RANJAK PITTA AND ITS AFFILIATES IN MODERN PERSPECTIVE: A REVIEW

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ABSTRACT
Science of Ayurveda is based on tridosha theory. Pitta, one among three doshas plays a major role in digestion and metabolism. Pitta dosha is of five types namely pachaka, ranjaka, alochaka, bhrajaka, and sadhaka pitta. Function of ranjaka pitta is to provide red coloration to rakta dhatu. Yakrit (liver), plecha (spleen) and amashaya (stomach) are the sites of ranjaka pitta mentioned in ancient literature. Raktagni and ranjaka pitta has an important role in the formation of rakta dhatu. Sushrut has mentioned about sarakta meda present inside the alpasthi (all bones except large bones) which is equivalent to red bone marrow and responsible for erythropoiesis. In modern physiology it is described that Liver, Spleen and Bone marrow are the site for erythropoiesis. Liver stores important factors like vitamin B₁₂, Folic acid, Iron. Red pulp of the spleen is a special reservoir of concentrated red blood cells. Intrinsic factor is a substance which is essential for absorption of vitamin B₁₂ in the ileum. It is secreted by the parietal cell of stomach. Erythropoietin, Growth inducers, Differentiation inducers, epinephrine, Norepinephrine, prostaglandin has an important role in erythropoiesis. In this article we are intended to identify the entities of modern medical sciences that have resemblance with Ranjaka pitta on the basis of its physiological functions. For this study, the basic materials have been collected from the Ayurvedic classics with the available commentaries, as well as text books of modern medical science for better understanding of the concept and its comparison with contemporary science.

Keywords: Erythropoiesis, Rakta dhatu, Raktagni, Ranjak pitta

1. INTRODUCTION
Many Ayurvedic principles have been described in Ayurvedic Samhitas. Among them theory of tridoshas is an important principle. Tridosha is responsible for homeostasis of human body. Vata, pitta and kapha doshas is not represented by a single entity in our body. We can understand these concepts on the basis of its functional aspects [1]. Again the function of each dosha is unique. All three doshas are equally important. A single dosha executes many actions. Therefore we cannot represent a single structure for the specific function of each dosha. All these are equally important and do their functions independently or sometimes with co-operation of other. Pitta dosha one among three dosha is responsible for digestion and metabolism in human body. Wherever any type of chemical reaction takes place in the body there should be involvement of enzyme, hormone, or neurotransmitter as a result there is production of heat or ATP like energy producing substance. Those substances may be considered as pitta [2].

Pitta dosha is present in cellular level, single system level, and organization level. Pitta dosha do not move in the body independently. It is circulated all over the body with the help of vata dosha. In modern physiology it has been mentioned that the basic theory of body’s control system allow the functional system to operate in support of one another [3]. The homeostatic mechanism involves Nervous system, Hormone system and Immune system. Similarly all these three doshas have equal importance and they together maintain homeostasis in our body. Here the function of pitta dosha may represent the enzymes, endocrine or neuroendocrine system in organization level.

Pitta dosha are of five subtypes on the basis of location namely paachak, ranjak, saadhak, alochaka, bhrajaka pitta. One of the most important liquid (drava) dhatu in our body is called rakta dhaatu. It is essential for nourishment and equilibrium. Raktagni (dhatwagni) and ranjak pitta helps simultaneously in the formation of rakta dhatu. There is a need of proper understanding for the formation of rakta dhatu in modern perspective. Ranjak pitta and raktagni cannot be represented by a single entity.
at all the time because Ayurveda is the science based on the concept of functional understanding. There is no specific correlation of Ranjaka pitta mentioned in Ayurvedic literature in terms of supporting modern literature. It seems to be a problem found in student life, particularly first year of Bachelor of Ayurvedic Medicine and Surgery to understand about the concept of Ranjaka pitta. Increased demand of Ayurveda science in the present scenario is required to understand the depth of Ayurvedic principles on criterion of modern medical science in an easy mode. In this review we are trying to identify anatomical structures based on its physiological functions retrospectively described under the function of Ranjaka pitta.

