INTRODUCTION

All artificial immunisations lead to more or less specific reactions. These reactions may occur at the site of administration of immunising agent; regionally in the area around it; at sites far removed, in the viscera specifically concerned with immune response and those to which the dissemination of the immunising agent may occur.

Normal Local Reaction:

BCG vaccination is given by intradermal injection with 0.1 ml. of suspension of a live but attenuated particular bovine strain of Mycobacterium tuberculosis in the left deltoid region. A weal is raised. This weal disappears in ½ to 2 hours depending upon the hydration of the skin tissue, leaving a small (5 to 10 mm) area of hyperaemia, a local sequela of injection trauma, for 2 to 4 days.

In the individuals previously uninfected by M.tuberculosis, about 2 to 4 weeks after the vaccination, erythema around an area of induration appears. Approximately at the site of prick of injection a nodule shows up. Within 3 to 10 days time, it softens giving rise to a pustule. Bursting of the pustule in about 2 to 5 days after its appearance results in an ulcer 4 to 8 mm in size. This painless depressed ulcer with undermined edges is soon covered by a thin crust or scab, which tends to peel off at the slightest provocation. The healing of ulcer in to a depressed, thin, shining scar with undermined edges in 4 to 6 weeks of its formation, marks the uneventful termination of sequence of occurrences at the site of BCG vaccination.

In an individual previously infected with Mycobacteria, exaggerated and accelerated reaction of similar nature as described above, is seen. The reaction in this case starts within hours after vaccination and ulcer, 6 to 12 mm in size, occurs within a week. Ulcer also heals into the scar earlier. Size of the erythema, induration, nodule, pustule, ulcer and scar all are bigger than those in the uninfected.

Similarly a repeat BCG vaccination also results in bigger local reactions. They are, however, smaller than those in the infected individuals. Onset of reaction in them, is almost similar to the infected.
It may be stated here that reactions described above, in the infected or uninfected, are painless. Slight tension is felt at the time of formation of nodule in the skin but before the subject concerned can complain, the tension disappears because of liquefaction of necrosed tissue.

Regional reaction:
Soon after the BCG vaccination, the bacilli traverse along the lymphatics to the regional lymphnode chains. From the deltoid region the biggest load is taken by the axillary region. The infraclavicular, supraclavicular and cervical lymph nodes also take a share. The involvement of different chains depends on the exact location of injection. The inflammatory reaction following the BCG in the glands leads to slight to marked enlargement of involved lymph nodes.

General reaction:
The BCG organisms are also absorbed into the blood stream and are disseminated to different sites in the body resulting in multiple reactions involving corresponding regional lymph nodes.

COMPLICATIONS

Definition of complication:
For purposes of simplicity and brevity, reactions other then those described above or those which do not conform to the stated time schedule are reckoned as complication. Most of the conditions listed under complications are actually harmless events and are misnomer. As far as local reactions are concerned, an ulcer or the one covered with crust not healing into scar for 12 weeks from the date of vaccination or the one having a size greater than 12 mm can be considered as complications.

Causes of complications:
The causes of complications are attributable to:

1. The vaccine; degree of attenuation of the BCG organism and their number in the vaccine

2. The technique of vaccination:
   a) depth of vaccination: into dermis, subcutaneous or muscular tissue.
   b) injection of larger volume of vaccine: The complications due to this factor, in fact in most cases, are due to a part of vaccine seeping into deeper layers of epidermis or dermis.
   c) the concentration of vaccine: Higher the concentration greater the chances of complication. Vaccine gets concentrated because of (i) lesser volume of diluent used for reconstitution of vaccine (ii) for lack of homogeneity at the time of reconstitution
and (III) sedimentation of bacilli at the bottom of the ampoule if it is not shaken before each filling of the syringe.

d) contamination of needles, syringes or vaccine due to inadequate sterilisation of equipment or carelessness at the time of reconstitution.

3. Infection of the ulcer from atmosphere by pyogenic organism

4. Constitutional factors in the subject.

5. Besides these there are conditions due to tuberculo-hypersensitivity. They manifest anywhere in the body. These conditions heal without leaving a scar. Like common cold, they take similar time to heal whether efforts are made at treatment or not. They are erythema nodosum, phlyctenular conjunctivitis, iritis, iridocyclitis etc.

Local Complication

Undulating ulcer:

As per definition, ulcer larger than 12 mm in size or not healing beyond 12 weeks are considered as complicated. They can be due to any of the first three causes. If they are due to deep vaccination i.e., ulcer is very deep in the subcutaneous tissue and does not show signs of infection, they are better left alone. What assistance intake of vitamin A & C and local application of sterile codliver oil renders, is difficult to gauge. In case signs of infection are suspected, intake of suitable broad spectrum antibiotics is useful. Antibiotic or chemotherapeutic agents should not be applied locally. Absorption of small quantity thereof from ulcer surface have been known to cause allergy. Local application of a drug, if the same is consumed systemically is, however, helpful.

