Haematology Research in India: Past, Present and Future

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Abstract Haematology research in India is relatively recent in origin. However the pioneers in the field not only did exemplary work when compared to advanced western countries, they also made it a point to develop centres of excellence and human resources for future of haematology work in this country. In this brief overview an effort has been made to give a taste of quality and expanse of haematology research in this country. This review does not claim to have described every bit of haematology research in this country. Our pioneers worked under extremely difficult and trying circumstances on a subject which was limited to funding available from Indian Council of Medical Research. Now the times have changed, several funding agencies in the country are able to provide substantial fund for research. Modern state of the art basic research institutions are tying up with medical colleges for good quality research and the seeds which our pioneers had planted have grown into a mighty tree. It would not be an exaggeration to say we are on the threshold of the golden era of haematology research in this country.

Keywords Haematology research · India · Nutritional anaemia · Haemoglobinopathy · Coagulation Disorders

Introduction

When one looks into the history of scientific research in any country, several facts stand out prominently.

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- (i) Good research work is possible only when a country is ready for one.
- (ii) Good research work is generated from a handful of research centers in any country.
- (iii) These research centers are usually directed by leading research workers and pioneers in the subject.
- (iv) Subsequently the able disciples trained in that center spread out elsewhere in the country expanding the vista of research.
- (v) Fruits of research finally reaches the common people either via industry –Institute co-operation or as in cases of medical research, Institutes may itself develop new advanced facilities to help common man.

Prof. J.B. Chatterjea was such a pioneer and he came at a time when the country had just come out of 200 years of British Colonial rule and was eager to develop itself and make a mark in the world of science. Bengali renaissance which was in the vanguard of Indian Independence struggle continued for some period even after independence, Haematology was a newly developing subject. Prof. J.B. Chatterjea made his center in Calcutta School of Tropical Medicine, a mecca for haematology learning and advanced research. After three decades of his pioneering research in haematology, he established himself as the father of haematology research in India. He had excellent knowledge of the subject, unparalleled ideas for research, leadership qualities to convert his ideas into action and last but not the least he was on a virgin territory of research which was developing over the last half a century.

The Pioneers

It will be seen that the haematology research centers in India which continued to deliver high quality research

work in the field of haematology were in the cities or centers where pioneers in this area worked or disciples of these pioneers developed new centers of excellence. The second oldest blood bank in the world was developed under Dr. U.C. Brahmachari at the present NRS Medical College Campus, Kolkata during second world war. Dr. Brahmachari's work in Kalazar is very well documented as was his association with School of Tropical Medicine where Prof. J.B. Chatterjea also worked.

Prof. C.R. DasGupta, Prof. J.B. Chatterjea represented the pioneers from Kolkata. Similarly Dr. Lucy Wills, Prof. J.G. Parekh, Prof. J.C. Patel worked on haematological problems in Mumbai. Prof. Selwyn Baker established a very good center at CMC, Vellore. Transfusion Medicine Research started at Bombay Blood Group Reference Centre (BGRC) under the aegis of Indian Council of Medical Research and under the leadership of Dr. H.M. Bhatia. National Institute of Nutrition did some pioneering work on Iron metabolism and continues to produce useful work in the same area.

The Pattern of Development of Haematology Research in India

Broadly research in medicine follows a similar path world over. A gifted physician first notices a patient with unusual disease or a cluster of patients with an unusual disorder, he/she does not stop at just describing the cases. These cases are investigated using the technology of that time in understanding its aetio-pathogenesis, causative agents, mode of spread/inheritance/prevalence in the community, means to manage these patients, development of new drugs etc. As the science progresses, successive generations of scientists look deeper into the problem. What appeared to be a single disorders/disease, under new investigations may show its heterogenous nature and the cause of this heterogeneity is sought again in the host/agent/environment. Hence the development of medical research looks something like this.

An- Unusual case/cases

Pathophysiologic/Aetiopathogenesis

Understanding of the case

New Mechanism of disease

Prevalence in the community

i. Means to control to the disease

ii. Screening technique

iii. Diagnostic technique

iv. Heterogeneity of the disease at the clinical/biochemical/
molecular level

v. Classification of the disease

Nature of Haematology Research in India: Past and Present

If we divide the era of haematology research in India as past (Pre 1980) and present (1980 till date). We will be able to see important changes in the emphasis of haematology research in India and around the world. It may be asked why have I taken 1980 as the watershed line to describe then and now?

