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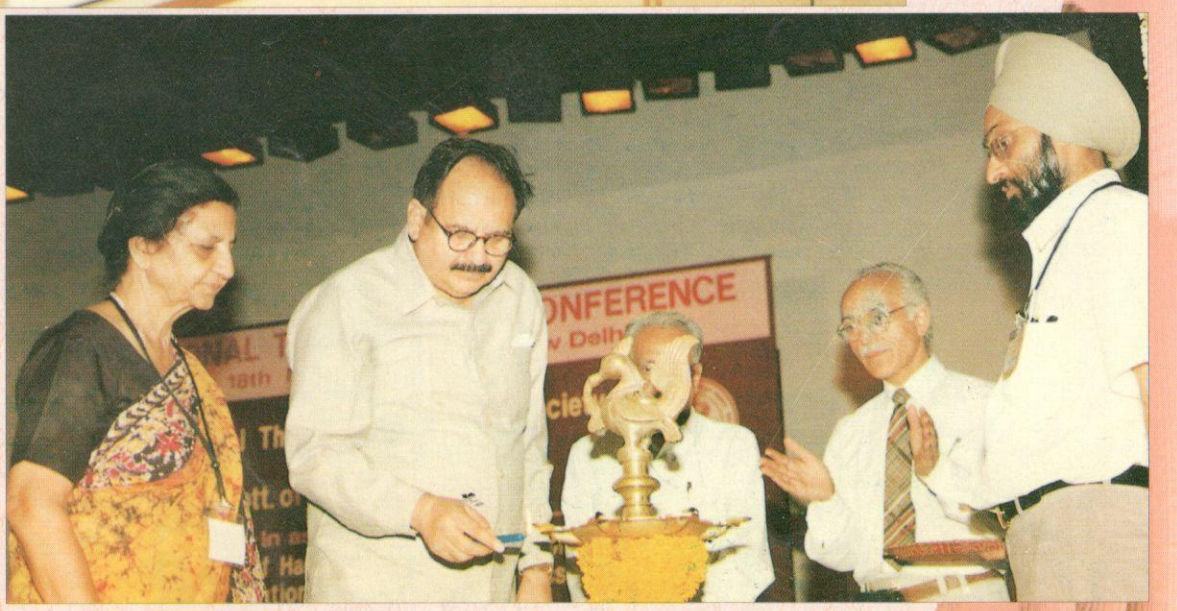
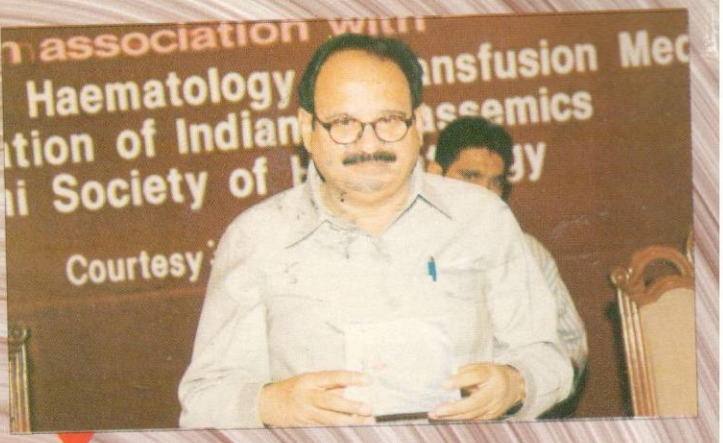


Hon'ble Minsiter of Health Govt. Of Delhi, Dr. Ashok Walia lightening the lamp to mark the inauguration of 4th National Thalassemia Conference

Address all correspondence to :
Dr. J.S. Arora, General Secretary, Federation of Indian Thalassemics,
KG-1/97, Vikas Puri, New Dehi-110018 Tel.: 25507483, 25511795 Fax : 91-11-5513576
Reliance Mobile : 31067011

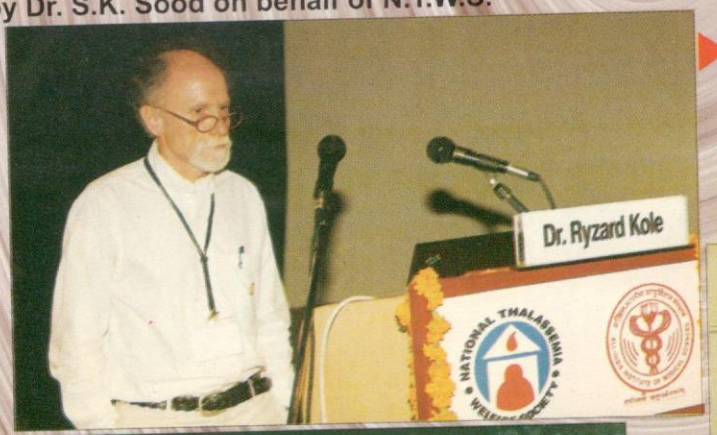
Minister of Health, Dr. Ashok Walia &
Dr. P.K. Dave (Director AIIMS)
alongwith Ms. Surrendar Saini & Dr. J.S. Arora
viewing the film "CHETNA" before its release.



Hon'ble Health Minister Govt. Of Delhi
Dr. Ashok Walia releasing CD of
Film "CHETNA" on Thalassemia Awareness.

Dr. M.B. Agarwal being honoured
with Dr. B.N. Dara Award
by Dr. S.K. Sood on behalf of N.T.W.S.

Mr. S.P. Ajmani & Dr. R.K. Marwah answering
the queries of audience on
"Wheat Grass Juice Therapy"



Dr. Ryszard Kole
Prof. at University of Carolina, USA
speaking on "Gene Therapy" in Thalassemia.

Jam-packed audience in the Conference.

Executive Members of various societies after F.I.T. Meeting

सम्पादकीय

ज्येष्ठ मास में जिस प्रकार मनुष्य एवं सभी पशु पक्षियों में मेघराज को देखकर उनके नेत्र चमक उठते हैं, कुछ ऐसा ही दृष्य चतुर्थ नैश्नल थैलासीमिया कान्फ्रेंस में भाग लेने आये थैलासीमिया बच्चों और उनके माता-पिता की आखों में देखा गया। एक के बाद एक डा॰ एम॰ बी॰ अग्रवाल द्वारा वर्णित ICL670C तथा Dr. Ryszard Kole द्वारा परिक्षित जीन थैरेपी रूपी बादलों की टोली जब डा॰ आर॰ के॰ मारवाह द्वारा अनुभवित गेहूं कोपल रस चिकित्सा तक पहुँची तो थैलासीमिक बच्चों को लगा जैसे मानसून आ गया।

