

A review on pathophysiology and treatment of aplastic anaemia

Jyoti Nayak*, Akanksha Singh, Sant Lal, Chetan K. Dubey, Pushpendra K. Tripathi and Shalini Tripathi

Department of Pharmacology, Rameshwaram Institute of Technology & Management, Lucknow, U.P., India

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ABSTRACT

Aplastic anaemia is a medical condition in which the bone marrow fails to make enough blood cells such as RBC, WBC & Platelets. It is mostly 2 types such as acquired and inherited and it is caused by exposure to chemicals (benzene and some carbmates), radiation (U.V), Drugs (Choramphenicol, carbamezepines etc), infection (virus) and immune disease. In aplastic anaemia diagnosis can be confirmed by bone marrow examination and it can be treated by immunosuppressive therapy, marrow stimulating agents and if aplastic anaemia is severe so used bone marrow transplantation.

INTRODUCTION:

Aplastic anaemia is a clinical syndrome in which the bone marrow is not capable to make enough blood cells.²

Where 3 types of blood cell is made:**Red blood cell:**

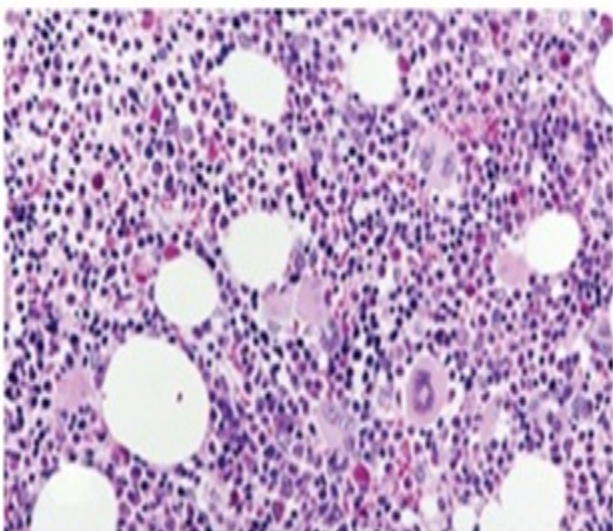
It is carry oxygen to the tissue from the lungs.

White blood cells:

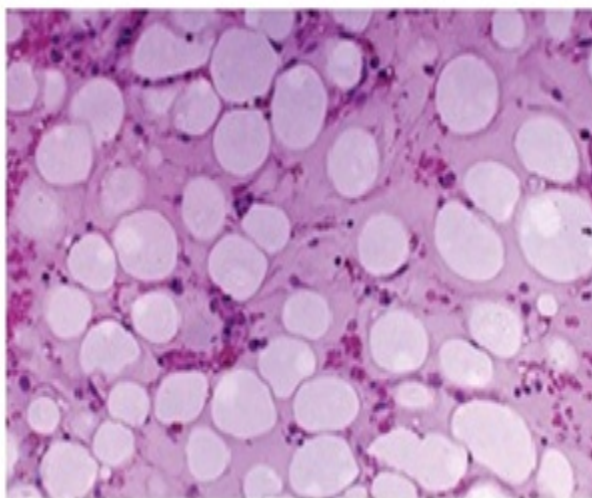
It is fight against infection

Platelets:

It is seal the damage blood vessels to prevent bleeding. These cells are made up by blood forming stem cell in the bone marrow. In this the stem cell are damaged and there are very few of them.^{2,5}



A. Normal marrow biopsy section
A normal marrow biopsy section of a young adult.



B. Marrow biopsy section of severe Aplastic anaemia
The marrow biopsy section of a young adult with very severe aplastic anaemia.

Figure1: (A) Normal marrow biopsy section. (B) Marrow biopsy section of severe Aplastic Anaemia

The specimen is devoid of hematopoietic cells and contains only scattered lymphocytes and stromal cells. The hematopoietic space is replaced by reticular cells (pre-adipocytic fibroblasts) converted to adipocytes.¹⁵

Aplastic anaemia is not a type of cancer but may be linked with certain cancer (Particularly those affect the bone marrow for Example Leukaemia) or Leukaemia Treatment. A small number of patients with aplastic anaemia may develop leukemia.

Aplastic anaemia may be inherited or acquired. Acquired aplastic anaemia is more common than the inherited type.

CAUSE OF APLASTIC ANAEMIA:^{22,26}

- Exposure to chemicals (Benzene)
- Drugs (Choramphenicol, carbamezepines, felbamate,

phytoin etc)

- Radiation (ultraviolet radiation)
- Infection (virus such as Non-A, -B, -C, -D, -E, -G Hepatitis Virus)
- Immune disease and heredity disease.