Site and function of ranjaka pitta by different acharya:

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<tr>
<td>Sthula Asthi</td>
<td>Aamashaya (stomach)</td>
<td>Aamashaya (stomach)</td>
<td>Yakrit (Liver)</td>
</tr>
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<td>Karma (Function)</td>
<td>To impart colour to rasa dhatu</td>
<td>To impart colour of rasa dhatu</td>
<td>Converts rasa into raka dhatu</td>
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2. RANJAKA PITTA AND RAKTAGNI

Aahar rasa is final absorbed product of food digested by jatharagni. From aahar rasa subsequent dhatus are formed and nourished by three laws [8]. Commentator provides three laws for the formation and nourishment of dhatus. Those are Kshiradadh nyaya, Khaalekapota nyaya, Kedarikula nyaya. Three laws work together simultaneously for the replenishment of dhatu. Kshiradadh nyaya work for the formation of dhatu where as kedarkulya nyaya and khaalekapota nyaya work for the nourishment of dhatu. Jatharagni act upon aahar and is converted into aahar rasa and mala [9]. In kshiradadh nyaya Acharya Charak has mentioned rasagni act upon rasa dhatu and is converted into raka dhatu [10] whereas in Sushrut samhita Raktagni act upon anu rakta which is formed from rasa dhatu by the action of rasagni and help in the formation of raka dhatu [11]. In kedarikula nyaya and khaalekapota nyaya rakta sadharmi ansa (nutrient specific to dhatu) of aahra ras (nutrient product) nourishes the formed dhatu. Blood should be regarded as pure when its color resembles red-gold, indragopa (scarlet fly), red lotus, mahavar, and gunja fruit (abrus precatorius) [12]. The function of raktagni is to synthesize the colorless raka dhaatu from anu part of rasa dhaatu.

Again Acharya Charak has mentioned that the teja portion of rasa is mixed with ushma of pitta (ranjak pitta) that is helpful for the coloration of raka dhatu [13]. Acharya Dalhana in the commentary of Sushrut Samhita has mentioned tejarama ranjak pitta is mixed with aayapanna vikar rahit rasa (diseased free rasa dhatu) to form raka dhatu [14]. Acharya sushruti has named all subtype of pitta by the name of agni. Acharya sushruti has mentioned the location of Ranjaka pitta as yakrit (liver) and pliha (spleen).

It helps in the formation of raka dhatu. Vagbhatta has mentioned its location as amashaya (stomach). According to all these views rasa dhatu is contributed in the formation of raka dhatu with the help of ranjaka pitta. The function of ranjaka pitta is to color the rasa dhatu to form raka dhatu. So, both ranjaka pitta and raktagni has an important role in the formation of raka dhatu.

The root of raktavaha srotas is yakrit (liver) and pliha (spleen) and raktavahi dhamani (blood vessels). Acharya Charak has described srotas are the channels which transport their respective dhatus which means yakrit, pliha and raktavahi dhamani carries the raka dhatu to hridaya through saman vayu [15]. Rakta dhatu is formed elsewhere in the body. The third kala is called as medodhara kala. Medas is found in the abdomen and small bones of all living beings. The long bone contains bone marrow (instead of medas). Further, Acharya Sushruta has classified bones as sthula asthi and other then sthoolasthi. Acharya Dalhan has commented alpa asthi for bones other then sthoolasthi. Bone marrow is found especially (vishestah) inside the sthula asthi (large bones) and sarakta medas (red bone marrow) is found in bones other then sthoolasthi (alpa asthi) [16].

Bone marrow is specifically present in sthulasthi. As per arthapatti tantrayuktta we can say that some less amount of other type of majja may be present and this other type of marrow may be red bone marrow. In some large bones like humerus and tibiae red bone marrow is present in the proximal portion. Acharya Sushrut has explained red bone marrow is present in the proximal portion. Acharya Sushrut has explained red bone marrow is present in alpapthi (bones like vertebrae, sternum, ribs, ilea).
3. MODERN ASPECTS
Erythropoiesis is the process of formation of red blood cells. In the early week of embryonic life red blood cells are produced in yolk sac. During the middle trimester liver is the main organ for production of red blood cells. Spleen and lymph node is also responsible for the production of red blood cell during this period. During the last month of gestation and after birth red blood cells are produced in bone marrow. Bone marrow of all bones produces red blood cells until 5 years old. The bone marrow of long bones except the proximal portion of humeri and tibiae becomes fatty and produces no more red blood cells after 20 years. After this age most of red cells are produced in marrow of membranous bone like vertebrae, sternum, ribs and ilia. The marrow of these bones becomes less productive as age increases [17].

All the cells of circulation blood are derived from pluripotential hematopoietic stem cell in bone marrow. Growth and reproduction of different stems cells are controlled by multiple proteins called growth inducers. Four major growth inducers have been described. Interleukin-3 promotes growth and reproduction of all different type of committed stem cells whereas others induce growth of only specific type of cell. Differentiation inducers are the proteins that promote differentiation of cells. Formation of growth inducers and differentiation inducers is controlled by factors outside the bone marrow [18].