लेकिन यह एक केवल Pre-mansoon shower ही था, क्योंकि डा॰ एम॰ बी॰ अग्रवाल के अनुसार ICL670C इस वर्ष के अंत तक उपलब्ध होने की आशा है। जीन थैरेपी अभी भी एक मरीचिका है, गेहूं कोपल रस को तो थैलासीमिक्स ने सच में एक मानसून की पहली बौछार मान ही लिया। यद्यपि डा॰ मारवाह ने अभी इसको खुलेआम प्रयोग करने की सहमति नहीं दिखाई और कहा कि इस पर अभी और अनुभव की आवश्यकता है तथा मशवरा दिया कि इसको केवल Haematologists की देखरेख में ही लेना चाहिए। उन्होंने एक विशेष बात कही कि इस चिकित्सा का लाभ दिखने में कम से कम 8 से 10 महीने लग जाते हैं अत: जिन व्यक्तियों में धैर्य तथा विश्वास हो उन्हीं को ही इसका प्रयोग आरम्भ करना चाहिए। तथापि यह हानिरहित एक घरेलू उपाय होने के कारण थैलासीमिक Parents ने इसे अपने बच्चों पर प्रयोग करने के लिए ठान ही लिया है। और उनके मुँह पर था 'कभी न कभी तो यह बादल बरसेगें'। हालांकि जिनके बच्चे बड़े थे अथवा उनमें कोई विकृति थी उनके होठों से कुछ ऐसा पढ़ा जा रहा था, जैसे कह रहे हों 'क्या करेंगे बरस के जब सूख जाएगा चमन'।

हीमैटोलोजी के विशेषज्ञों के अनुसार यह अब तक की सब से सफल कान्फ्रेंस थी। इस बात का अंदाजा इसी से लगाया जा सकता था कि हाल में बैठने की जगह बाकी नहीं बची थी, कुछ श्रोता खड़े हुये थे तो कुछ बालकोनी में चले गये थे। इस कान्फ्रेंस में इलाज की नई तथा तुलनात्मक आसान सम्भावनाओं की झलक से ऐसा प्रतीत होता है कि वह दिन दूर नहीं जब थैलासीमिया पर भी पूर्ण विजय प्राप्त की जा सकेंगी। अन्यथा कम से कम रक्तचाप अथवा मधुमेह रोग की तरह यह भी सरल चिकित्सीय हो जाएगा। अत: मेरी सभी थैलासीमिक बच्चों के माता-पिता से अनुरोध है कि वो इलाज में कोई कमी न छोडे। अब तो दिल्ली के लगभग सभी अस्पतालों में जैसे दीन दयाल उपाध्याय अस्पताल, लोक नायक अस्पताल, गुरु तेग बहादुर अस्पताल, कलावती सरन अस्पताल, आर॰ एम॰ एल॰ अस्पताल तथा चरक पालिका अस्पताल में मुफ्त Blood Transfusion और दवाईयों की व्यवस्था है। दिल्ली के बाहर चण्डीगढ़, जम्मू, अमृतसर तथा कुछ अन्य शहरों में भी काफी हद तक इलाज लगभग मुफ्त के बराबर ही है।

थैलासीमिक संस्थाएँ भी कुछ गरीब बच्चों के इलाज में सहायता करती हैं। जरुरत है तो सिर्फ इस बात की कि आप थैलासीमिया संस्था के साथ कदम से कदम मिला कर चलें।

डा॰ जे॰ एस॰ अरोड़ा

Editorial Board of National Thalassemia Bulletin intends to print directory of Societies working in the field of Thalassemia. Kindly send following information immediately:

1. Name, Address, Phone Nos. (Residence, Office, WLL, Cell), Fax and E-mail of Society, President and Secretary.
2. Transfusion Centre, Address, Phone No. and Name of Consultant with Phone No.
3. Blood Bank, Address, Phone No. and Name of Blood Bank Incharge with Phone No.

Gene Therapy of ß-Thalassemia

— *Ryszard Kole and Saovaros Svasti*
University of North Carolina, USA

Introduction

ß-thalassemia, a hereditary anaemia caused by defects in the ß-globin gene, is one of the most common genetic disorders in mankind. It affects populations in South East Europe, Middle East, China, Indian subcontinent and regions of South East Asia. Since the gene for ß-globin was one of the first cloned human genes there was early expectation that thalassemia and sickle cell anaemia will be the first disorders cured by the modern methods of molecular biology. Since cloning of the ß-globin gene tremendous progress was made in our understanding of the genetic nature and pathological mechanisms of the disease yet still more needs to be done before thalassemia is finally conquered.

The only cure now available for thalassemia is bone marrow transplantation. This treatment is limited by the scarcity of suitably matched donors and facilities and the high cost of the procedure. Moreover, even when available bone marrow transplantations carry significant risks. Thus, there is a need for other approaches, which even if not permanently cure the disease, lead to survival and improved quality of life of thalassemia patients.

Current treatment of severe thalassemia consists of regular, life-long blood transfusions. This procedure requires hospital visits and needs to be combined with iron chelation therapy, particularly bothersome for young patients (2). Although transfusions are not entirely satisfactory they did make a dramatic difference in the medical treatment of thalassemia. Nevertheless, faced with the above difficulties, the scientific community pursued a number of experimental approaches with goal to improve existing treatments. Recent progress in these efforts, particularly in gene therapy, gives reasons to be optimistic that better treatments for thalassemia will be found.

Gene Replacement Therapy

Since human ß-globin gene is small (approximately 1500 nucleotides) it was expected that replacing a defective gene with the correct one would be relatively easy. However, it was found that expression of the ß-globin gene is tightly regulated by a very large locus control region (LCR) and that available methods did not allow delivery of such a large fragment of DNA to the cells. Fortunately progress was made in both areas. The essential elements of the LCR were identified allowing removal of non-essential ones and reduction in the size of the construct required for proper expression of ß-globin. In addition, vectors that accept large fragments of DNA were obtained. The next hurdle, delivery of the constructs so that long term, appropriately regulated expression of ß-globin can be effected in vivo, was overcome by development of the vectors based on retroviruses and lentiviruses. Lentiviral vectors are particularly useful because they integrate into the genomes of haematopoietic stem cells. These accomplishments set the stage for recent experiments that showed the value of ß-globin gene replacement in a mouse model of thalassemia.

Sadelain and his co-workers developed transgenic mice that model thalassemia major or Cooley's anaemia. These mice exhibit pronounced anaemia with haemoglobin levels of 2-4 g/dL, splenomegaly and other symptoms typical of severe thalassemia. Fetal liver cells, a source of haematopoietic stem cells, were treated ex-vivo with lentiviral constructs that express normal human ß-globin and re-injected intravenously into the irradiated female recipients, establishing bone marrow chimeras. Remarkably, the levels of haemoglobin in the blood cells of most treated animals rose up to 12 g/dL of haemoglobin consisting of murine alpha-globin and human ß-globin subunits. Other pathologic indices also improved and remained at close to normal range for a period of 8 months. These results indicate that the lentiviral delivery of the ß-globin gene provide effective therapy, even in severe cases of thalassemia. It should be noted that the procedure, treatment of isolated stem cells and re-injection of the cells to the irradiated patient, is complex and in clinical application would require