Till 1980, most of the research in haematology the world over hardly included any molecular biology related work. Philadelphia chromosome was the hall mark of classical CML and detailed cellular mechanism by which Bcr-Abl oncogene worked was unknown. Bone marrow transplantation (BMT) as a therapeutic modality to treat serious haematological disorders was evolving; epidemiological data on various common haematological disorders, like nutritional anaemia, haemoglobinopathies etc. were mainly reported in the leading Haematology journals. Molecular targeted therapy and monoclonal antibody therapy was still a distant dream.

Indian haematologists were reflecting the similar trends in their research. Most of the write ups, conference presentations were on prevalence of common haematological disorders, interactions of nutritional deficiency and haemoglobinopathies, malaria, kala azar, microfilaria and other parasite related topics.

Myelodysplastic syndromes as new disease entity, classification of acute leukaemia by FAB criteria and its reproducibility, Immune dysfunctions caused by Iron deficiency anaemia, Vitamin B12/Folate biochemistry, Binding proteins of Vitamin B12 in different haematological disorders, evaluation of microchromatography for measurements of HbA2 compared to visual inspection/elution and measurement of HbA2 from electrophoresis strips, Cytochemistry in various types of leukaemias, marrow trephine biopsy in haematological disorders were the main areas of research in various Institutes in India. There were very little work on blood coagulation as the reagents were not easily available. One or two centers in the whole country were involved in some sort of coagulation research with home made reagents.

Post 1980 everything slowly changed. Published work in the area of thrombosis and haemostasis started increasing significantly. Allogeneic and autologous marrow transplantation data started coming out from few centers. The interest in work in the area of haemoglobinopathy, nutritional anaemia slowly dwindled. HIV infection finally arrived in our country and transfusion transmitted viral diseases became an important concern.

Increasing interest by young doctors to take up haematology and transfusion medicine started. Easy availability of large number of monoclonal antibody based reagents,

coagulation reagents and, molecular biology reagents made extensive research work possible in many Institutes around India. Several government funding agencies like Department of Science and Technology (DST), Department of Biotechnology (DBT), Indian Council of Medical Research (ICMR), Council of Scientific and Industrial Research (CSIR) funded large number of research projects in biomedical sciences. Some collaborative research work between scientists from reputed institutions in the west were also encouraged.

Glimpses of Research of Haematology (Pre 1980)

Nutritional Anaemia

Lucy Willis (1937) showed that nutritional megaloblastic anaemia can be treated by marmite [1]. Several Institutes were engaged in work on nutritional anaemia. I will not talk about the commendable amount of work done in School of Tropical Medicine under the leadership of Prof. J.B. Chatterjea as that had been chronicled elsewhere [2].

National Institution of Nutrition, an ICMR institute has done commendable work in the field of nutrition since its inception. Presently situated at Hyderabad this Institute has done extensive work on Iron absorption, Iron and other haemopoietic vitamins in various Indian foods. Dr. S.V. Apte, Dr. Srikantia and a series of workers worked on Iron reserves in the body. Some of the non haemopoietic consequences of Iron deficiency, role of vitamin A, other vitamins in Iron absorption [3], ergonomics of Iron Deficiency were also investigated at NIN.

Prof. S.K. Sood, at All India Medical Sciences, New Delhi under the able leadership of Prof. V. Ramalingaswami was studying the effect of protein deficiency in primate model [4]. Severe protein energy malnutrition was a real challenge to the paediatricians in India till 1980's hence it was not surprising to see this topic coming up again and again by many researchers of that time.

Clinically it was seen that many patients with Iron deficiency anaemia presented with recurrent infections and this needed to be studied at the level of a laboratory.

Prof. S.K. Saraya and his co-investigators along with young Dr. R. Chandra did their seminal work in this area [5]. Their work subsequently became a focus for many international studies and a multicentric study involving School of Tropical Medicine also. Their work focused on Immunoglobulin levels, changes of T&B lymphoid cells in nutritional iron deficiency and various infections [6]. Prof. J.C. Patel, Prof. B.C. Mehta studied various facets of Iron deficiency stretching over 3–4 decades and Prof. B.C. Mehta has now compiled his 40 odd papers on different facets of Iron deficiency in India in the form of a book [7].

