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ORIGINAL ARTICLE

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The Problem of Rabies Vaccination in  
Children; an Analysis of Children Bitten by  
Rabid and Rabid-Suspected-Animals

by

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**Abstract**

*The analysis of 234 Children, under 14 years of age, with the diagnosis of an animal bite was carried out in an attempt to find out problems of rabies vaccination in the children.*

*One of the most important factors in eliminating or at least greatly reducing rabies, is the public dissemination of information concerning not only the danger of uninjected animals, but how rabies can be prevented or terminated if treated immediately.*

*Two ml of NTV was given for 14 consecutive days regardless of the age of the victims, the site and the severity of the wounds, and the time span between the bite and the start of vaccination. ARS was never used regardless of the site and the severity of the wounds.*

*It is clearly seen from this analysis that the regime used in this report is safe and effective enough to prevent the victims from contracting rabies as long as the vaccination can be started within 10 days after being bitten.*

*ARS must be given to the victims with head or back bites when the lapse of time between the bite and the start of vaccination is more than 10 days and can justifiably be instituted in arm and leg bite victims when the time span between the bite and the start of vaccination is more than 21 days.*

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Received 20th. August 1979.

## Introduction

Rabies, caused by the rabies virus, is one of the oldest recorded diseases since Democritus in 500 B.C. and Aristotle in 322 B.C. described it clearly. Apparently there have been no changes since then.

The rabies virus belongs to the Rhabdovirus group, characterized by its neurotrophic effects, and is transmitted to man via the bite of infected dogs, cats, bats and carnivorous wild animals, such as foxes, wolves and skunks.

In Indonesia this disease is endemic and is transmitted to man mostly via the bite of infected dogs, and sometimes via cats and monkeys, since they are very popular domestic animals in this country. Because there is a lack of facilities and inappropriate community attitude toward the importance of rabies vaccination to those animals, the risk of becoming infected is high.

The prevalence of dog bites in North Sulawesi, North Sumatera, West Sumatera and West Jawa is the highest among the provinces of Indonesia. For example in North Sulawesi during the year 1978 there were 2765 reported victims, 1576 out of those were children under 15 years of age (Batuna, 1979).

The recovery from rabies in several animal species has been documented (Johnson, 1948; Pawan, 1936). But it is very rare for this to occur among men with rabies. Hattwick et al (1972) reported case of rabies, caused by a bat-bite

which case recovered without any sequelae after 6 months of onset.

However, this disease is still very lethal to man; nevertheless, it can be prevented effectively by active immunization. Shortly after being bitten by a rabid animal, vaccine should be instituted in a full course as early as possible.

The purpose of this analysis is to report the problems of rabies victims and rabies vaccination in children.

## Materials and methods

The data used in this analysis was collected from the medical records of the out patient clinic of the Surgical Department at Gunung Wenang Hospital, Manado, from January 1977 through December 1978.

The analysis 234 children, under 14 years of age, with the diagnosis of an animal bite, included :

- the age and sex group of children,
- the kind and the fate of the biting animal (dogs, cats or others).
- the time span between the bite and the start of the vaccination,
- condition of the victims and the side effects of vaccination during the course of inoculation.

SMB vaccines have been developed in Indonesia, however, NTV is still widely used, and in this report it was the only type of vaccine used. The regime of ARV in the out patient section of the Surgical Department is as follows :

- 14 consecutive daily inoculations of 2 cc of rabies vaccine were adminis-

tered regardless of the age, the site and the severity of the wounds, and the lapse of time from reception of the wound from the rabid or suspected-rabid animals.

- 2 boosters were administered at 10 and 20 days after the last course of vaccination.

- 1500 U of Anti Tetanus Serum (ATS) was given as soon as the victims came to the out patient clinic.

- ARS was never used regardless of the site and severity of the wounds.

- The patients were asked to come back to the hospital within 66 months after receiving rabies vaccine, if they experienced headache, paralysis, leg Cramps, or convulsions.

Home visits were done during this analysis to evaluate the condition of the children after receiving rabies vaccination.

Terminology and Abbreviations used in this report

— rabid animal: a biting animal with confirmed rabies as the result of an examination of the brain tissue.