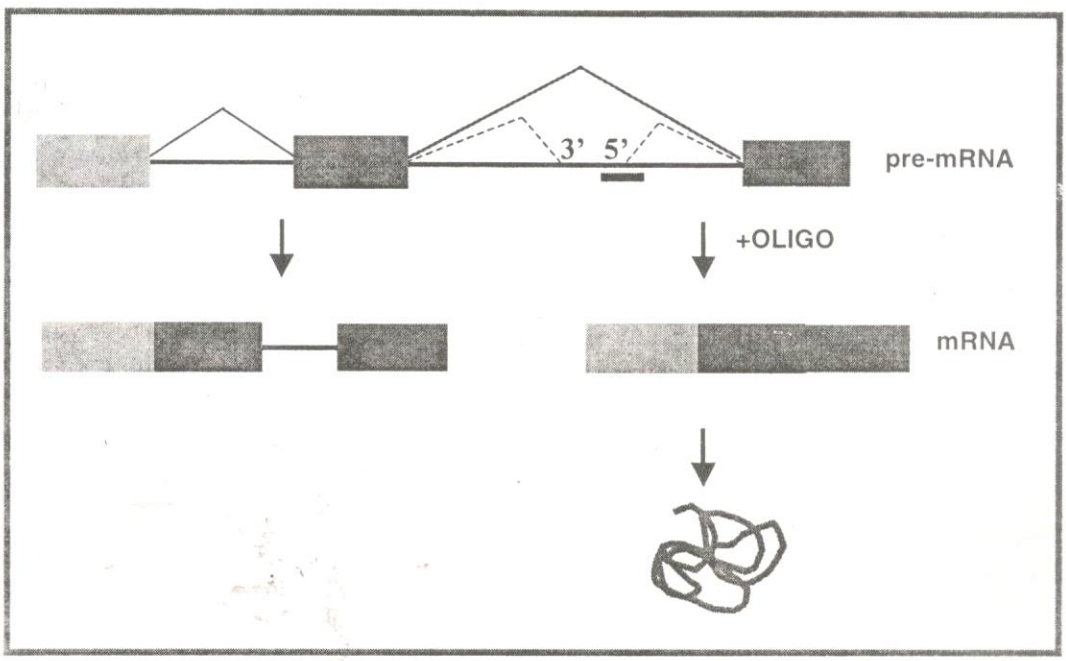
facilities similar to those needed for bone marrow transplantation.

RNA Repair Therapy

In this laboratory we are developing a form of gene therapy that, although not applicable to all types of ß-thalassemia, is simpler than gene replacement and promises direct treatment of thalassemia patients with antisense oligonucleotides. Antisense oligonucleotides do not require delivery vectors and can be used as drugs administered by injections and possibly orally.

Although ß-thalassemia is caused by close to 200 mutations affecting expression of the ß-globin gene, only 10 mutations are responsible for the majority of cases worldwide. Among those, some of the most frequent mutations cause aberrant splicing of the pre-mRNA transcribed from the defective human ß-globin gene. Our recent work focused on intron 2 mutations IVS2-654 (C>T), IVS2-745 (C>G) and IVS2-705 (T>G). These mutations activate aberrant splice sites within the intron, leading to inclusion of the intron fragment in the spliced mRNA. Inclusion of this fragment prevents proper translation of the resulting spliced mRNA, decreasing the levels of ß-globin and in consequence of haemoglobin, leading to thalassemia. Work in this laboratory has shown that blocking the aberrant splice sites with antisense oligonucleotides forced the splicing machinery to reselect the existing correct splice sites, restoring the correct splicing pattern (Fig. 1). The correction of splicing of thalassemic ß-globin pre-mRNA was accomplished in cell free extracts, in cell lines stably expressing the mutated ß-globin gene, and in erythroid mononuclear cells isolated from peripheral blood of ß-thalassemia patients.

The correction in erythroid cells from human patients has been achieved with the application of morpholino oligonucleotides. This type of oligonucleotide is resistant to nucleases and binds strongly to its complementary sequence within the target pre-mRNA. Because its backbone lacks negative charges present on inter-nucleotide linkages of DNA or RNA based oligonucleotides, its uptake and pharmacokinetic properties are expected to be different from those of standard oligonucleotides. We have found that morpholino oligonucleotides can be effectively delivered to cultured human primary erythroid cells from thalassemic patients by methods that temporarily distort the cell membrane ensuring its permeability to oligonucleotides. Under these conditions the morpholino oligonucleotides were more effective in repair of ß-globin pre-mRNA splicing than oligonucleotides with other backbones.



In more recent work we succeeded in delivering the morpholino oligonucleotides to the cultured erythroid cells from thalassemic patients without any adjuvant techniques. At high concentrations, the oligonucleotides restored correct splicing and expression of haemoglobin to the levels that approached 80% of normal. This was accomplished in erythroid cells from thalassemic patients with IVS2-654 and IVS2-745 mutations and in bone marrow cells from the

transgenic mouse model of IVS2-654 thalassemia. Thus, this oligonucleotide was able to penetrate the erythroid precursor cell membrane barrier, translocate to the nucleus and effectively rearrange the splicing machinery so that it reselected the correct splice sites. The results thus showed that the underlying molecular biology mechanisms and techniques operate effectively in early progenitors of erythroid cells, the very cells that need to be targeted during treatment of the patients. The level of correction was high such that if achieved during patient treatment it would be of clinical significance. The fact that bone marrow cells from the mouse model of IVS2-654 thalassemia responded similarly provided basis for pre-clinical animal studies now ongoing in this laboratory.

As pointed out above, the results showed that the correction of splicing of human ß-globin pre-mRNA is possible in appropriate target erythroid progenitor cells from thalassemia patients. If effective delivery of the oligonucleotides to bone marrow, the main site of erythropoiesis, could be achieved in vivo the procedure should be successful therapeutically. Thus, we focused on modifications of the oligonucleotides that improve their cellular uptake and biodistribution in the mouse model of thalassemia.

Based on the previous observations, in addition to morpholino oligonucleotides, we investigated oligonucleotides with peptide nucleic (PNA) and 2'-O-methoxy-ethyl (MOE) backbones. The PNA oligonucleotides are, similarly to morpholinos, uncharged while MOE oligonucleotides have negatively charged phosphorothioate backbone. In addition all three oligonucleotides were conjugated with positively charged peptides, e.g., four lysines, or with so called penetrating peptides tat and ant. This conjugation conferred positive charges to morpholino and PNA oligomers and reduced the negative charge of MOE compounds.

In vitro experiments showed that treatment of bone marrow cells from IVS2-654 mouse with peptide-conjugated morpholino oligonucleotides resulted in very effective, better than the other two backbones, correction of pre-mRNA splicing and restoration of haemoglobin levels close to 100% of normal. These compounds were used for in vivo experiments.

Intravenous injection of peptide-morpholino conjugates showed two days post injection an increase in correctly spliced ß-globin mRNA in bone marrow and in the liver of IVS2-654 mouse. More importantly, the peripheral blood from treated animals also contained correct ß-globin mRNA, the levels of which increased with additional time and subsequent injections. This indicated that the treated progenitor cells mature properly and are released from the bone marrow into circulation. Long-term experiments are underway and it is anticipated that under these conditions further accumulation ß-globin mRNA and haemoglobin will be observed.

In conclusion, the recent results of both, gene replacement and RNA repair experiments show effective restoration of haemoglobin expression in vivo in two different mouse models of ß-thalassemia. These very encouraging results set the stage for clinical trials of these techniques and drugs. Although each of the approaches has its own complications and limitations one can be hopeful that improved treatments for thalassemia will become available in not too distant future.

