Editorial

Current Scenario of Intra Dermal Rabies Vaccination in India

In India, Intra Dermal Rabies Vaccination (IDRV) started on 19th May, 2006. Credit should be given to Dr. M. N. Siddiqui and the Health Department of the Govt. of Uttar Pradesh for making it possible. In fact, there were no official guidelines available at the time when it was started. In fact, the history of mankind has many examples of pioneering acts by very courageous persons. Dr. M. N. Siddiqui is a pioneer and he is our hero. Then onwards IDRV has been implemented in different Indian States, one after another in, Orissa, Andhra Pradesh, Karnataka, West Bengal, Tamilnadu, Himachal Pradesh, Kerala and many more. In fact in every few months one more state recognized its benefit and started using it. IDRV is being given in some ARCs of Govt. hospitals and Autonomous Institutes only.

Dr. M. N. Siddiqui was the first person to use IDRV in regular Anti-Rabies Clinics of the Government, without even a National or State Guideline, for the vaccines being used for IDRV, in place. The **Drugs Controller General of India [DCGI] had issued its first directive in February 2006, permitting the use of IDRV in certain clinics fulfilling certain criteria. The package inserts of the vaccines had at that time no mention of IDRV usage.**

Dr. S. N. Madhusudana was the first person to do clinical trials on IDRV in India, from the late eighties onwards, initially at CRI Kasauli and later at NIMHANS where he was working. He started publishing his works from the early nineties onwards at regular intervals. He started using IDRV at CRI Kasauli in the late eighties, about 20 years before Dr. Siddiqui started to use it in a regular ARC set-up.

After the discontinuation of the use of Semple Vaccine (NTV) in 2005, the availability of adequate amount of TCVs for use in Govt. Hospitals and Health centers in India was a problem in many states for sometime. The states starting to use IDRV did not face vaccine shortages.

Where only, the ESSEN [IM] schedule was used for post-exposure prophylaxis against rabies, the crisis was more acute. **The number of vials of vaccine required for a full course of vaccination was more, when the ESSEN [IM] schedule of vaccination was used. When, the modified "TRC ID" schedule [2-2-2-0-2-0] was used, the total requirement of vaccine vials was much less than that for the "ESSEN" schedule**.

Not All, vaccines produced in INDIA are at present fit for ID usage as per facts revealed in the ICMR study evaluating the TCVs produced in India against a TCV pre-approved for IDRV by WHO and manufactured outside India [Verorab], This study was done in 2003- 2005 under a directive from the **Drugs Controller General of India [DCGI] prior to giving its approval for use of IDRV in India..** The "WHO Expert Consultation on Rabies", Technical Report Series 931, and the directives from the DCGI, from time to time also do not approve all TCVs for IDRV usage.

The WHO had approved IDRV in 1992, about 19 years ago. It is considered as an ethical and cost-effective replacement of NTV.

The **Drugs Controller General of India [DCGI] has issued directives from time to time regarding the regulatory guidelines for Intra Dermal Rabies Vaccination [IDRV] in India after detailed consultations with Experts Group, the Competent Authority, and the ICMR. The Drugs Controller General of India [DCGI] has allowed the use of only four of the eight commercially available vaccines against rabies [which can be used by IM route], to be used by the ID route also.**

The Drugs Controller General of India [DCGI] directive has mentioned that the vaccines to be used for IDRV should have a minimum potency of 2.5 IU per vial of single IM dose. Some vaccines come with Iml diluent and some with 0.5 ml diluent. The dose of each ID shot has been specified to be of 0.1 ml of the permitted vaccines after re-constitution with the diluent provided. The potency per each ID dose of 0.1 ml will be 0.25 IU per dose for some vaccines and 0.5 IU for some others. **However, in the ICMR study evaluating the TCVs produced in India against a TCV pre-approved for IDRV by WHO and manufactured outside India [Verorab], done in 2003- 2005 under a directive from the Drugs Controller General of India [DCGI] prior to giving its approval for use of IDRV in India, the potency of all vaccines used was above 5 IU per vial of single IM dose. Currently, in the Indian market almost all TCVs available have a potency of more than 5 IU per vial of single IM dose, though their labels mention of a potency of being greater than 2.5 IU per vial of single IM dose.**

The modified "TRC ID" schedule [2-2-2-0-2-0] is the only route approved by the DCGI. The dose of each ID shot has been specified to be of 0.1 ml of the permitted vaccines.