In aplastic anaemia, another cause of inherited aplastic anaemia is known as Diamond –Blackfan syndrome. In this red blood cell count is low, but the no. of other blood cell is normal. the a patient with D-B Syndrome, an increased risk of certain myelodysplastic syndrome, leukemia, bone cancer and colon cancer & in acquired aplastic anaemia is occur in adults , but the children also be affected.²⁰

TYPES OF APLASTIC ANAEMIA:

Table 1:

Sr. No	Types	Diagnosis	Cause	Treatment
1	Inherited	Bone marrow examination, red blood cell, white blood cell and platelets counts.	Fanconi anaemia, Dyskeratosis congenita D.B.syndrome	Immunosuppressive therapy Haemopoietic stem cell transplantation
2	Acquired Anaemia			
A	Immuno-haemolytic Anaemia	Red blood cell, white blood cell and platelet	Variety of extrinsic factor, antibody, mechanical factor direct toxic effect	Immunosuppressive therapy
B	Micro-angiopathic Haemolytic Anaemia	Bone marrow examination	Variety of extrinsic factor, antibody, mechanical factor direct toxic effect	Immunosuppressive therapy,antibiotic, haemodialysis
C	Haemolytic anaemia from direct toxic effect	Red blood cell, white blood cell and platelet	Variety of extrinsic factor, antibody, mechanical factor direct toxic effect	Immunosuppressive therapy, atagam
D	Drug induced haemolytic anaemia	Absolute reticulocyte count, serum haptoglobin Red blood cell count ,urine haemoglobin	Cephalosporins Dapsone, Levodopa Levofloxacin Methyldopa,etc	Immunosuppressive therapy,Special blood transfusion.

1. INHERITED APLASTIC ANAEMIA:

Anaemia is considered inherited. It is caused by gene mutations (abnormal copies of genes) that have been conceded from the parents to their child. Inherited aplastic anaemia is more common in children and young adults.³³

CAUSE OF INHERITED APLATIC ANAEMIA:

Fanconi Anaemia:

Fanconi anaemia is the most common form of legitimate aplastic Anaemia The most ordinary cause of inherited aplastic anaemia is called Fanconi Anaemia (FA). The many different genes can cause Fanconi anaemia. In order to get FA, a child must inherit to abnormal copies of one of these genes one from each parent. Someone with only one abnormal copy will not develop the disease and it is called a carrier.