— suspected-rabid-animal :

\* a biting animal dead within 14 days without having any rabies investigations performed afterwards.

\* any biting animal killed without a rabies investigation.

\* stray animal, known to have bitten a victim, then escaped after biting the victim,

- ARV : Anti Rabies Vaccine
- NTV : Nervous Tissue Vaccine
- DEF : Duck Embryo Vaccine
- SMB : Suckling Mouse brain Vaccine
- HDCV : Human Diploid Cell Vaccine.

## Result

Only one out of 234 victims was bitten by a rabid cat while the rest were bitten by dogs.

Sixtyeight of the victims were bitten by confirmed rabid dogs, and the other 166 victims were bitten by rabid-suspected-dogs. The Victims, bitten by rabid-suspected- dogs were as follows :

- 26 victims were bitten by dogs which were killed without rabies confirmation of any kind.
- 111 victims were bitten by dogs which died of unknown causes within 14 days.
- 29 victims were bitten by dogs which escaped after biting their victims.

## Figure 1.

Eighty-eight out of 234 victims were vaccinated within 5 days after being bitten. One hundred and one out of 234 victims were vaccinated within — 10 days after being bitten. Sixteen out of 234 victims were vaccinated within 11-21 days, and one of them contracted rabies 27 days after bitten, and died the day before the last inoculation had been given.

Only 3 out of 234 victims were vaccinated beyond 21 day after being bitten.

One out of 234 victims who did not seek help for vaccination reported to the hospital with rabies 4 months after being bitten, and died the following day.

The site of the bite wounds were as follows (figure 2) :

— head wounds were found in 19 out of 234 victims which represents 8.1%. 12 of these victims were vaccinated within between 11-21 days after being bitten.

None of these victims contracted rabies.

— back or chest wounds were found in 10 out of 234 victims or 4.3%.

None of these victims contracted rabies.

— Arm wounds were found in 66 out of 234 victims or 28.2%. One of these victims, who was not vaccinated, contracted rabies 4 months after being bitten.

— buttock or hip wound were found in 26 out of 234 victims or 11%.

The adverse reactions to vaccination were as follows :

Major reaction :

— Encephalitis post vaccination : none

— Anaphylactic reaction : none

Minor reactions :

Fever, in 28 out of 234 victims

Malaise, in 11 out of 234 victims

Myalgia, in 12 Victims

Pruritus, in 2 victims

Pain in, 3 out of 234 victims

Parasthesia, in 5 victims.

## Discussion

### Epidemiology

Rabies, which is mostly a disease of warm blooded animals, is transmitted to man through the infected salivary glands of those animals mostly by ways of a bite. Transmission can also occur when existing wounds or abrasions come into intimate contact with rabid salivary virus. Aerogenic transmission, although it occurs rarely, has been reported in a man who entered a cave where vampire bats were roosting, and again from laboratory exposure during vaccine preparation. In this report only 1 out of 234 victims was bitten by a rabbit cat, and the rest were bitten by dogs.

Investigation of negri bodies from the brain of a biting animal to confirm rabies is a simple procedure, and is of paramount importance, since not all of the biting animals are rabid. But this procedure is really difficult to conduct in this country today, because of the lack of facilities and inappropriate community attitude toward the importance of this procedure.

All biting animals killed or dead within 10 days after having bitten, without a rabies investigation, in a country where rabies is endemic, should be considered as rabid animals, and the victims, bitten by those animals, should be vaccinated as early as possible.

Twenty six out of 234 victims were bitten by different dogs which could not be identified, because all 26 dogs escaped after biting their victims. Apparently, the remaining 172 dogs, that bite 208 victims, could have been confirmed as to whether or not they were rabid, but only 58 dogs which bit 68 victims were confirmed as to having rabies by investigation of negri bodies. The rest of the 114 biting dogs were either killed or dead, without any awareness that rabies confirmation is very important. The dead bodies of the dogs in question were even thrown away into rivers or in beaches which are frequently used by swimmers. This situation might be very risky in the transmission of rabies, since oral infection has been demonstrated in experimental animals.

Age and sex prevalence of victims, bitten by rabid animals or rabid-suspected-animals in this report was most common among children of 5 - 14 years of age, and among males of all ages, since these children were frequently outside the house. One hundred and fifty four out of 234 victims or 65.8% were children of 5 - 14 years of age, and none of the victims was under 1 year of age.