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बीटा-थैलासीमिया की जीन थैरेपी

बीटा थैलासीमिया एक ऐसा अनुवांशिक रोग है जिसमें ß-globin जीन की विकृति के कारण शरीर में खून की कमी पाई जाती है।

मनुष्यों में यह सबसे अधिक पाये जाने वाला अनुवांशिक रोग है। यह दक्षिण पूर्व यूरोप, मध्य पूर्व चीन, भारतीय उप महाद्वीप और दक्षिण पूर्व एशिया के लोगों में अधिक पाया जाता है। क्योंकि ß-globin जीन का प्रतिरूप (clone) बहुत जल्दी बना लिया गया था। अत: यह आशा की जा रही थी कि थैलासीमिया तथा Sickle Cell Anaemia की आणविक जीव विज्ञान द्वारा जल्द ही चिकित्सा की जा सकेंगी।

यद्यपि जीन की प्रकृति और रोग की विकृति जानने में काफी प्रगति हुई है फिर भी थैलासीमिया पर विजय प्राप्त करने से पहले अभी बहुत कुछ करना बाकी है।

अभी तक थैलासीमिया की पूर्ण चिकित्सा के लिए एक ही उपाय है "Bone Marrow Transplantation"। उचित Bone Marrow की कमी, अधिक खर्चा तथा अत्याधिक खतरा इस चिकित्सा को अंजाम देने में रुकावट पैदा करते हैं। अत: यह आवश्यकता महसूस की जाती है कि इस रोग का कोई पूरा इलाज निकाला जाये जिससे थैलासीमिया रोगी भी अपनी सामान्य आयु जी सके।

वैज्ञानिकों ने थैलासीमिया के कठिन और पीड़ादायक चिकित्सा से राहत पाने के लिए बहुत से प्रयोग किए। हाल ही में जीन चिकित्सा पर कुछ सफल प्रयास किये गये हैं।

जीन प्रत्यारोपण चिकित्सा

मानवीय ß-globin जीन बहुत छोटी होती है अत: यह आशा थी कि विकृत जीन को उचित जीन से बदलना आसान होगा।

Retroviruses तथा Lentiviruses सम्वाहक के द्वारा ठीक जीन को रक्त बनाने वाली नवजात कोशिकाओं में डाला जाता है। वैज्ञानिकों ने चूहे को थैलासीमिया रोग से प्रभावित करके उसका Hb 2gm से 4 gm तक ले आए तथा उसके अन्दर तीव्र थैलासीमिया के सभी लक्षण दिखाई देने लग पड़े। उसके रक्त जनक मूल कोशिकाओं को ऐसे Lentivirus से मिलाया गया जिसके अन्दर ठीक मानवीय ß-globin जीन थे। इस तरह प्रभावित कोशिकाओं को एक ऐसे चूहे में डाला गया जिसकी Bone Marrow को विकिरण से नष्ट कर दिया गया था। इस प्रयोग से थैलासीमिक चूहे का हीमोग्लोबिन 12 ग्रा॰ तक बढ़ गया। यह प्रभाव 8 महीने तक रंहा। यद्यपि इस प्रक्रिया में लाभ तो हुआ परन्तु यह एक कठिन प्रक्रिया है और इसमें B.M.T. के समान सुविधायें आवश्यक हैं।

RNA Repair चिकित्सा

डा॰ रिर्ज़ड कोल ने अपनी प्रयोगशाला में कुछ विशेष तरह के बीटा-थैलासीमिया को Antisense oligonucleotides के द्वारा ठीक करने का प्रयास किया है। Antisense oligonucleotides को एक दवा की तरह injection अथवा मुँह के द्वारा लिया जा सकता है।

यद्यपि बीटा-थैलासीमिया 200 प्रकार की जीन विकृति के कारण होता है तथापि केवल 10 प्रकार की जीन विकृति ही सबसे अधिक पाई जाती हैं। डा॰ कोल ने IVS2-654, IVS2-745 तथा IVS2-705 जीन को Antisense oligonucleotides से ठीक करने का सफल प्रयास किया है। एक प्रयोग में उन्होंने थैलासीमिक रोगियों की कोशिकाओं को oligonucleotides के द्वारा ठीक करने में 80 से 100% तक सफलता प्राप्त की है। इसी प्रकार IVS2-654 से प्रभावित चूहे में Morpholino oligonucleotides का injection लगा कर ß-globin जीन को ठीक करने का सफल प्रयोग किया है। समय और दवा की मात्रा बढ़ाने से और अधिक लाभ होते देखा गया है।

उपरोक्त प्रयोग यह दशतिं हैं कि वह समय दूर नहीं जब हम जीन थैरेपी से थैलासीमिया रोग की पूर्ण चिकित्सा कर पायेंगे।

सम्पादकीय

उपरोक्त प्रयोग यह दशतिं हैं कि एक दिन थैलासीमिया रोग भी असाध्य नहीं रहेगा, और थैलासीमिक रोगी भी उचित चिकित्सा द्वारा बिना रक्त संचारण के अपनी पूर्ण आयु भोग सकेंगे। लेकिन इसका पूर्ण लाभ केवल वहीं थैलासीमिक उठा पायेंगे जो पूर्ण चिकित्सा आने तक उचित समय पर रक्त संचारण द्वारा अपना हीमोग्लोबिन 10 ग्रा॰ से अधिक रखेंगे तथा लोह निष्कासक दवाओं द्वारा S. Ferritin लगातार 1000 ng/dl से कम रखेंगे।

4th National Thalassemia Conference

National Thalassemia Welfare Society organized 4th National Thalassemia Conference in collaboration with Dept. of Haematology, AIIMS, New Delhi at Jawaharlal Nehru Auditorium, AIIMS, New Delhi. NTWS had already organized 3 National level Conferences and a Seminar on Thalassemia & Deferiprone in collaboration with Dept. of Haematology AIIMS

Dr. Ashok Walia, Hon'ble Minister of Health, Govt. of NCT of Delhi, inaugurated the conference on 17th May' 03.

During his inaugural speech he said that 5.5% of Delhi's population is Thalassemia carrier and Delhi Govt. has taken effective steps for prevention and control of this disease. He said, "We are providing free Thalassemia Screening to all expectant mothers visiting antenatal clinics at our Lok Nayak, Guru Tegh Bahadur and DDU hospitals". He said that we intend to extend this facility at other Govt. Hospitals so that whole Delhi can be covered under this programme. He also informed that Delhi Govt. is providing free blood and chelating agents to Thalassemics at these hospitals.

Dr. Walia also released a Tele film "Chetna" on Thalassemia awareness produced by DHS (Directorate of Health Services, Govt. of Delhi) in collaboration with NTWS. The story is based on a healthy looking couple that happens to be a Thalassemia carrier, luckily their first child is not Thalassemia Major but a carrier. The film highlights the basic problems faced by Thalassemics and motivates the audience for pre-marital Thalassemia screening and voluntary blood donation. **Dr. A.K. Walia also spared enough time to see full 27 minutes film. He appreciated the efforts being put-up by NTWS & DHS,** and directed his officers to use electronic media to show this film at various platforms. **He also said that under Bhagidari Scheme, Delhi Govt. has associated with National Thalassemia Welfare Society and formed a "Thalassemia Cell" to monitor the above activities.**

Ms. Surrendar Saini, President, NTWS urged the Delhi Govt. to include Thalassemia in the list of Disabled. She also asked the Minister to start a comprehensive National Thalassemia Centre in Delhi where Thalassemics can have all facilities under one roof.