Establishment of assays for folic acid and Vitamin B12 were a must to study these deficiencies in Indian population and as no easy assays were available at that time, time consuming and technically demanding microbiological assays had to be established in some of the centers to work in this area. School of Tropical Medicine, AIIMS, PGIMER, BARC, CMC Vellore, NIN are few such centers where such assays were available. The data on prevalence of these deficiencies in different Indian population groups came from those centres. Prof. Selwyn Baker and his group from CMC, Vellore made important contribution. They first showed that pigmentation over knuckles and other parts of the body occurs in nutritional Vitamin B12 deficiency [8]. He along with Prof. Mathan showed folate deficiency in idiopathic Tropical Malabsorption syndrome and did a very elegant epidemiologic study of that condition in an around Vellore. Later on Prof. Baker also described a simple technique to measure Vitamin B12 binding proteins but by that time he had left Vellore [9]. Prof. Bajpai from BHU showed association of Vitamin B12 deficiency with infantile tremor syndrome.

The original work on Vitamin B12 and folate deficiency for almost a decade originated from the department of haematology at PGIMER, Chandigarh under the able guidance and leadership of Prof. K.C. Das. He showed the very important contribution of folate coenzymes in transport of Vitamin B12 across the cell membrane [10–15]. Impact of dilantin in preventing the megaloblastosis was also demonstrated in the same lab. He devised a detailed Deoxyuridine suppression test to dissect mixed B12 and folate deficiencies in a test tube and unmarking of B12 & folate deficiency at biochemical levels in the presence of severe Iron deficiency. Another important classic observation made from this center was that lymphocytes remember past folate/B12 deficiencies long after these deficiencies were corrected. Based on his pre 1980 work later on he showed a spectrum of cytogenetic changes in lymphocytes at different time points after the B12/folate deficiency was corrected [15].

Coagulation Disorders

In India it was difficult to work on coagulation disorders before 1980's because of the nonavailability of the reagents required to study blood coagulation. However, inherited coagulation disorders, coagulation disorders due to liver failure, DIC, obstetric accidents, snake bites continued to confront the clinicians. Hence a lot of work on clinical description of these cases were seen. School of Tropical Medicine was one of the finest centers to learn blood coagulation and many of the leading haematologists of India did spend some time there. Prof. A.K. Basu, Prof. N.N. Sen who were trained on blood coagulation abroad

were available at School of Tropical Medicine and it gives me immense pride to say that Prof. J.B. Chatterjea's work was included in the Owen's biography of world's who's who of coagulation researches.

But what are the work in coagulation in pre 1980 era. Several workers from CMC, Vellore, PGIMER, Chandigarh, CMC Ludhiana worked on coagulation changes following snake bite. New factor VIII assay technique was introduced by Prof. K.C. Das [16] and factor IX assay technique by Prof. N.N. Sen at Oxford [17]. First case of antithrombin III deficiency was reported from the country by Dr. Dipika Mohanty in PGIMER, Chandigarh [18]. Prof. A.K. Saraya developed a technique of PF3 assay and described various types of thrombopathy using that technique [19]. He also described changes in platelet function in Diabetes [20] and Macroglobulinaemia [21].

Prof. B. Dube and his team at BHU, Varanasi was working on fibrinolysis in various disorders and comparative coagulation work in different animals. From Mumbai another stalwart in Haematology Prof. J.G. Parekh reported the first case of Von Willebrand Disease and Prof. B.C. Mehta reported an interesting results of spleen cell infusion in haemophilia [22]. This study has not been taken ahead any further. Technique for detecting antiplatelet antibody was adapted by Dr. Mohanty at PGIMER to study various thrombocytopenias [23].

Haemoglobinopathies

Prevalence work in haemoglobinopathies were conducted all over India by diverse groups, physicians, anthropologists, population biologists and so on. However, indepth study in this field was done by various workers in the School of Tropical Medicine and by Dr. Sukumaran at Wadia Children's Hospital in Mumbai. Mary Cut Bush showed for the first time the presence of sickle cell anaemia in India. Many new hemoglobinopathies were reported from the various part of the country. [24–27]. I am brief about the description of haemoglobinopathy research because, apart from finding certain new variants haemoglobin across the country, no other centres except the School of Tropical Medicine, Kolkata, did an in depth study of the biology of this disease. 'Prevalence studies were galore but in depth studies were few' summarises the state of haemoglobinopathy research of that time.