### **Rabies Vaccination**

Vaccination is the only effective way to prevent the development of rabies in man, regardless whether it is given before or after exposure to rabies virus.

Vaccination, given before exposure to rabies virus is called pre exposure vac-

ination, which is commonly given to the high risk people, such as nurses, doctors, veterinary students and laboratory workers who prepare rabies vaccine. While vaccination, given after exposure, is called post exposure vaccination. This is widely used in practice and highly effective in preventing the victims from rabies, which is almost always lethal.

Although there has been very little change in the regime of vaccination since it was introduced for the first time by Pasteurs, many different types have been developed and continue to be developed in the production of vaccines for the immunization of man. Two types of vaccines have been developed :

1. Nervous tissue vaccine, derived from the nervous tissue of adult or newborn animals.

One of the most common types of NTV in use today is the Semple type, another is the SMB vaccine which is prepared from suckling mice brain before myelinization occurs. These vaccination completely inactivated virus which has some superiority such as: they keep better under field conditions; they provide increased assurance of safety, and they lend themselves to an easier contralized production.

Fermi type vaccine, is another vaccine which contains residual infectious virus. Since this vaccine still contains residual live virus which has risk effects, the W.H.O. Expert Committee (1973) has recommended that the production of this

vaccine should be discontinued. Until recent years, the sole source of virus for vaccine production, was infected brain tissue, and this NTV is still the most extensively used since it is highly effective, even though it occasionally gives side effects of neuroparalytic reactions. However, these side effects are even less, in vaccines derived from newborn brain tissue, which do not contain myelin, considered to be a paralytic factor.

2. Non-nervous tissue vaccine such as, DEV, which is thought to contain little or no myelin, and HDCV which was developed by Wiktor et al. in the USA (1964) in the human diploid cell strain WI-38.

DEV is widely used in the USA, where it is estimated that more than 30,000 people are vaccinated with this vaccine each year. However, considerable doubts have been expressed about the efficacy of this vaccine (Crick and Brown, 1970). It is stated that DEV is effective enough in pre post exposure vaccination, and causes rare neurological adverse reactions or minor reactions. (Cohen et al, 1964; Moreira et al., 1972; Morgan et al. 1978).

HDCV is highly immunogenic. The antibody response due to a 2 dose inoculation is comparable with that evoked by 14 - 24 injections of ordinary NTV, and it seemed to respond faster (Shah et al., 1976). It is felt that further studies to evaluate the efficacy of this vaccine regarding the regimes used, are still needed,

The efficacy of human post exposure rabies prophylaxis with NTV rabies vaccine alone, can be seen in this analysis. Fourteen daily consecutive inoculations of 2 cc of NTV were administered without ARS regardless of the age of the victims, and the site and severity of the wounds. Contrary to the W.H.O. (1973) recommendation, where ARS should be given as early as possible to the victims who have been bitten on their neck or head, none of these victims in this report contracted rabies as long as inoculation with NTV was started within less than 10 days after being bitten. It is also found that ARS and boosters are not at all necessary within the first 21 days to those bitten on the arms or legs (Figure 2).

It is very important to note that addition of ARS reduces the active "humoral antibody" response to most rabies vaccines. Corey et al. (1976) showed that 23% of the victims who were vaccinated with SMB vaccines together with the addition of ARS, failed to develop adequate antibody. By giving more than I.U/kg bw of ARS, and corticosteroid, the antibody response is suppressed. It has been shown that this immunologic suppression could be overcome by additional "booster doses" of vaccine. ARS might be necessary among the victims bitten on their neck or head 10 days or beyond, prior to the vaccination. One of the victims who started the NTV regime on the 14th day after being bitten, contracted rabies on the 13th day of the course of vaccination, and died the next

day. The efficacy of post-exposure vaccination, most probably depends upon the time when the inoculation of vaccine is started, since the incubation period of human rabies ranges from 12 days to 6 or more months following exposure.

The average is between 30 - 60 days. The incubation depends upon the site and severity of the wounds, age of the victims, virulence of rabies virus, and the nervous system at the site of the wounds. It is stated that the bitten wounds on the neck and head have the shortest incubation period.