Pluripotent hematopoietic stem cell is converted to committed stem cell. The different committed stem cell grows to produce specific type of blood cells. A committed stem cell called colony forming unit-erythrocyte (CFU-E) produces erythrocytes. Under appropriate stimulation CFU-E stem cells is converted to proerythroblast. Once proerythroblast is formed it divides into multiple times to form many mature red blood cells. Proerythroblast is converted into basophil erythroblast/early normoblast. At this time the cell is accumulated with very little hemoglobin. In the next step early normoblast is converted into polychromatophil erythroblast/intermediate normoblast then to orthochromatic erythroblast then to reticulocyte. In this step the cells become filled with haemoglobin to a concentration of 34%. The nucleus condenses to small size and its final remnant is absorbed or extruded from the cell. During this reticulocyte stage, the cells pass from the bone marrow into the blood capillaries by diapedesis. The cell is then called mature erythrocyte [19].

4. SPECIFIC BLOOD RESERVOIR
Spleen can release 100 ml of blood into other area of circulation by decreasing its size sufficiently. The sinuses of liver can release about 450 milliliters of blood into remainder of circulation. Large abdominal veins can contribute 300 ml; venous plexus can contribute several hundred milliliters. Spleen has two areas for storing blood venous sinuses and pulp. The red pulp of the spleen is a special reservoir that contains large quantities of concentrated red blood cells. These red blood cells can be expelled into general circulation whenever sympathetic nervous system becomes excited and causes the spleen and its vessels to contract. 50 ml of concentrated red blood can be released into circulation, raising the hematocrit 1-2 % [20].

5. SITES OF RANJKA PITTA
The site of ranjak pitta is yakrit (Liver), pleha (Spleen), amashaya (Stomach) which is well proved by our Ayurveda masters. In modern literature it is mentioned that blood is formed in liver and spleen during intrauterine life. Hepatic stem cells in fetal liver migrate to bone marrow and become the major site for production of blood after birth. Liver is store house for Vitamin B12, Folic acid and iron. It is needed for the maturation of erythrocyte. The red pulp of the spleen is a special reservoir that contains large quantities of concentrated red blood cells. In liver and spleen diseases like hepatomegaly and splenomegaly there is reduction of hemoglobin concentration which denotes that there is importance of liver and spleen for the formation of blood. It is also seen that when liver and spleen are in normal condition still there is reduction in hemoglobin. It is due to the absence of intrinsic factor which is secreted from parietal cells of stomach (amashaya) and is required for the absorption of vitamin B12. In ancient literature it is also mentioned that when there excessive blood loss, one should drink blood with honey or he should eat goat’s fresh liver with its contained bile [21]. So these three structures yakrit (liver), pleha (spleen), and amashaya (stomach) help in maturation of erythrocyte and proliferation of erythroblastic cells which supports our Ancient Acharya.

In modern science it is described after 20 years of age blood formation occurs in red bone marrow of vertebrae, sternum, ilea, ribs and proximal portion of humerus and tibbie. The actual site of rakta dhatu formation (erythropoiesis) is not specified. Acharya Sushruta has classified bones as astula asthi and other then sthoolasti. Acharya Dalhan has commented alpa asthi for bones other then sthoolasti. Bone marrow is found especially
(visheshah) inside the sthula asthi (large bones) and sarakta medas (red bone marrow) is found in bones other then sthoolasthi (alpa asthi) [22].

Bone marrow is present in sthulasthi in significant quantity. As per arthapatti tanrayukti we can say that some less amount of other type of majja may be present and this other type of marrow may be red bone marrow. In some large bones like humerus and tibiae red bone marrow is present in the proximal portion. Acharya Sushrut has explained red bone marrow is present in the proximal portion. Acharya Sushrut has explained red bone marrow is present in alpasthi (bones like vertebrae, sternum, ribs, ilea). Rakta sadharmi ansa is present in aahar which is required for the nutrition of rakta dhatu. Food content which is required to nourish and proliferation the pluripotent stem cells may be called as rakta sadharmi ansa.

