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**Review Article**

# A brief review on bubble baby disease

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## ABSTRACT

Bubble baby disease is scientifically known as Adenosine deaminase - Severe combined immunodeficiency disease (ADA-SCIDS) which is a rarely occurring disease predominantly in infants (one in a lakh population). The disease is initiated by a complete deficiency of the immune system where the infants cannot tolerate even minor infections or allergies. Further, it is mainly caused due to the mutation in the gene IL2RG located on the X chromosome of the parents. To date, there is no particular test to diagnosis this disease, and delay in diagnosing this disease may lead to the death of a particular infant. Furthermore, in recent times researchers are concentrating on developing a test method to diagnose the disease rapidly. The treatment options include bone marrow transplantation, gene therapy, and pharmacotherapy (Calcarea phosp tablets) with reckeweg treatment (natural immunity booster drops). Though therapies very effective in improving the health of infants they possess few drawbacks like keeping the babies in sterile and isolated conditions which are done by placing the baby in a bubble made up of plastic. This short communication will cover about the disease and treatment options available in the present scenario.

**Keywords:** Bubble baby disease; Immunodeficiency; X chromosome; IL2RGgene; Infants

## INTRODUCTION

Severe combined immunodeficiency (SCID) is a group of genetic diseases causing profound developmental and functional impairment of T cells, affecting cellular and humoral immunities. Under this classification when an infant is unable to synthesize adenosine which decreases levels of T&B lymphocytes leading to a complete shutdown of the immune system and making the baby live in a bubble made of plastic is termed as bubble baby disease as shown in Fig 1. [1]Further, among the various genes that cause this disorder IL-2 receptor gamma chain gene (IL2RG) which accounted for more than 19% of total 45 cases prior and post T-cell receptor excision circle (TREC) in the USA

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and a major cause factor for bubble baby disease. [2] Infants suffering from this disease will be very sensitive even for mild infections like a common cold, ringworm infections, etc. [3]

**Fig 1. Boy in a bubble**

## SIGNS AND SYMPTOMS

Symptoms include rashes, diarrhoea, recurrent infections, and difficulty gaining weight, weakness, and/or growth delay.Organisms that would cause mild to moderate illnesses in healthy people may cause life-threatening infections in babies with this disease. And some of the infections observed are yeast (thrush or diaper rash), chickenpox, measles, herpes virus (cold sores), ear infections, meningitis (brain infections), or pneumonia that do not respond well to standard medical treatments. Children with SCID may also become infected with viruses (cytomegalovirus) from breastmilk, other live viruses (for example, the rotavirus or chickenpox) from vaccination or from common colds (viruses or bacteria) from siblings or surrounding children with healthy immune systems that can get rid of those infections.[4]

## CAUSES

Bubble baby disease is a recessive genetic disorder where an infant will acquire two recessive genes (abnormal gene) from each parent. The parent with one normal gene and one recessive gene will acts as a carrier for future generations without showing any symptoms. The chance for a child to become a carrier of the disease is 50% if only one parent has the one recessive gene. The risk for two carrier parents to both pass the altered gene and have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier like the parents is 50% with each pregnancy. The chance for a child to receive normal genes from both parents is 25%. The risk is the same for males and females.[5] Further, T-negative, B-positive, natural killer (NK)-negative (T-B+NK-) that occurs when T cells and NK cells cannot respond to growth factors (cytokines) needed to develop and survive in the body. The most common cause of T-B+NK- SCID, is X-linked recessive SCID (X-SCID) caused by an altered IL2RG gene found on the X chromosome which is the main cause for the occurrence of bubble baby disease. The *IL2RG* gene codes for the protein gamma subunit ($\gamma_c$) of the cytokine receptors for interleukin (IL-)2, IL-4, IL-7, IL-9, IL-15, and IL-21. The $\gamma_c$ receptor is defective in boys with X-SCID and cannot send signals from the growth factors needed to make functional T cells and NK cells. The B cells in these patients are also non-functional without help from T cells.[6]

## DIAGNOSIS[7]

A sequence of tests helps in the diagnosis of bubble baby disease in children. Most of these are blood tests. Here's a brief explanation of these screening techniques.