The ID route has been permitted to be used in selected anti-rabies clinics having an appropriate number of adequately trained staff for ID inoculation. These centers should be able to maintain cold chain for vaccine storage and be able to ensure adequate supply of suitable syringes and needles for administration by the ID route. These centers should be well versed in the management of open vial and safe storage practices.

Unfortunately, it has come to the notice of many experts that reconstituted vaccine vials are not being kept in a refrigerator when the clinic is open. They are kept on top of cooler bottles, directly under a ceiling fan, or merely in a thermocol box, with or without cooler bottles. With frequent opening of the boxes the temperature of the vaccine vials rise much above 8 degree centigrade [The upper limit of the required storage temperature].

In the race to start ID vaccination it is very important to remember that the **Intra Muscular (IM) route *is the preferred route for anti-rabies vaccination using modern TCVs or modern Avian vaccines in the immune compromised persons, persons on immunosuppressant drugs or therapy and on chloroquine therapy. Persons suffering from Diabetes Mellitus of a long duration, persons having malnutrition, and many other medical illnesses, where the patients are expected to have a poor immune response, the use of ID route for post-exposure prophylaxis against rabies, can be very risky.***

Centers using IDRV, should also have provision for IM vaccination by ESSEN IM schedule in selected cases

If ID dose is given sub-cutaneously (SC) then there is a possibility of poor immune response due to low antigen load. This may be life threatening. WHO recommends in cases where the characteristic change in the skin over the injection site has not appeared, the patient should receive another dose of vaccine at a site nearby where the characteristic change in the skin over the site of the shot, appears. It has come to the notice of many experts that this is not being implemented in many ARCs using IDRV. This is very dangerous.

It has come to the notice of experts that in many centers the staffs arenot knowing that they are using IDRV. The staffs, including doctors, are saying that they are using "Sub-Cutaneous Rabies Vaccination". This is very dangerous.

It has come to the notice of many experts the fact that many IDRV centers in reputed teaching and in non-teaching institutions are not co-operating with APCRI when they are being approached for collecting blood samples of patients on specified dates for the purpose of monitoring the effectiveness of IDRV. There is a great need for a survey evaluating the proper implementation of IDRV in India and its effectiveness in reducing the "Burden of Rabies in India", at present.

In the race to bid for the Govt. supply tenders, some manufacturers, whose registered packs contained only ONE 0.5ml ampoule of diluent, started supplying TWO ampoules of 0.5ml diluents, overnight. They did it to mislead the tender committees, that their vaccine also comes with ONE ml of diluent and as a result, its use should be economical. This is an unscientific act, and is not permitted by law. **Whenever, the diluent's volume is increased or decreased, some characteristics of the vaccine changes. It becomes a new drug, and as a result has to undergo fresh clinical trials, before it can be accepted as being safe for human use.**

Currently, some pharmaceutical companies are importing & marketing rabies vaccines without carrying out an appreciable number of authentic clinical trials in reputed centers in the country. Some of these vaccines are being procured by some State Govt. institutions for use in their ARCs. **This means that unsuspecting patients are being treated with untried vaccines and some are also using these vaccines for IDRV. This is very dangerous.**

As an offshoot of the IDRV program, certain faulty implementation of Rabies Post-exposure prophylaxis is going on in some hospitals and its surrounding areas. In the ESSEN [IM] protocol of one vial of rabies vaccine is to be administered by IM route on D0, D3, D7, D14 and D28, the D14 dose is omitted. **This becomes a new schedule, being used to treat actual patients, without any clinical trial, and without any regulatory approval, and not recommended by any one of the manufacturers in their package inserts. This is a very dangerous act.**

The use of Rabies Immunoglobulins [RIGs] has not picked up to the desired level. RIGs are being used in only some centers. The use of RIGs is also not proper. There is a deficiency in the training of doctors and staff manning ARCs. **APCRI's Manual on Rabies Immunoglobulin (RIG) Administration, February, 2009 will be very useful for the doctors working in the ARCs.**

All changes are very good if they can provide more safety and efficacy to the patients. However, changes which endanger the lives of the unsuspecting patients seeking treatment are not desirable. I believe that in the long run truth will prevail.