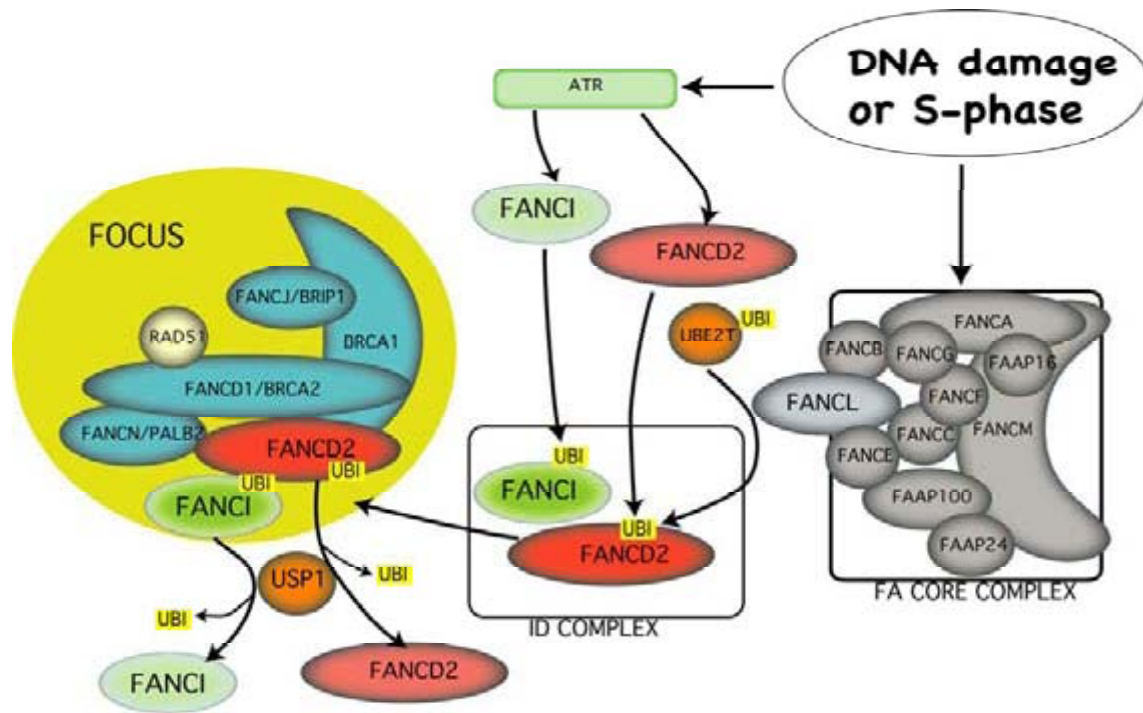


Figure 2: DNA damage response pathway, linking the FA and BRCA pathways.²⁷

A sequentially diagnose FA anaemia, a chromosome breakage test will be ordered. For this test, a small sample of blood is taken from the patient. After that some of the cells in the blood (the lymphocytes) are exposed to a certain chemical to see if it causes the chromosomes in the cells to break and rearrange. Chromosomes in normal cells are not damaged easily, but the chromosomes in Fanconi Anaemia cells will be damaged.²⁰

Dyskeratosis Congenita:

An additional inherited cause of aplastic anaemia is called Dyskeratosis Congenita (DC). Some of the genes are help to protect the chromosomes cause this disease. The chromosomes in our cells are fitted with caps at each end called. Telomerase is the protein that maintains the telomeres. Two different genes, are called TERC and TERT, are needed to telomeres make telomerase. An abnormal copy of either one of these genes can cause DC. Another gene, *DKC1*, makes a protein called dyskerin that is needed for telomerase to work.

Abnormalities in this gene also cause DC. Signs of this disorder include abnormal skin pigmentation, abnormal nails, and white patches in the mouth (called leukoplakia).⁷ The patient is likely to appear pale. If the anaemia progresses, decreased oxygen circulating in the blood may lead to an increase in heart rate and the sudden appearance of a new heart murmur.²⁶

2. ACQUIRED HAEMOLYTIC ANAEMIA:

It is caused by variety of extrinsic factor, namely antibody, mechanical factor direct toxic effect (in malaria/clostridial infection etc), splenomegaly & certain acquired membrane abnormalities. Most acquired aplastic anaemia (AA) is the result of immune-mediated destruction of hematopoietic stem cells causing pancytopenia and an empty bone marrow, which can be successfully treated with either immunosuppressive therapy (IST) or hematopoietic stem-cell transplantation (HSCT).

These includes below:

(A). Immunohaemolytic anaemia:

The Immunohaemolytic anaemia is a group of anaemia occurring because antibody production by the body against its own red cells.

Immune haemolysis in these cases may be induced by one of the following these types of antibody:

- 1-Autoimmune Haemolytic Anaemia.
- 2-Drug induced Immunohaemolytic Anaemia.
- 3-Isoimmune Haemolytic Anaemia

(B). Microangiopathic Haemolytic Anaemia:

It is caused by abnormality in the microvasculature. There are 3 different pathways by which Microangiopathic Haemolytic Anaemia results:

- Cardiac haemolysis
- External impact
- Fibrin deposit in microvasculature

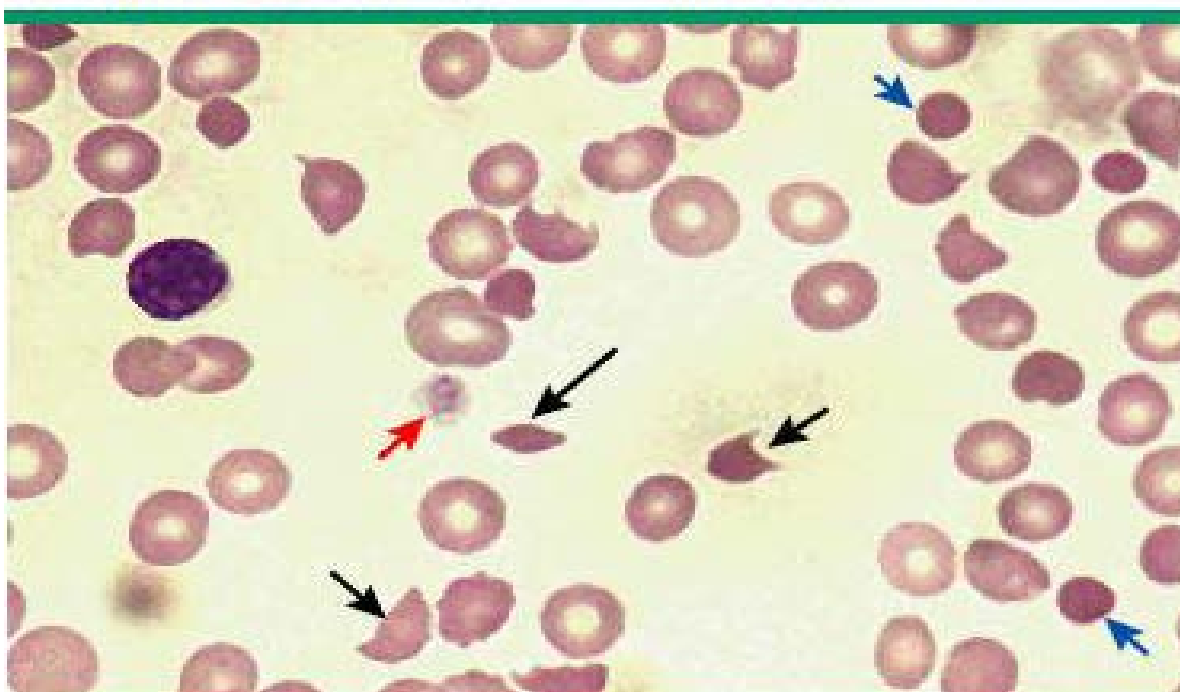


Figure: 3 Peripheral smear of Microangiopathic haemolytic anaemia showing presence of Schistocytes.¹²

Peripheral blood smears from a patient with a Microangiopathic haemolytic anaemia with marked red cell fragmentation. The smear shows multiple helmet cells (small black arrows), other fragmented red cells (large black arrow), microspherocytes are also seen (blue arrows). The platelet number is reduced the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction. Courtesy of carola von kapff,SH (ASCP).

(C). Haemolytic Anaemia From Direct Toxic Effect:

Agocyte the damage red cells.²⁰ **Haemolytic anaemia** occurs when red blood cells die sooner than the bone marrow can produce them. The scientific term for red blood cell destruction is **haemolysis**. There are two forms of haemolytic anaemia: **intrinsic** and **extrinsic**.

Extrinsic haemolytic anaemia develops when the spleen traps and destroys healthy red blood cells. **Intrinsic haemolytic anaemia** develops when the red blood cells produced by the body are defective.⁴

(D). Drug-induced haemolytic anaemia:

Drug-induced immune haemolytic anaemia is a blood

disorder that occurs when a medicine triggers the body's defence (immune) system to attack its own red blood cells. This causes red blood cells to break down earlier than normal, a process called haemolysis. Some drugs cause this type of anaemia such as Cephalosporin's, Dapsone, Levodopa, Levofloxacin, Nitrofurantoin, Nonsteroidal anti-inflammatory drugs (NSAIDs), Penicillin and its derivatives Drug-induced haemolytic anaemia is rare in children.³¹

CLINICAL FEATURE OF ANAEMIA:

Onset of aplastic anaemia may occur at any age and it is usually dangerous infection of mouth and lymph node and throat are generally present. The hemoglobin level at which symptoms and sign of anaemia develop depends upon 4 main factors

(1). The speed of onset of anaemia:

Frequently progressive anaemia cause more symptoms than the anaemia of slow onset. There is less time for physiologic adjustment.

(2). The severity of Anaemia:

Table 2:

Diagnostic Categories	Hemoglobin	Reticulocyte Concentration	Neutrophil Count	Platelet Count	Marrow Biopsy	Comments
Moderately severe	<10 g/dl	<40×10 ⁹ /L	<1.5×10 ⁹ /L	<50×10 ⁹ /L	Marked decrease of hematopoietic cells.	At the time of diagnosis at least 2 of 3 blood counts should meet these criteria.
Severe	<9 g/dl	<30.0×10 ⁹ /L	<0.5×10 ⁹ /L	<30.0×10 ⁹ /L	Marked decrease or absence of hematopoietic cells.	Search for a histocompatible sibling should be made if age permits.
Very Severe	<8 g/dl	<20.0×10 ⁹ /L	<0.2×10 ⁹ /L	<20.0×10 ⁹ /L	Marked decrease or absence of hematopoietic cells.	Search for a histocompatible sibling should be made if age permits.