**Complete Blood Count**: The clusters of white blood cells are the main pillars in maintaining the immunity of an individual. Further, this complete blood count will reveal the total number of lymphocytes present in the body. Infants or kids suffering from this disease will have a low count of these white blood cells and they are extremely vulnerable to infections, even the mild ones.

**T cell, B cell, and NK cell count**: These cells are also part of the human immune system which will be absent for the infants suffering from bubble baby disease.

**Immunoglobulin levels (IgG, IgM, IgA, IgE)**: These are antibodies produced by the body to fight the microbes. A child suffering from bubble baby disease will be low on the count of these antibodies.

**Specific genetic testing:** This is another effective way of screening for bubble baby disease because many known genetic factors are contributing to this disease.

A clinical study was performed by Yu Lung Lau with 147 patients of Asia and North-Africa origin and the results stated that performing an early lymphocyte subsets for any infant with one or more of the following clinical features: family history, persistent candidiasis, BCG infections and ALC less than 3x10^9/L which would confirm the diagnosis of SCID. [8]

## TREATMENT

Various approaches can be used to manage this bubble baby disease which includes gene therapy,

bone marrow transplant, and pharmacological therapy.

**Gene therapy:** Gene therapy is a process where the affected gene is identified, removed, modified, and reinserted into the body to normalize the conditions. Further, **Kit L. Shaw et al** have performed a phase-2 clinical trial study on Autologous hematopoietic stem cell transplantation (HSCT) of gene-modified cells is an alternative to enzyme replacement therapy (ERT) and allogeneic HSCT. Results suggested that except for the oldest subject (15 years old at enrolment), all subjects remained off ERT with normalized peripheral blood mononuclear cell (PBMC) ADA activity, improved lymphocyte numbers, and normal proliferative responses to mitogens and demonstrated that clinical therapeutic efficacy from gene therapy for ADA-deficient SCID, with an excellent clinical safety profile.[9]

**Bone marrow transplantation:** A typical bone marrow transplantation procedure involves infusing healthy bone marrow cells by removing the unhealthy bone marrow. **EyalGrunebaum et al** have compared outcomes and immune reconstitution for the patient who has undergone bone marrow transplantation and the results suggested that in the absence of a relative with identical HLA, bone marrow transplantation may provide better engraftment, immune reconstitution, and survival for patients with SCID. [10]

Though bone marrow transplantation and gene therapy are effective in treating bubble baby disease but possess few disadvantages like exact blood group for transplantation. Further, in gene therapy when the effected gene is removed and modified and reinserted may lead to new viral infections.

**Pharmacological approach:** The other treatment options include immune system boosting with the help of gamma globulins which can be used to treat the influenza virus, rotavirus, poliovirus, mumps-measles-rubella, etc. Further, enzyme replacement can also be considered as an alternative approach where there is a mismatched transplant or a graft failure. Therapy includes injecting polyethylene glycol coupled with adenosine deaminase which metabolizes the toxic substances of the ADA and prevents their accumulation in the body. This therapy is widely used for patients who don't have a potential donor. Furthermore, Reckeweg is a homeopathic drug that is invented and widely used in Germany with beneficial results. [11]

## CONCLUSION

Bubble baby disease is a life-threatening inherited disorder which is scientifically known as Adenosine deaminase severe combined immunodeficiency disease (SCID). It is a condition where one in one lakh babies are getting affected by this disease. It is one of the types of severe combined immunodeficiency disease which affects and degrades the immune system slowly in the body. The patients with this disease shows the inability to produce this enzyme (adenosine) which is important for the production of the lymphocytes which helps to fight against the infections hence its (ADA) deficiency leads to the decreased levels of T&B lymphocytes where there is the complete suppression of the immune system and cannot resist even mild infections like a common cold, ringworm infections, etc can be fatal. Treatment approaches includes gene therapy, bone marrow transplantation and pharmacological approach. Though, various treatment approaches are available in order to keep the infant safe from the outer environment scientist came with a novel thought of keeping the baby in a bubble made of plastic.

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