18th May 2003 was a day of surprises and joy for the Thalassemics. First they were glad to note that a new oral iron chelator is on the anvil when Dr. M.B. Agarwal, a renowned Haematologist from Bombay presented the results of the clinical trials of ICL 670C the new oral iron chelator. He mentioned that the new drug may have fewer side effects and be given just once a day orally.

Dr. M.B. Agarwal was honoured with prestigious Dr. B.N. Dara Award initiated by National Thalassemia Welfare Society. The award was conferred by Dr. S.K. Sood who is well known as father of Haematology in India. The award was 3rd in series; the first two awards have been conferred to Dr. Mammen Chandy and Dr. V.P. Choudhry respectively.

Thalassemics were overjoyed to hear the new indigenous developments in the treatment of Thalassemia, when Dr. R.K. Marwah, Prof. of Paediatrics, PGI, Chandigarh presented his talk. He said that Division of Haematology-Oncology Advanced Paediatric Centre PGIMER Chandigarh has 340 Thalassemics registered. Dr. Marwah cited an example of one Mr. Tarun Nanda, a Thalassemia Major from Ludhiana registered at PGI Chandigarh in 1983, who was getting blood transfusion since infancy. In Oct. 83 his BT interval was 26 days, which reduced to just 11 days in May 91 with Hb, maintained at 7-9gm/dl. Then he went under splenectomy and his BT interval raised to 25 days in June 91, which again came down to just 18 days by Feb. 99 with Hb maintained at 8-10gm/dl. After initiating wheat grass juice therapy in March 99 his BT interval again rose to 26 days in 1999 & 2000. Blood requirement further reduced to once in 44 days in 2001. As per our information lately he has not taken blood transfusion for the last 90 days and he is maintaining Hb between 10-12gm/dl.

He also gave reference of **Wheat grass juice in the treatment of active distal ulcerative colitis by** Dept. of Family Medicine, The Technion, Israel Institute of Technology. Ref: Scand J Gastroenterology Apr, 2002.

He said before starting trial he got approval from ethical committee of PGI Chandigarh. 60 patients with mean age 9.7 yrs ± 5.44 yrs (range 1yr – 21.5 yrs) were enrolled after informed written consent. Splenectomized & patients on Hydroxyurea were excluded. Patients themselves acted as control. Study was conducted from Sep. 2001-Oct. 2002. 7 months pre therapy and 4 months wheat grass therapy was considered for evaluation. Final analysis could be possible only in 44 cases. Response observed in 11 of 44 patients (25%). He concluded:

1. **Definite improvement observed**
2. **Success in some cases proven**
3. **Benefits apparent after at least 9 months of therapy**
4. **The results do generate enthusiasm; a need for a multicentric evaluation is obvious**

Around two years back Amit who is now 29½ years old and weighing 47 Kg was on regular blood transfusion every 2 weeks. Within 2 years of starting this therapy, his interval between two last transfusions has been increased to over 60 days with Hb maintained at 10.8gm/dl despite of the fact that he is not maintaining regularity in its use.

Then it was the turn of doctors and the Thalassemic parents who believe more in research in the west. Prof. Ryzsard Kole, Prof. of Medicine at University of Carolina, U.S.A. said that experiments with gene replacement have shown good results in mouse model of Thalassemia but this required irradiation of the patient similar to those needed for Bone MarrowTransplantation and there is always risk of radiation & vector related complications.

He said out of 200 mutations affecting beta Thalassemia gene only 10 mutations are common. He has worked on 3 mutations IVS2-654, IVS2-745 and IVS2-705. By repairing them with antisense oligonucleotides, he found correction in erythroid cells from Thalassemia patients. The results have been from 80%-90%. The antisense oligonucleotides can be used as drugs administered by injections or orally.

Both days The Hall was jam-packed. Over 600 persons participated. To everyone's surprise this was the most attended Thalassemia conference. Participants took keen interest during the Question-Answer session. The new developments have raised a ray of hope among the thousands of depressed & disheartened Thalassemics.

These new developments will boost the morale of Thalassemics and bring sense of bright future among them. It will also encourage them to effectively utilize the available facilities so that whenever the new developments are available for regular use they can be benefited.

At the end of the day every body left with a relief, joy, optimism and a new ray of hope at the end of tunnel.

Review of the conference by the participants/experts

DearDr. Arora,

The conference was very well thought out & executed, a very enjoyable experience. I was grilled by my patients as to the latest in therapy – a sure sign that you have to hold the next conference in Kolkata.

I thank you again for the warm hospitality and your keen interest in Thalassemia.

Yours sincerely,

(Dr. S. Chandra)

Dear Dr. Arora,

I enjoyed my stay in India very much. It was very touching to see how eagerly the patients are awaiting progress in our research. In this regard **I am pleased to tell you that since I came back we have detected repaired haemoglobin in the peripheral blood of the oligonucleotide treated IVS2-654 mouse. One more small step towards the treatment.**

The conference was excellent. Since I do not deal with medical issues on a daily basis it was very informative and instructive for me to hear the problems that the

contd. page 12

अन्तर्राष्ट्रीय थैलासीमिया दिवस 8 मई, 2003
मुख्य अतिथि यू0पी0 विधानसभाध्यक्ष पं0 केसरी नाथ त्रिपाठी
अध्यक्ष निशा यादव, सचिव डॉ0 आर0एन0 मेहरोत्तरा
एवं एस.सी.एफ. अनिरूद्व पाण्डेय, थैलासीमिया सोसाईटी ऑफ इण्डिया इलाहाबाद

थैलासेमिक सोसाइटी ऑफ इण्डिया, इलाहाबाद द्वारा आयोजित
'स्वास्थ्य एवं रक्त परीक्षण शिविर– में अध्यक्ष निशा यादव,
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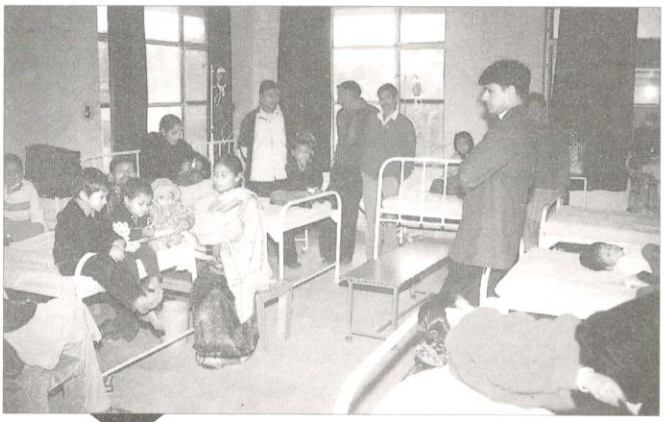
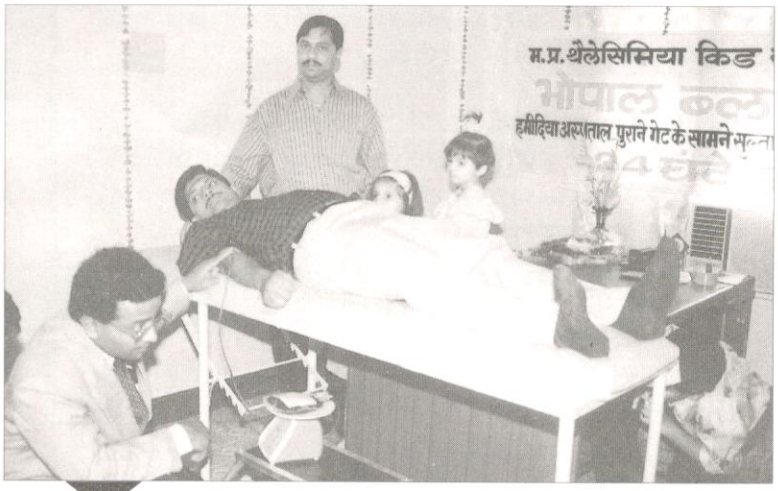