NOTE These values are approximations and must be considered in the context of an individual patient's situation (In some clinical trials, the blood count thresholds for moderately severe aplastic anaemia are higher, e.g., platelet count <100×10⁹/L and absolute reticulocyte count <60,000×10⁹/L.). The marrow biopsy may contain the usual number of lymphocytes and plasma cells; "hot spots," focal areas of erythroid cells, may be seen. No fibrosis, abnormal cells, or malignant cells should be evident in the marrow. Dysmorphic features of blood or marrow cells are not features of acquired aplastic anaemia. Ethnic differences in the lower limit of the absolute Neutrophil count should be considered.¹⁵ Mild anaemia produced no symptoms or sign but a quickly developing severe anaemia may produce significant clinical feature.

(3). Age of patient:

The young patient owing to good cardiovascular reimbursement tolerate anaemia quite well as compared to the elderly patient develop cardiac & urbral symptoms is more significantly due to associated with cardiovascular disease.

(4). The Hemoglobin dissociation curve:

In anaemia, the affinity of hemoglobin for oxygen is depressed as 2, 3-BPG in the red cell amplified .as a result oxyhaemoglobin is dissociated more readily to discharge free oxygen for cellular use, causing a shift of the oxyhaemoglobin dissociation curve to the right.²⁰

SIGN & SYMPTOMS:^{20,24}

Only some sign and symptoms are common to all type of anaemia are as under

1. Whiteness: which may seen in the mucous membrane,

conjunctivae & skin.

2. Cardiovascular system: A hyperdynamic circulation possibly present with tachycardia collapsing pulse, congestive heart failure.

3. Central nervous system: In elder patient may develop symptoms referred to the CNS such as attack of faintness giddiness, headache and drowsiness.

4. Ocular appearance: In ocular appearance retinal hemorrhages may occur if there is associated vascular disease or bleeding diathesis.

5. Reproductive system: In reproductive system some Menstrual disturbance is occur such as amenorrhoea & menorrhagia and loss of libido are some of manifestation involving the reproductive system in anaemia subject.

6. Renal system: In renal system some sign and symptoms is occur such as mild proteinuria and impaired concentrating capacity of the kidney may occur in severe anaemia.

7. Gastrointestinal system: if anaemia is occurring in GIT some symptoms is occurs such as anorexia, flatulence, nausea, constipation & weight loss may occur.

8. Thrombocytopenia: (low blood count): in thrombocytopenia, leading to increased risk of hemorrhage, brushing, & petechiae.

9. Leucopenia: (Low White Blood Bount): In Leucopenia, leading to increased risk of infection.

PATHOPHYSIOLOGY:

(1). T-Cell Mediated Destruction of Bone Marrow

Recovery of autologous haematopoiesis in patients who failed to engraft after stem cell transplant and responsiveness to immunosuppressive therapies are the

major clinical evidences supporting an immune pathophysiology underlying acquired AA. Although a non-immune pathophysiology has been inferred from a failure to respond to immunosuppression, refractoriness to

therapy is also consistent with very severe stem cell depletion, a “spent” immune response, or immunological mechanisms resistant to current therapies.