**Correlation of functions of raktagni and ranjaka pitta:**

<table>
<thead>
<tr>
<th>Raktagni and its correlation</th>
<th>Growth inducers, Differentiation inducers, Erythropoietin, Norepinephrine, Epinephrine, Prostaglandin, Androgen hormones</th>
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<tr>
<td>Ranjak pitta and its correlation</td>
<td>Intrinsic factor, Vitamin B&lt;sub&gt;12&lt;/sub&gt;, Folic acid, Iron, Copper</td>
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### 6. GROWTH INDUCERS AND DIFFERENTIATION INDUCERS

The cells of circulation blood are derived from pluripotential hematopoietic stem cell in bone marrow. Growth and reproduction of different stems cells are controlled by multiple proteins called growth inducers. Differentiation inducers are the proteins that promote differentiation of cells. As the function of raktagni is to synthesize the rakta dhatu so the function of Growth inducers and Differentiation inducers comes under the function of Raktagni.

#### 6.1. Erythropoietin

Conditions that decrease the partial pressure of oxygen in the blood increase the rate of red blood cell production. It helps in formation of growth inducer and differentiation inducer as a result there is increased number of erythrocytes. This process is carried out by erythropoietin. So Erythropoietin enhances red blood cell production. Thus the function of Erythropoietin comes under the function of Raktagni.

#### 6.2. Norepinephrine, Epinephrine, Prtostaglan din, Androgen

Norepinephrine, epinephrine and several of prostaglandin stimulate kidney for erythropoietin production. The effect of testosterone to increase red blood cell production may be at least partly indirect because of the increased metabolic rate that occurs after testosterone administration. So norpeinephrine, epinephrine, prostaglandin, testosterone have an important role in erythrocyte production. So the function of norepinephrine, epinephrine, prtostaglandin, and androgens are come under the functions of raktagni.

#### 6.3. Intrinsic Factor

The parietal cells of the gastric gland secrete a glycoprotein called intrinsic factor, which combine with vitamin B<sub>12</sub> in food and makes it available for absorption by the gut. Intrinsic factor binds tightly with vitamin B<sub>12</sub>. In this bound state vitamin B<sub>12</sub> is protected from digestion by gastrointestinal secretion. Intrinsic factor binds to specific receptor site on the brush border membrane of the mucosal cells of ileum. A common cause of red blood cell maturation failure is failure to absorb vitamin B<sub>12</sub> from gastrointestinal tract. In diseases like atrophic gastric mucosa stomach fails to produce normal gastric secretions. Lack of intrinsic factor decreases the availability of vitamin B<sub>12</sub> and failure in maturation of RBCs. So, the functions of intrinsic factor come under the function of ranjak pitta.

#### 6.4. Vitamin B<sub>12</sub>, Folic Acid

Vitamin B<sub>12</sub> and folic acid plays an important role for final maturation of red blood cell. These two are essential for the synthesis of DNA because this is required for the formation of thymidine triphosphate which is the essential building blocks of DNA. Lack of either vitamin B<sub>12</sub> or folic acid causes abnormal and diminished DNA consequently failure of nuclear maturation and cell division. The erythroblastic cells of the bone marrow due to failing of proliferation rapidly produce larger than normal red cell called macrocyte. These poorly formed cells are capable of carrying normal oxygen but their lifespan will have shorter one third to half. Vitamin B<sub>12</sub> is transported into the blood during next few hours by the process of pinocytosis, carrying intrinsic factor and vitamin B<sub>12</sub> together through the membrane. Once vitamin B<sub>12</sub> is absorbed from GIT it is first stored in liver and then released slowly as needed by the bone marrow. Folic acid is normal constituent of green vegetable, fruits, and meats (especially liver). Failure of maturation of
RBC is also caused by the deficiency of folic acid. In certain case like sprue there is difficulty of absorption of folic acid and vitamin B₁₂, which causes failure of maturation of RBC. Therefore function of vitamin B₁₂, and folic acid come under the function of ranjak pitta.

6.5. Iron
Iron has an important role in formation of hemoglobin. When iron is absorbed from the small intestine with the help of vitamin C it immediately combines in the blood plasma with a beta globulin (apotransferrin) to form transferrin which is then transported in the plasma. In the cell cytoplasm iron combines with apoferitin to form ferritin. The hepatic cells contain large amounts of a protein called apoferitin, which is capable of combining reversibly with iron. Therefore, when iron is available in the body fluids in extra quantities, it combines with apoferitin to form ferritin and is stored in this form in the hepatic cells until needed elsewhere. This iron stored as ferritin is called storage iron. When quantity of iron in the plasma fall low, iron in the ferritin storage pool is removed easily and transported in the form of transferrin in the plasma to the areas of the body where it is needed. Transferrin molecule binds strongly with receptors in the cell membrane of erythroblast. There the transferrin delivers the iron directly to the mitochondria where heme is synthesized. People who do not have adequate quantities of transferrin in their blood can cause severe hypochromic anemia. So iron has an important role in maturation of RBCs. That’s why functions of iron come under the function of ranjak pitta.