Bandaging, covering the ulcer with sticking plaster, application of antiseptic agents can lead to local irritation.

Abscess formation:

It is not a common complication. It is the consequence of deep vaccination into subcutaneous or muscular tissue. It is more likely to occur in young subjects, new borns or infants because of thin epidermis. Children of higher ages who struggle or otherwise move at the time of vaccination also are likely to get deep vaccination and therefore abscess formation. Like any cold abscess it is not a painful condition, unless super-infect with pyogenic organisms. One or two aspirations, under cover of antibiotics is helpful.

If an abscess bursts open on its own, it leads to a rugged crater of large size. Sinus formation is also possible. The overall management in these conditions is similar to that described under ulcer.
Scrofuloderme and Eczematous lesions:

They generally occur because of local irritation of the skin around the ulcer by the discharge. If antiseptics, dressings etc. of the ulcers are avoided vast majority of such episodes can be prevented. Depending upon the clinical picture, intake of antihistaminics or bacteriocidal or bacteriostatic drugs are helpful.

Lupoid reactions:

In India 5 cases have been known to occur. Two each were siblings in two families and one in an other. None of them have been documented so far. Healing in three cases occurred without any interference, within 4 months. Anti tuberculosis treatment in the other two took similar time to heal. It is possible that a few more cases may not have been seen by medical profession or not diagnosed or not reported. From the above it is not fair to conclude that there is a particular diathesis for development of lupoid reactions.

Squamous Epitheliosis:

A local proliferative condition, very rare in India.

Hypertrophied scar:

Instead of a depressed thin normal scar delayed healing of ulcer or foreign body (sand particle etc.) can lead to a thickened scar coming up almost in line with the surrounding skin. A scar protruding out 1 mm beyond the level of the skin is termed as hypertrophied scar. It is found predominantly in area having high prevalence of non-specific tuberculin sensitivity. Highly concentrated vaccine, presence of hyper sensitivity, resembling tuberculous, are other possible factors for their occurrence. It is also seen often as a consequence to second BCG vaccination. Except that it poses cosmetic problem in the fair sex, the condition is painless, does not spread or grow in size.

Keloid formation:

Reported more commonly among the yellow races and in African countries, keloid following BCG vaccination is a very rare condition in India. It has biscuit like appearance, grows with time causing intense itching. Its cause is not known. Many theories are rampant. Surgeons may be consulted for this condition. Excision generally leads to more fulminating condition. Superficial X-ray therapy is stated to be useful.

Regional complications:

Lymphnode involvement together with lymphangitis and local ulcer formation are indicative of establishment of Primary Complex. But clinical enlargement of the glands can be termed a complication. Its prevalence is known to vary between 0.1 to 0.3%. It is found more oftener among
the new borns and infants perhaps because of deeper vaccination involving injection of greater volume of vaccine than skin can hold. It is easily preventable. Half the dose (0.05ml) of vaccine for those under 1 year of age and carefulness in vaccination can reduce gland involvement. Since immune response is related to the log of the dose, reduction of dose of BCG vaccine to half is not likely to affect hypersensinvity or degree of immunity.

The lymphnodes can also enlarge because of contamination of needles, syringes, vaccine etc. This condition has an elament of pain and non specific inflammatory reaction in the tissue around the glands. They also suppurate faster. Enlargement of lymphnodes induced by vaccine alone also some times show signs of softening, less frequently bursting out resulting in sinus formation. Some times scrofuloderma  and eczema also likely to occur around month of the sinus.

The non-flectuating hard glands subside slowly in 6 to 8 months. Fluctuating glands are better aspirated or even excised. In case of non-specifically inflamed gland, broad spectrum antibiotics alone may help early cases. In late cases besides the drugs, aspiration and excision may have to be resorted to.

The anti tuberculosis drugs are better avoided. If at all necessary, they may be given 6 months after the date of vaccination. By this time cell mediated immune response would have been positively completed and elimination of BCG organisms may not affect the immunal status of the individual. However, caution being better part of valour, another BCG vaccination after some time would ensure that interference in the immune mechanism had been vacated.

It may be stated here that BCG vaccination results in enlargement of lymphnodes only among the non-infected . Lymphnode reaction in reinfection or BCG vaccination of infected or second BCG vaccination is marked by absence of lymphnode involvement.

**General complications:**

The general conditions at sites far removed from that of BCG vaccination attributalbe to tuberculo allergy have been discussed earlier.

Besides these, generalised tuberculous disease has also been described in literature but has not been reported from India. Children with conditions like Agamma-globulinaemea or hypogamma-globülinaemia have been mistakenly diagnosed as tuberculous. BCG organisms were isolated from their viscera but the pathological conditions were due to reasons other than BCG vaccine. They occurred because of poor protective mechanism in the body.

Solicotic lungs in experimental animals have been seen to develop tuberculous lesions, after BCG vaccination. But these very organisms, removed from diseased lungs of silicotic animals, failed to produce any tuberculous animal with healthy nonsilicotic lungs.

-o0o-