

## *International Journal of Scientific Research and Reviews*

### **Parasite-Vector-Host Conscious Mechanism as Determinant of Parasite Virulence, Vector Infectivity and Host Susceptibility: Reproductive Success of Malaria Parasites in *Plasmodia*-Mosquito-Human Troika**

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#### **ABSTRACT:**

The whole intelligent mechanism starting from the human hosts and the mosquito vectors and their anatomical, physiological, biochemical and molecular organization is the manifestation of the psyche of the *Plasmodia* parasite to serve its virulence and reproductive success. It is a conscious mechanism of '+/+' interaction of the vector species and the *Plasmodia* species to be the reason of human malaria. The virulence (ability to invade, replicate and continue inside the host) in pathogen is the powerful ingredient which ensures the pathogen to succeed over the host. Virulence is the core of pathogens and they evolve by enhancing their more and more specialized and lethal virulence factors. All these factors can interact at the host genetic level and can cause alteration of host genetic activity and thus can bring a favour for its higher pathogenicity by its evolved virulence. The psychic make up of an organism is deeply lodged in its genetic make-up.

**KEY WORDS:** Parasite-vector consciousness, virulence, infection, infectivity, pathogenicity, reproductive success, genetic make-up

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## **INTRODUCTION:**

The presence of oocyst and sporozoites in the mosquito vector establish infection. Vector infectivity is defined as the proportion of the vectors found with sporozoites and that determines the vectorial capacity<sup>1,2</sup>. The degree of infectivity of the vector depends on:

- 1) Susceptibility of the vector species to get infected while feeding on the infected host.
- 2) The number of the mature gametocytes in the blood of host at the time of feeding of vector species.
- 3) The affinity of the vector species to establish contact with man.
- 4) Longevity of the vector species.
- 5) The environmental and climatic conditions like temperature, humidity, rainfall<sup>3,4</sup>.

Now the fundamental questions that arise are: what factors determine which mosquitoes and which of their sibling complexes are to be vectors<sup>5</sup>? What determines their degree of infectivity? Is the vector conscious of its vectorial capacity<sup>6,7,8,2</sup>? Is vector infectivity a conscious mechanism? Is infectivity in any way advantageous for the vectors? In what way the vector infectivity modulates or affects the vector psyche and physiology<sup>8</sup>? Does the vector have an urge to acquire vectorial capacity? Why does the mosquito vector transmit malaria parasite? Is the process of transmission of the parasite by the vector species a conscious mechanism? Why some species show relatively high susceptibility to malaria parasite infection, thus making them more potent as vectors?

## **VECTOR-PLASMODIA INTERACTION:**

The susceptibility of the vector to plasmodia depends on the genetic constitution of vector species which modulates the morpho-physiological characteristics, thus making it either favorable or unfavorable to infect Plasmodia<sup>2</sup>. The genetic constitution also must be determining size of the blood meal that the vector species can feed on, the intake of number of gametocytes, number of infective gametocytes from circulating blood of the host. Temperature of the environment of the vector species also affects its susceptibility towards Plasmodia.

Other hidden factors which work for the susceptibility of vector species are two adaptations: (a) the adaptation of malaria parasite in the vector species and (b) the adaptation of the vector species to take upon itself the responsibility of growth, reproduction and transmission of the parasite. How does the parasite recognize and choose the respective vector species as its niche<sup>9</sup> to fulfill its urge for growth, reproduction, transmission and finally to manifest its virulence<sup>10</sup>? Why does the vector species dissipate its energy to adapt to take up the responsibility of the fulfilment of the urge of the Plasmodia? Is it because the vector species also gets to manifest its virulence through infectivity by supporting the stepwise process of expression of virulence of the Plasmodia parasite? Thus, is it a conscious mechanism of '+/+' interaction of the vector species and the Plasmodia species to be the reason of human malaria<sup>11</sup>. Does the parasite

reservoir play any role in this interaction with regard to containing a number of mature gametocytes in the blood?

The gonotrophic cycle of the vector species is defined as a physiological process which includes digestion of its ingested food and development of the ovaries<sup>[12]</sup>. Digestion of blood is usually accompanied by development of ovaries in the vector species and called gonotrophic concordance. But there are situations such as hibernation during winter, when the blood is digested and development of ovary does not occur.