6.6. Copper
Copper profoundly influences the absorption of iron. This suggests that a copper protein may be involved in the mechanism by which iron is absorbed from the gastrointestinal tract. The daily turnover rate of iron through the plasma and into the red cells is increased rather than decreased in copper-deficient swine suggests that movement of iron within the body is not reduced. The relation of copper to iron metabolism must be in some way concerned with the role of copper in red cell synthesis. Anemia develops in the absence of copper because of the limited capacity of the marrow to produce cells. It is suggested that deficiency of the erythrocyte copper compound erythrocuprein, is related to these alterations in erythrocyte production and survival [23]. Thus function of copper come under the function of ranjaka pitta.

7. DISCUSSION
Basically Vata, Pitta, Kapha constitute three regulatory systems i.e. nervous, endocrine and immune system respectively of all living system. Among five types of pitta, Ranjaka pitta has an important role for the coloration of rakta dhatu. Raktagni (one type of Dhatavagni) helps in formation of rakta dhatu. Raktagni acts on anu rakta (pluripotent stem cells) and convert it into rakta dhatu (blood cells). Ranjak pitta during the process of hemopoiesis provides coloration (hemoglobin) to rakta dhatu. Acharya Sushrut has mentioned the site of ranjaka pitta as yakrit and pliha, Acharya Sharngadhhar has mentioned it as yakrit and Acharya vagbhatta has mentioned as amashyaya (Stomach). Acharya Charak has not mentioned the site for ranjak pitta. Acharya Sushrut and Vagbhatta have mentioned the function of ranjaka pitta is to impart coloration whereas Acharya Sharngadhhar has mentioned the function of ranjaka pitta is to convert rasa dhatu into rakta dhatu. Acharya Charak has mentioned teja portion of ahara rasa is mixed with ushma of pitta (ranjak pitta) that is helpful for the coloration of rakta dhatu.

In modern physiology hormone like erythropoietin, androgen, thyroid hormone, corticosteroid hormone vitamins like vitamin B₁₂, folic acid, pyridoxine, vitamin C (helps iron absorption), minerals like iron and copper, norepinephrine, epinephrine, intrinsic factor, Growth inducers, differentiation inducers are the major factors that is responsible for erythropoiesis and maturation of RBC. From the above discussion functions of Growth inducers, differentiation inducers, erythropoietin, epinephrine, norepinephrine, prostaglandin and testosterone may be correlated with the functions of raktagni. Functions of Intrinsic factor, Vitamin B₁₂, folic acid, iron and copper may be correlated with the functions of ranjaka pitta.

8. INADEQUECIES
Across all Ayurvedic textbooks, the following inadequacies are found in relation to blood physiology.

- There is no direct reference for the site of production of rakta dhatu (blood) in fetal life as well as adult life which are clearly described in modern literature.
- Name of the specific bones is not mentioned where sarkta meda (red bone marrow) is present.
- Acharya Sushrut has mentioned sarkta meda are present in asthis (alpasthi) other than sthulasthi. Examples of sthulasthi and alpasthi are not mentioned in the text.
- Function of sarkta meda is not specified.
• Acharya charak has mentioned the role of rasagni in the production of rakta dhatu where as Acharya sushrut has mentioned the role of raktagni in the production of rakta dhatu.
• Stage wise haemopoiesis is not mentioned clearly by our ancient acharya.
• Location of Raktagni (dhatavagni) is not mentioned.
• In most of the text books the word prasadaja is considered for dhatu nirman. Dhatu poshana is the actual meaning for prasadaja of dhatu [24].

9. CONCLUSION
Pitta dosha is divided into five types namely pachaka, ranjaka, sadhaka, alochaka, and bhrajaka. The site of ranjak pitta as described in ancient literature is yakrit, pliha, and amashaya. Ayurveda is based on functional understanding. From the above discussion functions of Raktagni may be correlated with Growth and differentiation inducers, erythropoietin, norepinephrine, epinephrine, prostaglandin, and testosterone. Functions of Ranjak pitta may be correlated with intrinsic factor, vitamin B₁₂, Folic acid, Iron and copper. There is a need of further research to evaluate in detail of all other doshas. So, that student joining BAMS can understand easily the basic concepts of rakta dhatu and ranjaka pitta.

10. REFERENCES