None of the 17 out of 234 victims, bitten on their heads or necks contracted rabies, even though their inoculations were started even without ARS within 10 days after being bitten. Four of these were vaccinated without boosters. However, it is very risky not to give ARS to the victims bitten on their head or necks for whom inoculation was started later than 10 days. The reason is one of 2 victims who commenced vaccination on the 14 th day after being bitten contracted rabies, on the 13th day of daily consecutive inoculation (Figure 2).

It is easily seen in this report that the bite-wounds on arms or legs, have a longer incubation period than the bite wounds on head or necks, since none of

the 65 arm-bite-victims and none of the 112 leg-bite-victims contracted rabies even though the inoculation was started 21 days or more after being bitten, and without ARS of course, prospective studies of the efficacy of NTV regarding the age, the site of the wounds, the dosage schedule, and the time span between the bite and the start of vaccination can not be conducted for ethical reasons. However, post exposure vaccination should also be instituted even if the victims have been bitten by rabid or suspected-rabid-animals 3 or more months before. One of the victims in this report who was not vaccinated, contracted rabies 4 months after being bitten on his arm by a suspected-rabid-dog.

It is also easily seen that 2 booster doses 10 days apart are not necessary, since 89 out of 234 victims did not continue the vaccination to the booster stage. And none of those victims contracted rabies. But further studies, like the determination of antibody levels to support this finding are still necessary.

Although further studies are needed especially whether or not a late institution of ARS is still effective enough rather than early institution, from this analysis the following scheme can be recommended for post exposure vaccination of 2 cc NTV for 14 consecutive days :

Site of the wounds	Status of biting animals	Recommended Treatment					
		Time space between a bite and the start of inoculation.					
	At time of exposure	10 day observation from time of biting	0—5 days	6—10 days	11—21 days	21+ days	
Head or Neck	Rabid	—	V+B	V+B	ARS V+B	ARS V+B	
	Suspected	Start vaccination	Stop V	None	None	None	
		Health confirmed by 10th day	Killed	V+B	V+B	V+B ARS	V+B ARS
		Escaped Died					
2. Other parts of the body	Rabid	—	V	V	V	V	
arm	Suspected	health confirmed	None	None	None	None	
leg		by 10th day					
buttock or hip	Rabid	Killed	V	V	V	AVS	
chest or back		Escaped Died				V+B	

Note : ATS 1500 U should be given to the victims regardless whether a biting animals is rabid or not

V — vaccine

B — booster

ARS — Anti rabies serum

### Side effects of Rabies Vaccination

Besides preventing the victims from contracting rabies, the vaccine also could give deleterious reactions. These deleterious effects can be divided into :

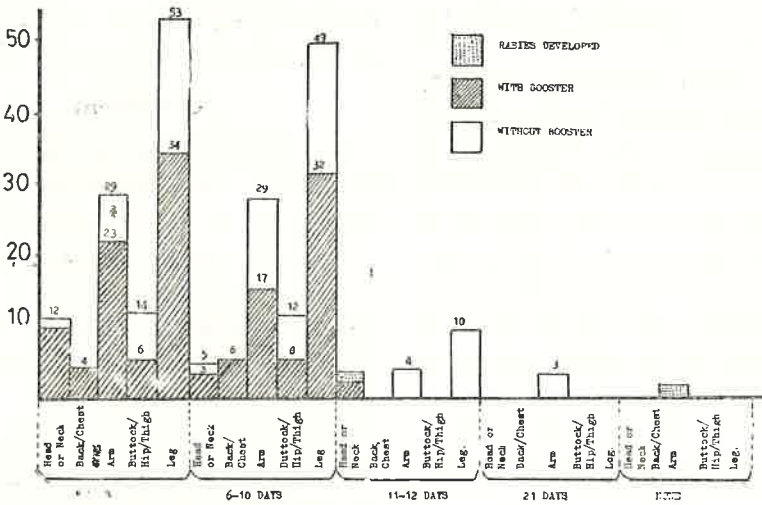
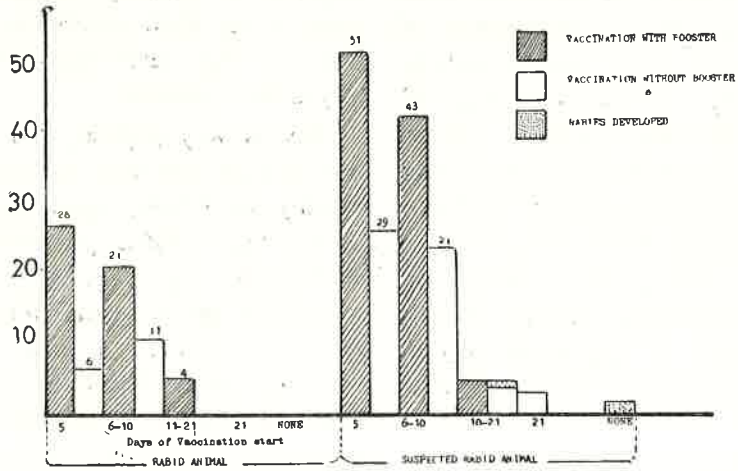
1. Minor reactions including erythema and pruritus.