Haematological Malignancies and Hypoplastic Anaemias

Now a days these conditions occupy most of the working hours of a haematologist in practice. Pre 1980 era was handicapped in studying these disorders because of the lack of presently available tools and many of the drugs which

we now regularly use. However, like all other disorders prevalence of these disorders continued to be gathered from various places. Tata Memorial Hospital and Cancer Research Centre Mumbai contributed to major research work in this field.

What is very interesting and not often recognized that Prof. R.N. Roy who later on retired as the Prof & Director, Department of Medicine from Medical College, Kolkata was involved as a Rockefeller fellow in one of the earliest bone marrow transplantation programme involving cadaver marrow along with Hugh Chaplin Jr. [28]. Incidentally it may not be out of place to mention here that he also developed a technique of plasma haemoglobin measurement with the same boss [29] and the same technique is used till date.

Cytochemistry became one of the tools to classify or categorise acute leukaemias since Hayhoe and Quaglino (1964) published their MRC data on its utility in classifying leukaemia. In 1976 FAB classification of acute leukaemias was published and in India, several Institutes tried to present their leukaemia data based on FAB sub class and correlating them with cytochemistry [30]. Many of the haematologists who were stalwarts on nutritional anaemia research were looking after these leukaemia patients hence they superimposed their insight of nutritional anaemia research on understanding some of the leukaemia biology, this understanding resulted in demonstration of Deoxy Uridine suppression test which remains largely normal in acute erthro leukaemia where megaloblastic and dyserythropoietic features are common [31], showing that morphological megaloblastosis does not necessarily require defective B12, folate utilization, karyotyping became an important tool in understanding the biology of leukaemias. Chronic myeloid leukaemia provided the early cytogeneticists to study Ph' chromosome in this disease [32]. Prof. K.C. Das at Chandigarh combined his unique skills of autoradiography using ^{59}Fe and cytogenetics to show superimposition of radioactive iron granules with Ph' chromosomes in CML proving that erythroid and myeloid elements in CML descends from the same leukaemia progenitor. Subsequently monoclonal antibodies were used by Dr. DasGupta at Tata Memorial Hospital to classify some of the acute leukaemias and correlated them with existing cytochemistry [33, 34].

Prof. K.C. Das at PGIMER, continued to study the standard non banded karyotypes in acute leukaemias, chronic myeloid leukaemias. His cytogenetic study in multiple myeloma and macroglobulinaemia were published in "Blood" [35]. ^{59}Fe incorporation technique and reticulocyte count in exhypoxic polycythaemic mice was used as the bioassay for erythropoietin in various disorders including hypothyroidism and aplastic anaemia [36]. The work on hypothyroidism showing erythropoietin resistance is widely mentioned in the literature [37]. Prof. Das also used ^3H thymidine uptake in many of his research work in

haematology. It will be unfair if I do not mention his famous du suppression test which has enthralled many of his students. He initiated a study of antileukaemic drug sensitivity of leukaemic cells based on ^3H thymidine uptake. In addition his laboratory made extensive use of beta and gamma ray emitting radioisotopes to study many facets of different haematological disorders using ferrokinetics, red cell survival, autoradiography etc.

Research in Haematology Post 1980

In post 1980 era, haematology research in India have changed both qualitatively as well as quantitatively. This tempo accelerated several fold in post 1990s due to opening up of Indian economy and development of molecular biology technology for investigation of haematological disorders. There were development of new concepts for treatment of hitherto untreatable haematological disorders with use of BMT and recombinant protein molecules like G-CSF, GM-CSF, erythropoietin and other proteins. Development of apheresis technology, availability of interferon, large number of chemo therapeutic agents, emergence of monoclonal antibody therapy, improvement of management of cytopenias, development of new concepts of antileukaemic therapy by differentiation stimulating agents, emergence of the concept of molecular targeted therapy, unprecedented development in the technology in transfusion medicine and HIV infection changed the tempo and direction of haematology research. Haematology research became more and more specialized and increasingly institutes with strength in basic science entered the arena of haematology research in this country.