The normal development of the ovary depends on temperature, a full blood meal and fertilization. A full blood meal in the vector species stimulates the secretion of gonotrophic hormone (from corpora allata) and neurosecretory cells of the brain. The duration of the gonotrophic cycle of the vector species depends on

- 1) Time required to find a host to feed on
- 2) Time required for digestion of blood and development of ovary
- 3) Time taken from blood feeding and oviposition.

Temperature influences gonotrophic cycle of the vector. The duration of the vector gonotrophic cycle affects its vectorial capacity through its transmission potential of the Plasmodia species from infected host, to a new healthy host<sup>12</sup>. The whole process seems as if it were designed for transmission of the parasite, so that unfailingly the plasmodia will retain their reproductive success along with that of the vector species and maintain their virulence through symbiotic interaction<sup>11</sup> and as if they have their own way of cognition and processing to achieve their goal through different frequency bands<sup>13, 14</sup>.

Anthropophagic Index (Human Blood Index) is an important parameter to find out the vector contact with human being to estimate the biting frequency on man. Though the mosquito takes the blood meal of mammals, birds, reptiles, amphibians etc. only humans get malaria, not other species. But what might be the reason that the plasmodia have chosen humans as their preference to complete the asexual phase of their life cycle? Do they prefer anucleated Red Blood Cells (RBCs) for their reproductive success? Is the parasite itself the intelligent designer of human RBCs for its own purposes? And, did it, for its own purposes, design the whole “intelligent” mechanism involving the human hosts and the mosquito vectors along with their anatomical, physiological, biochemical and molecular organization as the manifestation of its psychic urges to propagate its virulence and its species? And the fight of the host against the parasite and vector is an ordering mechanism in its physical and biological systems to ensure its existence and evolution<sup>15</sup>. Recent researches by us have all pointed<sup>16,17,18,19,11</sup> to the role of consciousness (*i.e.* urge) in evolution of life and of species<sup>16,17,18,19,11</sup>.

The effort to eradicate mosquitoes using insecticides exercises selection pressure on the vector species and they develop ability to survive contact with insecticides by various mechanisms and thus they

become resistant. The resistance of the vector species or the *Plasmodia* may be because of vigour tolerance or physiological resistance or behaviouristic resistance. Finally whatever may be the mechanism but ultimately the vector species develops resistance to the insecticide and the *Plasmodia* to the drug<sup>[2,4]</sup>. By that they ultimately develop more vigour in terms of survival, longevity, reproductive fitness (by giving rise to resistant progeny), infectivity and vectorial capacity<sup>2</sup>. It seems, all these advantageous preparations of developing resistance are only to strengthen their virulence as well as pathogen city in terms of transmission potential of human *Plasmodia* species<sup>5</sup>.

## **PATHOGEN ABILITY**

Pathogens are probably the masters of cell biologists and have identified special niches by subverting host's physiology and immune defense<sup>16</sup>. The virulence (ability to invade, replicate and continue inside the host) factors in the pathogen are the powerful ingredients which ensure the pathogen to succeed over the host.

The ability of the pathogen to proliferate and to counter the defense mechanism of the host is its survival success. Because of that they have developed advanced mechanisms to acquire phenotypic diversity as their efficient adaptability by rapidly evading the host immune defenses. There is no doubt that pathogens ever possess the capacity of adhesion, toxin production and many other virulence factors in terms of genes<sup>20</sup>. And simultaneously novel virulent genes are also acquired by transduction, conjugation, transformation or by any other method of their multiplication to strengthen and bolster their pathogenicity. Virulence is the core of pathogens and they evolve by enhancing more and more their specialized and lethal virulence factors. They may include more powerful toxic enzymes, advanced reproductive success, drug resistance, more capable proteins for invasion and a strong capsule etc. After all these can interact at the host genetic level and can cause alteration of host genetic activity and thus can favour higher pathogenicity by its evolved virulence.

