritional problems should not represent contraindications to vaccination unless sufficiently severe to be immediately life-threatening.

#### 8. Concomitant Acute Febrile Disease

In industrially developed countries, it is routine to postpone vaccination until resolution of any acute febrile disease. This practice is, for the most part, totally impractical in the prosecution of mass campaigns. There is little evidence to suggest that the common acute communicable diseases increase the risk of complications of vaccination.



The numbers to be excluded, were, such a contraindication in effect, would in all probability be high. For all of these reasons, there appears no justification for a contraindication based on febrile illness unless that illness is immediately life-threatening.

#### SPECIAL CONSIDERATIONS FOR TROPICAL AREAS

As most smallpox endemic areas are tropical, certain disease processes of importance in the tropics should be considered.

##### 1. Scabies and Pyoderma

Both are common in the tropics. In general, these diseases tend to involve relatively small skin areas. Experience during jet vaccination studies in Tonga, and in the Federal Territory of Amapa, Brazil, has shown that secondary infection of this type of lesion with vaccinia virus occurs rarely if at all. In both areas, many children with scabies and pyoderma were vaccinated without complications.

##### 2. Leprosy

There is evidence to indicate that, both smallpox and vaccination are more severe in persons with leprosy.<sup>20,21</sup>

Primary vaccination may provoke the erythema nodosum leprosum (ENL) reaction or neuritis in the leprosy patient with either the lepromatous or tuberculoid form of the disease; it is more common in those with the lepromatous form. In revaccinees, the likelihood of an ENL reaction is small, unless a patient is subject to such reactions. Pettit and Waters,<sup>22</sup> reviewing ENL, point out that the precipitation of reactional phenomena may favourably influence the evolution of lepromatous leprosy and cite instances where smallpox vaccination has been deliberately applied to lepromatous patients to induce such reactions. Available evidence therefore does not support leprosy as a contraindication to vaccination.

SUMMARY AND CONCLUSION

There are few conditions for which smallpox vaccination is contra-indicated in endemic areas. Among those generally listed, only two appear justified on the basis of increased risk and feasibility of detection : frank eczema and life-threatening concomitant disease. These are conditions which can be identified readily and which carry the clearcut risk of disastrous results for the patient and/or the eradication campaign; the limited numbers of persons refusing vaccination for these conditions would have no epidemiologic consequence in the prosecution of an eradication effort. In contrast to this, pregnancy should never be considered a contraindication to vaccination in endemic areas. The occurrence of complications following vaccination in pregnant women are so rare as to be considered medical exotics while smallpox in the pregnant woman is awesome in its destruction of both mother and child. Reorienting present concepts of pregnancy and vaccination deserves a high health education priority. Present practices of screening in West Africa indicate that sufficient resources exist in endemic areas to screen for eczema and life-threatening disease.

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