Nutritional Anaemia

Though nutritional anemia remained a substantial problem, the research in nutritional anaemia dwindled and a small number of research work in this area continued to be published from University College of Medical Sciences, Delhi by Dr. S.K. Sood and his group. Some studies on Vitamin B12 binding proteins were initiated at AIIMS and PGIMER Chandigarh. NIN at Hyderabad continued its study on the area of food fortification. Several interesting studies at PGIMER showed involvement of folic acid in microbial defense in experimental folic acid deficiency in the monkey model [38] and a sprue like syndrome was produced in monkey's by experimental folate deficiency. Meanwhile a hospital based study showed bleeding diathesis in nutritional megaloblastic anaemia [39] and platelet functional defect in Vitamin B12/folate deficiency [40]. A similar defects in platelet functions in nutritional iron deficiency was demonstrated from AIIMS New Delhi by

Dr. Saraya and his team [41]. Several studies showed nutritional deficiency in the back ground of unsuspected celiac disease but these studies were initiated by gastro enterologists and internists.

Hemoglobinopathy and Red Cell Enzymopathy

Haemoglobin electrophoresis as a tool to look for abnormal haemoglobin continued all over India in the same way as it was done before 1982. These activities were undertaken by diverse groups of people which included Haematologists, Biologists, Anthropologists etc. Many abnormal haemoglobins from various centers were reported. Haemoglobin E was reported from north western India [42]. However, the major contribution was detailed studies of haemoglobin S by Serjeant et al. in association with Prof. B.C. Kar from Orissa [43–45].

Institute of Immunohaematology started to contribute significantly in haemoglobinopathy research during this period, Dr. Colah (nee :Pavri) under the leadership of Dr. H.M. Bhatia developed Prenatal Diagnostic Technology for B-thalassemia using globin chain synthesis studies [46] later on they modified the technique based on DNA technology [47] and further simplified it in the favour of 2nd trimester diagnosis using cordocentesis and HPLC [48]. Several centers including one in Delhi and at CMC Vellore developed DNA technology based for prenatal diagnosis. One of the major development during this time is accumulation of robust data on the results of bone marrow transplantation on more than 300 patients from the haematology department of CMC, Vellore [49]. The availability of molecular biology technique lead to characterization of B thalassemia mutations [50] and the prevalence of alpha thalassemia prevalence in India [51, 52]. Several studies on transfusion transmitted viral infections were published during this period. Sickle cell anaemia continued to be studied in Gujarat, Maharashtra, Madhya Pradesh, Orissa and in South India by various groups, these are prevalence, detection and severity related studies [53] without in depth study to unravel the biology of the disease or how to alter it. Several aspects of research on G6PD and Pyruvate Kinase Deficiency was published during the period but unfortunately they all emerged from one or two Institutes in India [54, 55] which was most unlike more extensive interest in the area of haemoglobinopathies.

Haematological Malignancies and Aplastic Anaemia

Apart from many prevalence studies on various aspects of the disease that was published during this period several studies were published covering the cytogenetic data, molecular markers, results of different therapy, results of allogeneic and autologous stem cell transplantation from

various centers of the country. Tata Memorial Hospital, CMC Vellore, AIIMS were the premier Institutes which continued to publish their data.

However, basic medical research made significant contribution during this time. Institute of Chemical Biology at Kolkata reported several striking results using lectin from haemolymph gland of snails on ALL cells showing its possible therapeutic and diagnostic application and study on betel leaf also provided an agent with possible therapeutic use in CML [56, 57]. These products required further attention to develop them into applicable form. CMC Vellore also published their results on multicentric trials on indigenous arsenic compound on promyelocytic leukaemia patients. They also developed a HPLC technique with foreign collaboration to study plasma busulphan kinetics for conditioning therapy for marrow transplantation.

Technologically many Institutes like our own progressed in developing FISH, molecular cytogenetics, flow cytometry, minimal residue disease detection by RT PCR but no striking findings were made using all these advanced technology which could further understanding of these disorders which were already not known from Western Studies.

Transfusion Medicine and Immunohaematology

Institute of Immunohaematology was already well known all over the world for its discovery of Bombay Blood Group and In^a/In^b blood group system. It was also one of the leading centers in India which studied the biology of Rh isoimmunisation. It developed procedures of intrauterine transfusion and techniques to quantify the density of blood group antigens on red cells [58].