Thalassemia Clinic organised by Vivekanand Hospital & Research Centre on 4.4.03



Blood Donation Camp at Bhopal Blood Bank organised by M.P. Kid Care Society

A Thalassemia Tableau marching in the "Health Parade" Organised on World Health Day, the 7th April, 2003 by Directorate of Health Services, Govt. Of Delhi

Dance & Painting Competition organised by Ajmer Ragion Thalassemia Welfare Society

अन्तर्राष्ट्रीय थैलासीमिया दिवस 8 मई, 2003
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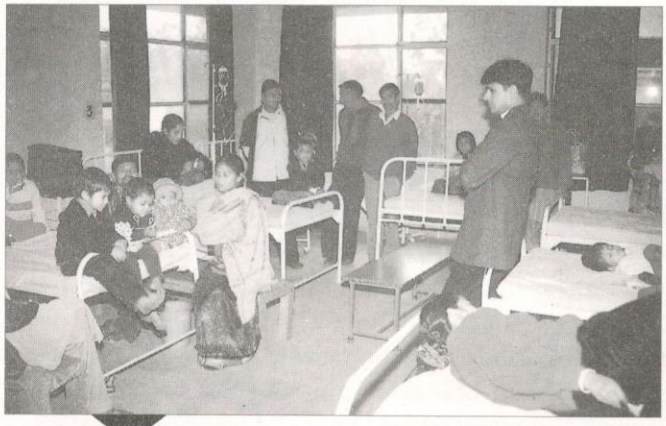

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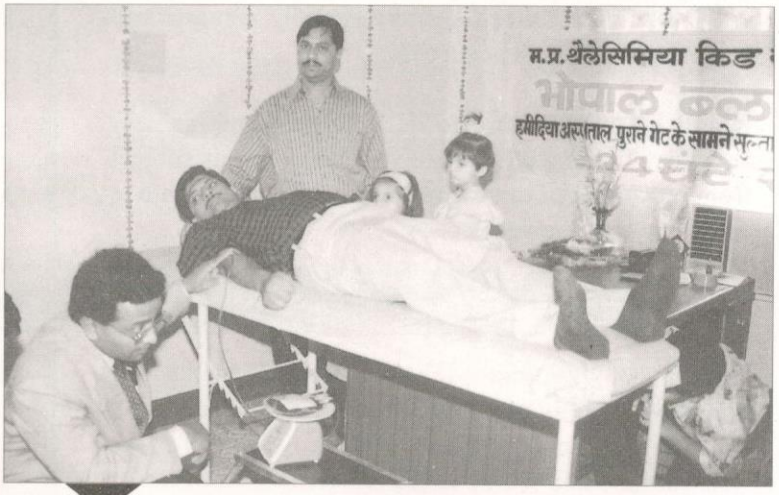

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patients and their doctors face every day. I congratulate you on the job well done and wish you best of luck in you future work. My best wishes and my heart go out to the patients as well.

With best regards,
Ryszard Kole

❖ ❖ ❖

Dear Dr. Arora,

I must mention it is one of the successful conference I ever attended. All lectures were above the marks, arrangements were wonderful. Everyone was very polite and helpful. It is really feather in your cap and conference was a great success.

It will be my pleasure to help Thalassemia society anywhere in the world as I have interest in this subject from beginning of my career. Kindly do not hesitate to write to me whenever necessary.

With kind regards,

Yours sincerely,
Dr. M.R. Lokeshwar

❖ ❖ ❖

Dear Dr. Arora,

Heartiest congratulations for a wonderful meeting. I also thank you for your kind hospitality. I am sure that this meeting would add to the enhanced treatment of Thalassemics and they would benefit in a big way.

With regards,
Dr. M.B. Agarwal

❖ ❖ ❖

Dear Dr. Arora,

My regards and best wishes. The Conference was indeed a grand success. The Society is doing great work under your able leadership. God Speed.

Your's sincerely,
Lt Col. (Dr.) D.K. Mishra

National Thalassemia Welfare Society

Well Done Mr. Jewesh Manuja – 2nd Consecutive Century

Once again Mr. Jewesh Manuja helped us in organizing "2nd Thalassemia blood donation camp" in collaboration with the Jail Road Shopkeepers Association and Anand Vihar Welfare Association at Suhag Banquet Hall, Hari Nagar on 8th June 2003. His efforts were so fruitful that in his second attempt he scored century and we could collect 130 units of blood. Red Cross team once again appreciated his arrangements and hard work in making the camp a super success. Now Jail Road Shopkeepers Association and Anand Vihar Welfare Association have promised us to hold at least one blood donation camp every year in the month of June. Once again 3 kudos to Mr. Jewesh Manuja.

Vikas Puri achieved one more milestone by organising two consecutive Blood Donation Camps on 15th and 16th June 2003. Credit goes to Dr. J.S. Arora, General Secretary, National Thalassemia Welfare Society for roping in as many organizations as possible in supporting the camp. The First in series i.e. 15th Thalassemia Blood Donation Camp was organized in association with Manav Avam Yog Seva Sansthan, Mianwali Voluntary Blood Donors' Association, Vikas Puri Main Market Association and KG-I Residents Welfare Association. 110 units of blood were collected. 2nd Camp in this series was organized on 16th June, 2003 on the occasion of "Shahidi Guru Purabh of 5th Sikh Guru, Guru Arjun Devji" at Gurudwara Guru Singh Sabha C-Block, Vikas Puri in association with Gurudwara Prabhandhak Committee. 55 units of blood were collected. Though it was first attempt yet it was very successful. Mrs. Neelam Kohli made special efforts in persuading the young devotees to donate blood for the noble cause. Dr. J.S. Arora gave a brief talk on Blood Donation to the audience in the Gurudwara.

Free Hepatitis B & C Screening Camp

Free Hepatitis B & C Screening Camp for Thalassemics was organized on Sunday the 13th July 2003 at National Thalassemia Welfare Society run Special Thalassemia

- To know level of awareness on the issue among CBO's, health organizations and community/ children.
- To know different parameters/factors that are responsible for severity of this disease in Kutch (social, economical, cultural)
- To identify gaps in the current mechanism of interventions on the issue of Thalassemia.
- To have effective networking with allied systems.

To have advocacy with government to undertake **Thalassemia Eradication Campaign** in high risky zones of Gujarat.