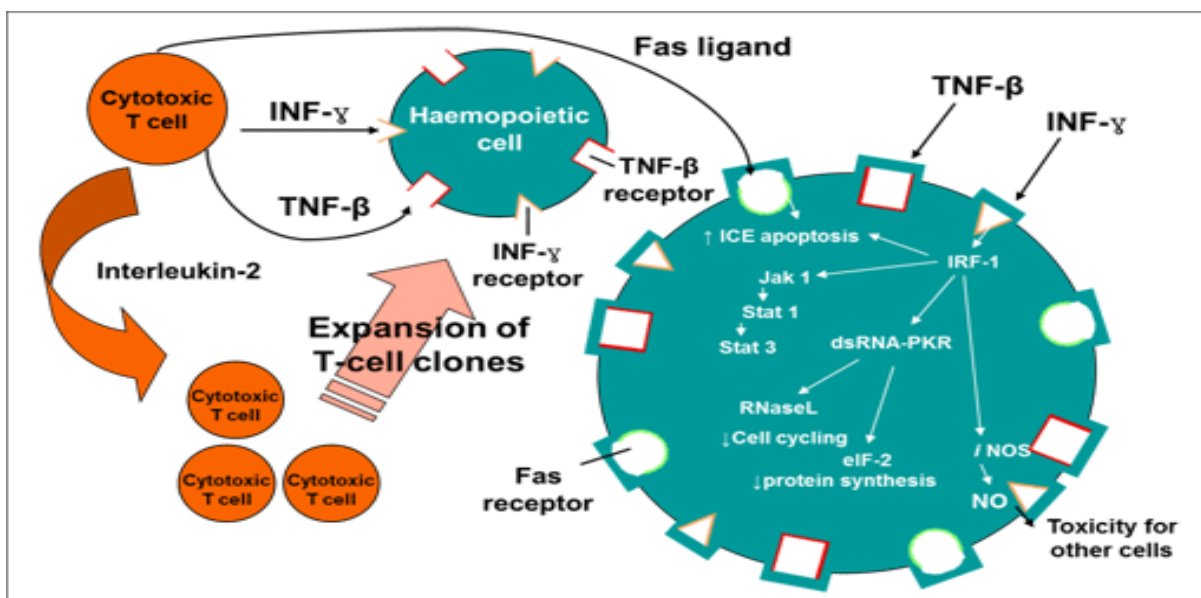


Figure 4: T-Cell Mediated Destruction of Bone Marrow

Removal of lymphocytes from aplastic bone marrows improves colony numbers in tissue culture, and their addition to normal marrow inhibited haematopoiesis in vitro.⁴⁴ The effector cells within the lymphocyte subset are activated cytotoxic T cells bearing a Th1 profile, expressing and secreting interferon-γ.³⁴

T-bet, a transcription factor that binds to the interferon-γ promoter region and is critical for Th1 polarization, is up-regulated in T-cells of patients with AA.³⁵ Specific CD8+CD28- cell clones are expanded in AA peripheral blood, as manifest by skewed usage of the Vβ repertoire; and oligoclonal recognize and induce apoptosis of autologous myeloid cells. Regulatory T cells, which control and suppress auto-reactive T cells, are decreased at presentation in almost all patients with AA.³⁷ In a mouse model of immune-mediated marrow failure, addition of T regulatory cells abrogated pancytopenia induced by the infusion of lymph node cells.⁹

Why T-cells are activated in AA is unclear. HLA-DR2 is over-represented among patients, suggesting a role for antigen recognition, and its presence is predictive of a better response to cyclosporine.^{25,28} Polymorphisms in cytokine genes, associated with an increased immune response, also are more prevalent, such as for tumor necrosis factor-α (*TNF2*) promoter at -308.10 interferon-γ¹³ and interleukin 6 genes.¹⁷

These alterations in nucleotide sequence and in gene regulation suggest a genetic basis for aberrant T cell activation in bone marrow failure.

DIAGNOSIS:

In aplastic anaemia the diagnosis is confirmed by bone marrow examination and red blood cell, white blood cell and platelets counts.

The following tests aid in determining differential diagnosis for aplastic anaemia:

Bone marrow aspirate and biopsy: to rule out other causes of pancytopenia (i.e. neoplastic infiltration or significant myelofibrosis).

History of iatrogenic exposure to cytotoxic chemotherapy: can cause transient bone marrow suppression

X-rays, computed tomography (CT) scans, or ultrasound imaging tests: enlarged lymph nodes (sign of lymphoma), kidneys and bones in arms and hands (abnormal in Fanconi anaemia)

Chest X-ray: infections

Liver tests: liver diseases

Viral studies: viral infections

Vitamin B₁₂ and folate levels: vitamin deficiency

Blood tests for paroxysmal nocturnal haemoglobinuria.

This **physical examination** can reveal tenderness in the abdomen as well as a swollen liver.³⁹

Blood Transfusion:

A blood transfusion is given to quickly increase your red blood cell count and to replace destroyed red blood cells with new ones.

Intravenous Immune Globulin:

A low blood cell count can negatively affect the way your immune system fights infection. You may be given **immune globulin** through an IV in the hospital to improve your immune system function.

Corticosteroids:

In the case of an extrinsic form of hemolytic anaemia of autoimmune origin, corticosteroids are used to stop your immune system from making antibodies that destroy red blood cells.

Surgery:

In severe cases, your spleen may need to be removed.

TREATMENT:

In treatment of aplastic anaemia are as under:

A. General management: in aplastic anaemia firstly identify the causative agent and then eliminate the possible cause.

B. specific treatment: it includes below-

Marrow stimulating agents: the marrow stimulating agent such as androgen.