After the advent of HIV 1 infection transfusion medicine got extra boost and NACO funded for upgradation of many blood banks and research on prevention of HIV and transfusion transmitted hepatitis. Unfortunately research from various blood banks of India were mostly prevalence data. SGPGI Lucknow, did some study on Parvovirus seropositivity, CMV seropositivity in Indian population. Cryopreservation using standard technology was tried and used for preserving red cells and haemopoietic stem cells.

Technique to expand haemopoietic stem cells were also attempted from this Institute [59] successfully, however the applicability of these expanded stem cells have not been tested formally. Several small studies have been published in National Journal on the results of plasmapheresis for management of TTP and the Quality of pheresed platelets using various machine and techniques. Indepth investigation of red cell antigens using monoclonal antibody and, molecular biology has only been published from a single Institute [60–62].

Coagulation Research

Thrombosis and Haemostasis Research in India

I have taken 1980 as the watershed to divide the story into past and present. The reasons for selecting 1982–1983 as the watershed in the history of haemostasis research are several fold. The most important reason being establishment of Haemophilia Federation of India by late Mr. Ashok Verma, a patient with severe haemophilia. This organization subsequently established 70 centres all over the country. This society increased the awareness of congenital coagulation disorders. Meanwhile with more extensive availability of cryoprecipitate and factor concentrates from abroad, the hemophilia patients could get better treatment. Indian Council of Medical Research initiated a task force for the Collaborative study of Haemophilia, to collate some data on various aspects of haemophilia patients in India [63]. Around that time coronary artery by-pass surgery and subsequently coronary angioplasty, streptokinase therapy etc. for acute myocardial infarction became more extensively available, demand for coagulation studies in different parts of the country increased. Qualitatively in early 1980s patient care service in India started changing. Many corporate hospitals in Mumbai, Chennai, Hyderabad and subsequently in Delhi started coming up and they were often associated with state of the art laboratories which also included haemostasis laboratories. Thrombophilia started becoming an important problem and by that time in addition to antithrombin III, Protein C and Protein S deficiency factor V Leiden mutation as a cause of thrombophilia was also documented by Leiden Thrombophilia Group.

One of the major difficulties in starting a haemostasis laboratory in the past was the lack of availability of commercial reagents. Handful of laboratories which were doing coagulation research were preparing their own thromboplastin and APTT reagents. Over the years as the economy of India opened up to the external world, coagulation reagents from some of the best companies in the world became easily available in the market. In addition automated and semi automated coagulometers, which became easily affordable also contributed to spread of coagulation testing in the country. Another extremely important development in mid 1980's was the development of molecular biology techniques which reached the labs by early 1990s paving the molecular revolution in coagulation research.

However, with all these developments present day haemostasis research is also originating from few centers in India, though coagulation studies are more extensively available as a service from many government hospitals, corporate hospitals and private laboratories.

(a) Christian Medical College Vellore

Under the able guidance of Prof. Mammen Chandy, this centre has become one of the important centres of haemostasis research today. Several important aspects on the management of surgery in haemophilia, Von Willebrand disease, [64–66]; mutations in haemophilia B [67]; international studies involving Von willebrand disease [68], mutations in rare factor deficiencies [69, 70] originated from this centre. Indian Society of Haematology and Transfusion Medicine as well as Haemophilia Federation of India through this Institute and through active guidance of Prof Alok Srivastava runs a quality assurance programme for the country and this will improve the quality of the data that comes out of the haemostasis laboratories in this country. The centre also provides carrier detection and prenatal diagnosis facilities for haemophilia patients. This centre also highlighted the increased frequency of Glanzmann's thrombosthemia in South India.

(b) All India Institute of Medical Sciences

This centre continues to be an active centre in haemostasis research. Following Prof. A.K. Saraya, Prof. M. Bhargava continued her work in the area of haemophilia, von Willebrand disease. Presently Prof. Renu Saxena's major interest is in the area of thrombophilia research [71–75]. Prof. V.P. Choudhary has published work in the area of Von Willebrand disease [76], use of soyabean for platelet function defects. Prof. H. Pati, another illustrative worker in this field has published his work in the area of afibrinogenaemia and Budd Chiari syndrome. Prenatal diagnosis and carrier detection in hemophilia are now available in the Genetics department of the Institute with Dr. Madhulika Kabra as well as with Prof. I.C. Verma at Sir Gangaram Hospital, New Delhi.