TASWELS, Orissa

Thalassemia & Sickle Cell Anaemia Welfare Society, Orissa observed International Thalassemia Day on 8th May 2003 at Shishu Bhawan, Bhubaneshwar. Sri Prafulla Chandra Ghadei, Hon'ble Minister, was the Chief Guest. Blood Donation Camp, Screening for Thalassemia in collaboration with RMRC, Bhubaneshwar, General Check-up of Thalassemia patients by Haematologist and a meeting were its major activities.

Amritsar Thalassemia Welfare Society

In the month of June, 2003, a deputation of the society consisting Shri Satnam Singh (President) and Shri Rajinder Singh Arora (Vice President) led by Mr. G.M. Pathak met Dr. Karnail Singh Professor and Head Dept. of Paediatrics, Govt. Medical College Amritsar and requested to allot a separate room for Thalassemia patient as Day Care Centre. The request was acceded to by the Head of Deptt. A hall in the Children Hospital of G.M.C. Amritsar was allotted for Thalassemia Day Care Centre. The society started its renovation at its own and completed the work by the end of the month.

The office bearers of the Amritsar Thalassemia society Shri Satnam Singh and Shri Rajinder Singh Arora also attended the 4th National Thalassemia Conference held in the A.I.I.M.S., New Delhi accompanied by Dr.Karnail Singh, Prof. & Head, Dept. of Paediatrics, Govt. Medical College, Amritsar, 17th-18th May, 2003.

On 5th June 2003, the Thalassemia Day Care Centre was inaugurated by Dr. P.S. Bedi, Principal, Govt. College, Amritsar. The Amritsar Thalassemia Welfare Society in association with the Dept. of Paediatrics, Govt. Medical College, Amritsar organized the programme. On the occasion Dr. Karnail Singh Prof. & HoD. of Paediatrics, Dr. (Mrs.) Karuna Thaper Asst. Prof., Dr. Pannu, Dr. Dhillon, Dr. Naresh Sharma, Dr. (Mrs.) Arora of the Paediatric Deptt., Dr. Jaya Deep Dept. of Blood Transfusion Medicines, Govt. Medical College, Nursing and paramedical staff, Thalassemia and other patients, parents of Thalassemic children, social workers, press reporters including Sh. Satnam Singh and Sh. Rajinder Singh Arora, Sh. G.M. Pathak, Gen. Secretary, J&K Thalassemia Welfare Society & other executive members of the Amritsar Thalassemia Society were present.

Dr. P.S. Bedi, Principal G.M.C. Amritsar in his address said that all required facilities would be provided for the care of Thalassemia patients by the G.M.C. in the care centre very soon with total treatment free of cost. Dr. Karnail singh & other also appreciated the Principal, Mr. G.M. Pathak and Dr. Jaya Deep requested the Principal to provide oral iron chelating medicine "KELFER" to the needy Thalassemia patients. Shri Rajinder Singh Arora thanked all the staff, members of the hospital for attending the function. Cold drink and light refreshment was served to all by the society.

Children's Corner

Abhinav Wadhwa made a sketch of Chief Minister, Smt. Shiela Dixit on the spot while inaugural address at St. Stephen's Hospital. He also made sketches on the entrance glass doors of Thalassemia ward at St. Stephen's Hospital. He is a keen artist and has won many drawing competitions. He has been awarded 'Kala Shri' Award in painting. He has won bronze medal at Nehru Bal Mela.

डा॰ के॰ के॰ कौल की भेजी गई टीम करती है जोकि बिल्कुल मुफ्त हैं। अर्थात् थैलासीमिया रोगियों का सारा उपचार बिल्कुल मुफ्त हैं।

8. J&K सरकार से हमारी सोसाइटी ने कड़े परिश्रम के बाद थैलासीमिया रोगी और एक Attendent को सरकारी बसों में मुफ्त सुविधा भी दिला रखी है।

9. Govt. Medical College, Jammu के प्रिसिंपल महोदय हमारी सोसाइटी के Patron हैं और मुख्य मंत्री जी Patron-in-chief। यह हमारा सौभाग्य है और इस college और अस्पताल के डाक्टर, स्टाफ, Paramedical staff और सोसाइटी का आपस में पूरा तालमेल और पूरा सहयोग है।

10. प्रिसिंपल महोदय ने हमारी सोसाइटी के लिए Medical Advisory Board बनाया हुआ है। डा॰ डी॰ बी॰ शर्मा, डा॰ कुम कुम शर्मा, डा॰ अशोक गुप्ता और डा॰ के॰ के॰ कौल इसके सदस्य हैं।

अब प्रिसिंपल साहब ने हमारी मांग पर थैलासीमिया रोगियों के लिए साल में कम से कम दो बार Cardiologist, Endocrinologist, Haematologist, Gastrocrinologist and nephrologist से consolidated total check up कराने के लिए कह दिया है।

हमारे देश की थैलासीमिया societies के लिए अभी बहुत कुछ करना बाकी है जोकि हमारे लिए एक challenge है। इसलिए तमाम societies से हमारी प्रार्थना है कि वह थैलासीमिया रोगियों के उपचार के लिए Awareness और Prevention के लिए और अधिक मेहनत करें। इससे ही रोगियों को normal life मिल सकती है और इस रोग की रोकथाम हो सकती है।

अजमेर रीजन थैलासीमिया वेलफेयर सोसायटी

अजमेर रीजन थैलासीमिया वेलफेयर सोसाइटी के तत्वाधान में अंतराष्ट्रीय थैलासीमिया दिवस के अवसर पर आज जोनल बल्ड बैंक ज॰ ला॰ ने॰ चिकित्सालय अजमेर में स्वेच्छिक रक्तदान शिविर का उद्घाटन डा॰ ए॰ के॰ सिंघल नियंत्रक एवमं प्रधानाचार्य ज॰ ला॰ ने॰ मेडिकल कॉलेज अजमेर के कर कमलों के द्वारा किया गया। उक्त अवसर पर डा॰ सिंघल ने थैलासीमिया रोग की रोकथाम हेतू समाज को जागरूक करने एवं रक्तदान के प्रति समाज में चेतना जगाने का आवहान किया साथ ही स्वेच्छिक रक्तदान हेतू प्रेरित करने वाली संस्थान का सेमिनार जून, 2003 में ज॰ ला॰ ने॰ मेडिकल कॉलेज के सानिध्य में कराने का आवहान किया।

श्री पारवानी ने बताया कि उक्त रक्तदान शिविर में 75 रक्तदाताओं के द्वारा रक्त दान किया गया जिसमें अधिकतर ज॰ ला॰ ने॰ मेडिकल कॉलेज के छात्रों के द्वारा रक्तदान किया गया। साथ ही 150 छात्रों का बल्ड ग्रुपिंग किया गया ताकि समय पर आवश्यकता पड़ने पर रक्तदान करवाया जा सके। उक्त स्वेच्छिक रक्तदान के प्रति जागरूकता पैदा करने का कार्य सोसायटी उपाध्यक्ष डा॰ महेश केसवानी एवं डा॰ विकास सक्सैना तथा छात्रसंघ के जनरल सैकेट्री कमलेश अग्रवाल एवं जितेन्द्र आहुजा के द्वारा किया गया।