C. Bone marrow transplantation: it is used in severe case under the age of 40 year.

Immunosuppressive therapy: In immunosuppressive therapy with agent such as anti-thymocyte globulin and anti-lymphocyte serum has been tried to 40-50% success rate. Horse anti-thymocyte globulin (ATGAM (R); h-ATG) is the only drug approved by the Food and Drug Administration for the treatment of AA. While it is generally believed that h-ATG administration leads to depletion of immune competent cells, its exact mechanism of action remains unclear.⁴² H-ATG preparations contain a variety of antibodies recognizing human T-cell epitopes, many directed against activated T-cells or activation antigens.⁶

Aplastic anaemia treatment guideline:

Investigations:

Complete Blood Count with differential Reticulocyte count

Peripheral blood smear examination

Bone marrow aspiration and biopsy

Bone marrow cytogenetic study

Flow cytometry for GPI-anchored proteins

Vitamin B12 and folate level

Liver function test

Viral studies : Hepatitis A, B and C, EBV, HIV

Antinuclear antibody and anti ds DNA

Chest X-ray

Abdominal ultrasound (optional)

Cardiac echocardiogram (optional)

Peripheral blood chromosome breakage analysis to exclude Fanconi anaemia or peripheral blood gene mutation analysis for Dyskeratosis congenita if clinical features.³

AYURVEDIC TREATMENT OF APLASTIC ANAEMIA:

In aplastic anaemia Ayurvedic herbal treatment can be thoughtfully utilised to effectively treat and cure patients affected with aplastic anaemia.

Herbal medicines have a dominant effect on the bone marrow and stimulate it to start producing normal red blood cells, white blood cells and platelets.

This process usually takes three to six months, and the time of period is depending upon the immune status and overall physical condition of the affected individual. The majority of affected individuals usually go into a complete remission within six months of starting Ayurvedic herbal treatment.

Mostly affected individuals do not require blood transfusions after three to four months of commencing Ayurvedic treatment. Once the blood picture comes to a complete normal, medicines which are initially given thrice daily can then be gradually reduced to twice daily for a few months and once daily for another few months, and then stopped completely. This gradual tapering of medicines helps in bringing about a prolonged remission of affected individuals for the treatment of aplastic anaemia. This disease, which is considered currently incurable and has a high mortality rate, can be treated quite satisfactorily with the help of Ayurvedic herbal medicines. This is probably a major contribution of Ayurveda in the treatment of a serious medical condition like aplastic anaemia.¹

List of Herbal Plants Which Is Used In Treatment of Aplastic Anaemia ⁴¹

Table 3:

S.No	PLANTS NAME	WORK	DOSE
1.	Spirulina, or blue-green algae	It is used to suppress the immune system	1 Heaping tsp. per day
2.	Alfalfa (<i>Medicago sativa</i>)	It is used to fortify and cleanse the blood	1 tsp in one cup of water
3.	dandelion(<i>Taraxacum officinale</i>), yellowdock (<i>Rumex crispus</i>)	It is used to fortify and cleanse the blood, it may be help to bring level of haemoglobin in normal range	1 tsp in per cup of water, in root for 20 min. & leave for 5 min.
4.	Gentian(<i>Gentiana lutea</i>)	It is used to stimulating the digestive system.	1tbs. about a half hour before eating.

SOME OTHER HERBAL MEDICINE USED IN TREATMENT OF APLASTIC ANAEMIA:

Medicines like Arogya Vardhini, Punarnavadi Mandur, Panch-Tikta-Ghrut-Guggulu, Laxadi Guggulu, Laghu-Malini-Vasant, Heerak Bhasma and Abhrak Bhasma are used to stimulate the bone marrow function. In addition, medicines which act on the "Rakta" and "Majja" dhatus (tissues) of the body are also used, as these again act on

the metabolism regulating bone marrow production. These medicines include Manjishtha (*Rubia cordifolia*), Saariva (*Hemidesmus indicus*), Patha (*Cissampelos pareira*), Musta (*Cyperus rotundus*), Kutki (*Picrorrhiza kurroGuduchi* and Amalaki (*Embilica officinalis*).¹ Plants used in treatment of aplastic anaemia such as *Tinospora Cardifolia*, *aizadirecta indica*, *Embilica officinalis*.³⁸

FOLLOWING PLANTS ARE USED TO TREAT APLASTIC ANAEMIA:



Tinospora cordifolia

Embilica officinalis

Azadirachta indica

Figure 4: Name of the plants

ALLOPATHIC TREATMENT OF APLASTIC ANAEMIA:

In allopathic treatment of aplastic anaemia, the immune system effect are achieved by daily medicine intake or in more severe cases used bone marrow transplants.²⁴ In this transplanted bone marrow replaces, a potential bone marrow cell with a new one from a matching donor. The multipotent stem cell in the bone marrow reconstitutes all three blood cell line, than giving the patient a new immune system, red blood cells, and platelets. But, also the risk of graft failure, there is also a

risk that the newly created white blood cells may attack the rest of the body. In Medical therapy of aplastic anaemia frequently includes a short course of anti-hymocyte globulin (ATG) or anti-lymphocyte globulin (ALG) and several months of treatment with a cyclosporine is modulate the immune system. In this used mild chemotherapy agents such as cyclophosphamide and vincristine it is very effective. Another therapy, such as targets T-cells, ATG, It is believed to attack the balsone marrow. Steroids is generally unsuccessful, although are often

used to combat serum sickness and it is caused by ATG use. One potential study involving cyclophosphamide was terminated early due to a high incidence.⁴⁰

In the past, before the above treatments became available, patients with low leukocyte counts were often confined to a sterile room or bubble.³⁰

MEDICINES USED IN ALLOPATHIC TREATMENT OF APLASTIC ANAEMIA:

Table 4:

S.No.	MEDICINES	WORK	DOSE
1.	Leukin	It is a form of a protein that stimulates the growth of white blood cells in your body.	iv-200mcg/day, for 14 day
2.	Atgam	Atgam is a lymphocyte-selective immunosuppressant; it is used to prevent organ rejection during transplantation.	10 to 20 mg/kg daily for 8 to 14 days.
3.	Filgrastim	It stimulates the production of Neutrophil (WBC).	5 Mcg/kg/day,daily ,up to 2 weeks.

SIDE EFFECT OF ABOVE DRUGS:

LEUKIN:

Side effect:

- White patches or sores inside your mouth or on your lips.
- Easy bruising, unusual bleeding (nose, mouth, vagina, or rectum), purple or red pinpoint spots under your skin.
- Swelling, rapid weight gain.
- Chest pain, fast or uneven heart rate.
- Weakness or fainting.
- Black, bloody, or tarry stools.
- Coughing up blood or vomit that looks like coffee grounds.
- Painful or difficult urination.
- Dark urine, clay-colour stools, Jaundice (yellowing of the skin or eyes).
- Breathing problems; problems with vision, speech, balance, or memory

ATAGAM:

Side effect:

- **Gastrointestinal** - Diarrhoea, nausea, vomiting, rectal fissure and mouth ulcer.
- **Musculoskeletal** - Joint pain and back pain.
- **Respiratory** - Difficulty in breathing and abnormal breathing sound.
- **Heart** – Chest pain and low blood pressure.
- **Skin** - Rash, itching and hives.
- **Miscellaneous** - Fever, chills, decrease in white blood cells/platelet counts and pain at injection site.

FILGRASTIM:

Side effect:⁸

- **Most common**-mild to moderate bone and muscle pain and allergic reaction.
- **CNS**-Dizziness, fatigue and headache.
- **Skin**-Rash, hair loss, inflammation of blood vessels in the skin, redness or swelling in the site of injection.
- **Gastrointestinal** –Nausea, mouth ulcer loss of appetite, diarrhoea.
- **Respiratory**-Shortness of breath, trouble breathing.

SOME OF THE MEDICINES LINKED TO APLASTIC ANAEMIA INCLUDE:

- Non-steroidal anti-inflammatory drugs (NSAIDs). Medicines used to treat pain and inflammation. Examples include Indomethacin (Indocin), Piroxicam (Feldene), and Diclofenac (Voltaren)
- Antibiotics, including sulfonamides (“sulfa drugs”) and forms of penicillin
- Anti-thyroid drugs, such as Propylthiouracil and Methimazole (Tapazole)
- Carbonic anhydrase inhibitors, including Acetazolamide and Methazolamide (these are used to treat glaucoma)
- Diabetes medications, including Tolbutamide, Carbutamide, and Chlorpropamide
- Ticlopidine used to prevent strokes and heart attacks
- Anti- seizure drugs like Carbamazepines (Tigerton), Phenytoin (Dilantin), and Valproic Acid.
- Choramphenicol, an antibiotic (no longer available in the United States)
- Mesalazine which is used to treat ulcerative colitis

and Crohns disease

- This is only a partial list of the drugs most often associated with aplastic anaemia.

Other drugs may also cause this disease. The best way to avoid aplastic anaemia from drugs is to take medicines only if they are necessary.³²

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