(c) National Institute of Immunohaematology, Mumbai

It gives me immense pleasure and pride to summarise the work of this Institute in the area of hemostasis Research. Hemostasis Research was initiated in this Institute by the former Director Dr. Dipika Mohanty and myself with my colleague Dr. Shrimati Shetty. Dr. Mohanty came to this Institute with a wealth of experience in hemostasis research, which she gained from Hammer Smith Hospital, London and Oxford Hemophilia Centre. Dr. Mohanty and myself learned lot of our hemostasis work from Prof. K.C. Das's laboratory, where she was instrumental in establishing von Willebrand factor electro immunoassay, assay of platelet related immunoglobulin and initiated the work on hemostasis in leukemia [77] malaria [78]. We continued our work on hemostasis in malaria in the Institute [79] and initiated both functional and molecular biology studies both in the area of coagulation disorders as well as the thrombophilia. In association with Haematology department of KEM Hospital and Hemophilia Society (Mumbai Chapter), several studies on treatment of haemophilia were published [80–82].

Several new techniques to assay inhibitors, to study the effect of EACA on inhibitors, to show the VWF binding activity to factor VIII was established [83–86]. One of the most extensive work on thrombophilia was published from this centre [87]. Strong association of Factor V Leiden with Budd Chiari syndrome was also published from this center [88]. This centre was one of the first centres in the country to document in Intron-22 inversion in hemophilia A patients in the country.

One of the most extensive studies on Glanzmanns thrombasthenia with the mutations of GPIII gene was published from this centre [89–91]. It may not be out of place to mention here that Dr. Uma Khanduri from CMC Vellore first pointed this disease to be common in South India [92]. One of the major contributions of this centre is in the area of prenatal diagnosis where both molecular and phenotypic methods have been combined to be able to give the diagnosis for at risk foetus in almost all the patients [93–95].

Another area on which this centre has done phenomenal work is in the area of inhibitor formation in hemophilia patients. This centre was also one of the few centers in the world to point out that thrombophilia modifies the clinical phenotype of severe factor VIII or IX deficiency into milder one.

(d) Other Centres in India

Many other centers are coming up and are actively contributing to hemostasis research in India. Army hospitals are actively involved in the work of thrombophilia and high altitude complications. Many corporate hospitals like P.D. Hinduja hospital in Mumbai, Dr. M.B. Agarwal at the Bombay Hospital Medical Institute, Dr. Sunil Parekh at his clinic in Mumbai are actively contributing to hemostasis research. On the Eastern side of the country at the Institute of Hematology and Transfusion Medicine, Calcutta Medical College are doing some interesting work in platelet biology. Hemostasis work has been initiated in many other hospitals in India and they are going to come up in a big way in future. It is quite possible that I have missed a few centers which are conducting fruitful research in this area.

Discussion and Conclusion

In this short overview I have tried to develop a landscape of hematology research in India. Haematology research in this country is extremely indebted to the stalwarts of the stature of Prof. J.B. Chatterjea and others of his era.

Many of the research workers in the field of haematology were either direct students of Prof. Chatterjea or are student's students who have heard a lot and read a lot about this colossus of haematology research in our country without personally knowing him.

History of haematology research clearly showed the rise and fall of various centers of excellence over time. Disciples of Prof. Chatterjea migrated and opened up new centers of excellence in this field. Unfortunately very few centers have gone from strength to strength, mainly because many of the government institutes of research have fallen apart due to poor funding, lack of incentive, indecisiveness about future course of the institute and lack of a comprehensive roadmap for developing and retaining human resource. One of the most interesting finding of haematology research in India today is the increasing participation of basic biological scientists and scientists from various physical and information sciences to solve some of the intraceable problems of apoptosis, cell cycle, epistasis, epigenetics, structural biology, membrane biology which plagues some of the haematological disorders. Traditional medicine is also being increasingly explored in search of medicines for disorders which was hitherto fatal.

Kolkata has an immense potential to capitalize this modern wave. IICB, Bose Institute, Saha Institute of Nuclear Physics, Jadavpur University and Science of College of Kolkatta University have a large number of experts in various basic sciences. Our medical profession need to interact with these Institutes as well as with many renowned practioners of ancient Indian medicine with a view to bring this city in the forefront of haematology research in the country bringing the saga to a full circle and that will be our greatest guru dakshina to this doyen of haematology research in India. A beginning to this effect has already been made!

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