श्री पारवानी के अनुसार शिविर का समापन डा॰ आर॰ के॰ चौधरी अधिक्षक ज॰ ला॰ ने॰ चिकित्सालय के द्वारा किया गया। इस अवसर पर डा॰ चौधरी ने थैलासीमिक बच्चों को बल्ड बैंक से निरंतर रक्त आपूर्ति करने का आश्वासन दिया। साथ ही इलाज की समस्त प्रकार की सुविधाएँ अस्पताल में मुहैया कराने का भी आश्वासन दिया। साथ ही आश्वस्त किया कि रक्तदान किया गया रक्त भी थैलासीमिक बच्चों को रक्त संचारण हेतू दिया जाएगा।

उक्त शिविर को सफल बनाने में इनर क्लब की भूतपूर्व सैकेट्री श्रीमति प्रतिभा गहलोत, श्री अशोक सैन, गिरधर शर्मा तथा सोसायटी के अन्य पदाधिकारियों ने भरपूर सहयोग दिया। ज॰ ला॰ ने॰ चिकित्सालय एवं मेडिकल कॉलेज के डा॰ आर॰ एल॰ सौलंकी, डा॰ महेश केसवानी, डा॰ नानक जेठानी (इनचार्ज बल्ड बैंक), डा॰ भरत छबलानी, वरिष्ठ तकनिशियन श्री श्यामसुन्दर शर्मा, आनन्द शर्मा एवं प्रकाश शर्मा ने रक्तदान शिविर में भरपूर सहयोग किया। सोसायटी ने यह भी निर्णय किया कि सभांग के टोंक, भीलवाड़ा एवं नागौर जिलों में भी थैलासीमिया बच्चों के रक्त संचारण हेतू रक्तदान शिविर आयोजित किया जायेगा।

Facts About Cricket

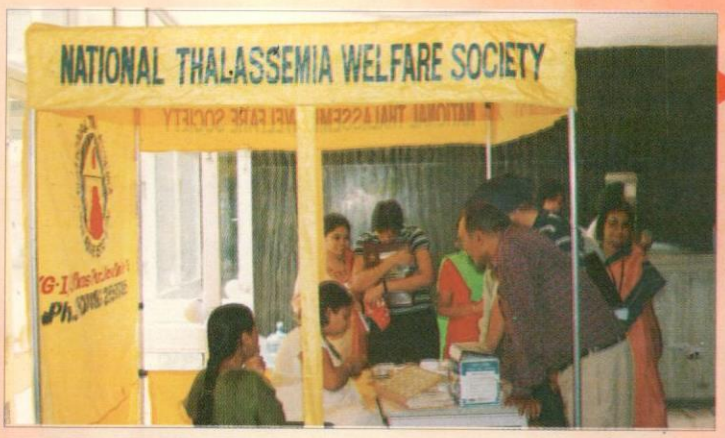
India refused to continue the match against Pakistan when Sarfaraz Nawaz bowled four successive bumpers and the umpire took no action. The game was at Sahiwal in 1978-79.

The first ODI in which 'wides' and 'no balls' were added to the bowlers' analysis was India vs. Pakistan at Jaipur on Oct. 2, 1983.

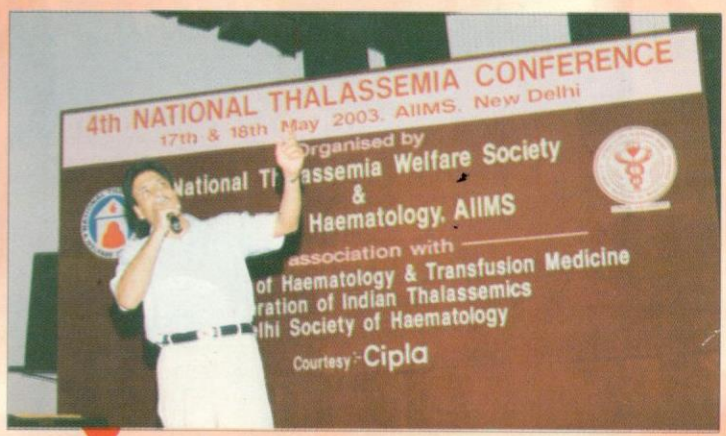
The match between New-Zealand and India at Auckland on February 14, 1981 was the first in New-Zealand in which coloured clothing, white balls and black sightscreens were employed.

25,000 spectators turned up to watch England play its first ODI match at Chandigarh. Unfortunately violent thunderstorm flooded the ground. In order to placate the crowd a 15 over game was staged in unplayable conditions.

P A de Silva refused to leave the field when given out "obstructed; field" in the Sri Lanka vs. New-Zealand match at Wellington in 1977. Under pressure the umpire was persuaded to reverse his decision.

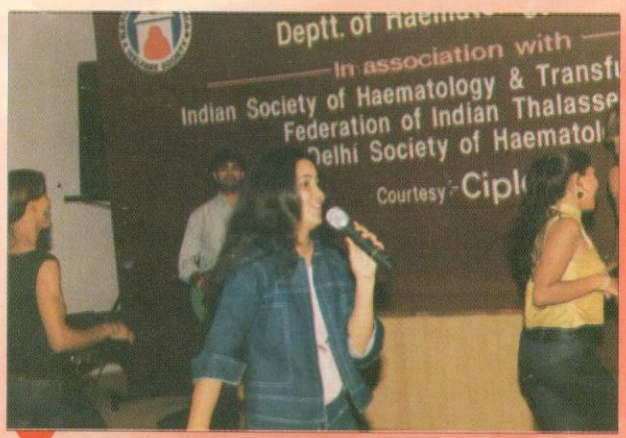


Serum Ferritin samples being taken at NTWS stall during the conference.

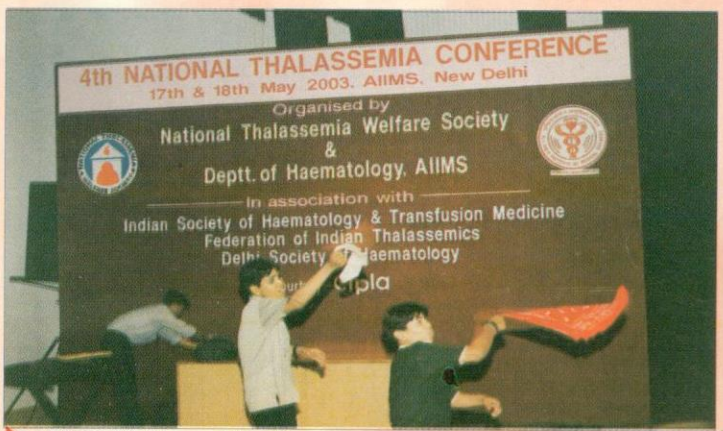


Dr. K.K. Kaul of Jammu mimickering as film actor Raj Kumar

Thalassemic children enjoying the Cultural Evening on Ist Day of the Conference.



M.T.V. Star Ms. Harsh Deep sang her numbers in the Cultural Evening on Ist day of the Conference.



Mst. Abhinav Wadhwa & Mst. Munish dancing on the floor

M.T.V. Stars Lucky Singh & Harshdeep with Mr. Gautam Seth & Dr. Arora enjoying the cultural evening on Ist day of the conference.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14 Jamshedji Tata Rd., Mumbai -400 020.(INDIA).
Tel.: 022 285 1111 Fax : 022 285 3720 / 022 204 7857