1.1. local reactions such as pain, erythema and pruritus.

1.2. systemic reactions such as fever, malaise, myalgia and adenopathy.

2. Major reactions such as central nervous system reactions to vaccines, and anaphylactic reactions.

In this report none of the victims vaccinated with NTV had either encephalitis post vaccination or anaphylactic reactions. It is interesting to note that the occurrence of neuparalytic accident due to NTV used in immunization, varies from one country to another.





Many factors are to be considered when taking into account the development of these accidents. Those factors include, the physiology of the individual, the species of the animal used in vaccine production, the method of inactivating the vaccines, and the dosage schedule.

Minor reactions which were found in this report were : fever during the course of vaccination (12.8%), malaise (4.7%), myalgia (5%) pruritus only in 2 out of 234 victims or 1%, and parasitosis (2%).

### **Pre-Exposure Vaccination**

Pre exposure vaccination in Indonesia is not yet practised. It is not known yet exactly whether pre exposure vaccination in Indonesia is more costly than post-exposure vaccination, but it seems evident that pre-exposure vaccination is a paramount necessity in highly endemic areas like North Sulawesi, especially among the age group of 5 - 15 years. Of the 3 age groups less than 2 years, 2 - 5 years and 5 - 14 years, the prevalence rate of rabid or suspected-rabid-bite is the highest in the 5 - 14 years age group. By implementing pre-exposure procedure, it is hoped that the development of rabies can be prevented effectively even though the lapse of time between the bite and the start of vaccination is longer than the safety time for starting vaccination.

SMB vaccine which contains almost a complete lack of the encephalitogenic factor is preferred for human vaccination. Moreira et al (1973) found a positive

response of antibody formations to 3 doses of 1cc SMB vaccine at one week intervals. These levels were still satisfactory after 6 months.

DEV is very popular, and is widely used for pre-exposure vaccinations, especially in U.S.A., since this vaccine causes less adverse reactions. Cohen et al. (1964) reported that the antibody response of the individuals who one year previously received 4 doses of DEV with one week intervals, significantly increased starting from one day after vaccination. However, Moreira et al. (1973), recommended that a booster shot will be reasonable if it is given after 6 months, since it produces a new increase in the rate of neutralizing antibodies.

Morgen et al. (1978) found that pre-exposure prophylaxis by intradermal inoculation with 0.1 cc of DEV is comparably effective to 1 cc of DEV.

### **Conclusion**

In conclusion, we can see then that one of the most important factors in eliminating or at least greatly reducing rabies, is the public dissemination of information concerning not only the danger of uninjected animals, but how rabies can be prevented or terminated if treated immediately.

Furthermore we can see that effective treatment of rabies has been carried out by using NTV on an across the broad administration of 2 cc at one day intervals for 14 consecutive days, regardless of the age, the site and the severity of the wounds.

We further realize that NTV, although effective enough at the present time, is not the most effective and preferable drug available for post exposure vaccination in Indonesia. The reason is, inappropriate community attitude toward the danger of rabies. It is our hope that the most currently developed vaccine HDCV, which is highly immunogenic will soon be available in this country.

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