

Vaccinations in stem cell transplant patients

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Factors determining the immune status after stem cell (STC):

- the persistence of recipient immunity for both allogeneic and autologous SCT,
- the transfer of immunity from the donor for allogeneic SCT.

Long-term follow-up of allogeneic BMT patients shows no difference in the proportion of seronegative patients with a seropositive or seronegative donor. In both cases, the patient will lose immunity through the transplant procedure.

The strength of previous antigen challenge is probably important (Ljungman *et al.*, Blood 1994).

Non-live vaccines in STC transplant patients

In STC transplant patients, non-live vaccines are not associated with evident major risks. Repeated doses are necessary in patients who have undergone myeloablative SCT. This has been shown for tetanus, diphtheria, *Haemophilus influenzae*, and inactivated poliovirus vaccines. The rate of loss of immunity suggests that immunization is not needed before 6 months after transplant. In most studies, immunization is started at 12 months.

With the pneumococcal polysaccharide vaccine, no effects of early vaccination, before 12 months, (Parkkali *et al.*, 1996), repeated doses (Guinan *et al.*, 1994), and donor vaccination (Molrine *et al.*, 1996) have been reported. In a pilot study, one single dose of conjugate vaccine gave far better responses than one single dose of polysaccharide vaccine in patients with relatively severe chronic graft-versus-host disease.

Influenza is another important infection with a substantial mortality in SCT patients (Ljungman *et al.*, BMT 2002), but whether vaccination will decrease the severity of the disease is not known. One year after transplant, only half of the patients were responders (Pauksen *et al.*, 2000) and whether a better immune response can be obtained with two doses of vaccine is debatable.

Live vaccines

Live vaccines have far more side effects.

BCG: contra-indicated in STC transplant patients (since risk/benefit ratio not really favorable).

Yellow fever immunization: very limited data available.

Mumps: probably not indicated.

Rubella vaccination: probably safe.

Measles vaccination: safe (Ljungman *et al.*, 1990; King *et al.*, 1996) for both adults and children.

Varicella vaccination in seronegative patients: apparently no side effects (Sauerbrei *et al.*, 1997).

Vaccination recommendations

(EBMT 1995 and 1999; CDC 2000)

Tetanus toxoid	All patients	3 doses	6-12 months
Diphtheria toxoid	All patients	3 doses	6-12 months
Inactivated polio	All patients	3 doses	6-12 months
HIB	All patients	2 doses	6-12 months
Pneumococcal	All patients	1 dose	6-12 months
Influenza	Seasonal	1 dose	4 months
Measles	Individual	1 dose	24 months
HBV	Regional	3 doses	6-12 months

Immunity to

	Tetanus	Polio
One year after vaccination	87%	90%
Five years after vaccination	89%	88%
Six to 14 years after vaccination	72%	79%

These results are encouraging (Ljungman *et al.*):

Alternative strategies

Donor vaccination

Donor vaccination has been shown to improve recipient immunity for:

- *Haemophilus influenzae* (Molrine *et al.*, 1996)
- Tetanus toxoid (Wimperis *et al.*, 1986; Molrine *et al.*, 1996)
- Hepatitis B (Wimperis *et al.*, 1986; Ilan *et al.*, 1993, 1994)
- Conjugate pneumococcal vaccine (Molrine *et al.*, 2003)

and should be combined with early post-transplant patient vaccination.

Addition of cytokines

GM-CSF added to influenza vaccination induced a somewhat better early response to vaccination with influenza B, but no improvement regarding the response to influenza A.

Hot topics for the next few years

With the advent of new techniques such as non-myeloablative SCT, “tailored stem cell infusions”, addition of other cell types – mesenchymal stem cells: it is necessary to revisit previous studies.

A comeback of measles could be a problem: less vaccine coverage in the population.

Vaccination with peptide-pulsed dendritic cells produced positive preliminary results *in vitro* against CMV (Einsele *et al.*) to boost immunity in an already positive patient. Whether it can work against adenovirus and aspergillus is not yet known.