It is assumed and quite generally accepted that during the process of evolution, the homo sapiens has evolved to protect itself against pathogens<sup>21</sup> and it is also established that 90% of the human body is possessed by microbes<sup>22</sup>. So in the process, who evolves? The man evolves in a network of microbes or the microbes evolve inside the network of humans? The microbes alter genes, bring mutations and make man more suitable for evolution of their pathogenicity. They can utilize host molecules for their own benefit and they have evolved ability to switch off and switch on their genes to regulate transmission. They have developed specialized enzymes to capacitate them to invade, to survive in an intracellular habitat, to evade the immune defense of the host, to move from one cell to the other, and to get nutrients from host cells (lysed cells) by their toxicity. And all these capacities of the pathogen are of course genetically encoded in their genome.

For example, in case of bacterial toxins they are mostly carried by bacteriophages<sup>23</sup>. The bacteriophages have great ability to carry DNA, to survive harsh environmental conditions which can kill bacterial populations. The virulence factor of bacteriophages enables the bacterium to expand its ability and fitness in its niche by enhancing its ability to invade the hosts' barriers including their immune defense<sup>24</sup>, Virulence is the core of the pathogen and that is conferred on it by other pathogenic characters such as proliferation, colonization (to proliferate and survive), enzymes for adhesion, invasion, evasion and other nutrients) all such characters that manifest as pathogen city and all of them too are encoded in their DNA. They call these virulence genes as pathogen city islands<sup>25</sup>.

The complex life cycle of human *Plasmodia* in its two hosts is another challenge for the parasite which starts from ingestion of blood meal from infected host to the attainment of virulent infective sporozoite stage in mosquito (in ambient temperature, pH, xanthurenic acid)<sup>26</sup>, as if the parasite has designed both the hosts and their machinery to confidently attain its virulence and reproductive success.

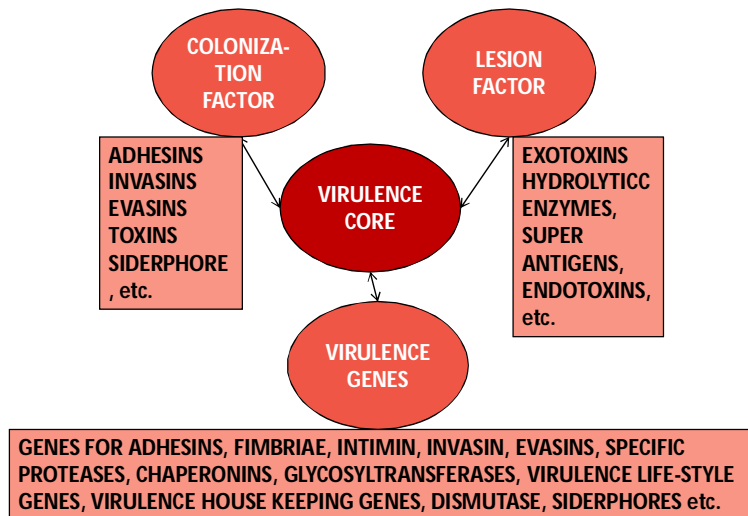


Figure: The diagrammatic representation of virulent core and its traits; To show that the traits are the manifestation of its original core.

Changes in their environment can bring rapid mutation in them to preserve and enhance their virulence through speedy evolution. The psychic make up of an organism is deeply lodged in its genetic make-up. The corresponding urges for their manifestation and the respective processes required for them are also encoded there and accordingly they learn, adapt and ensure their existence, proliferation, virulence and pathogen city etc.<sup>10</sup>. The new adaptive urges remain encoded in the form of epigenetic marks and biochemical substrate as well as mechanisms<sup>27,28,29, 30</sup>.

## CONCLUSION

The virulence is the core character which forms the pathogen city island by an assembly of virulence genes. The complex design of the virulence system seems to point to the fact that the whole

cellular, biochemical and physiological systems of the host are determined by the pathogens. The pathogens undergo chromosomal shuffle and reshuffle to add to their virulence genes to evolve by acquiring better virulence factors. The pathogens' ability to infect and incapacitate by direct toxic mechanisms and by other indirect mechanisms that ensure their survival and proliferation are all manifestations of their such urges stemming from their virulent core. They seem to determine the course of evolution of all higher organisms in a surprisingly definite bottom-up manner and fashion them as their prospective and operational niches by all kinds of manipulations of genes as well as ecological and physiological adaptations. It is thus difficult to say which factors and organisms actively contributed to the evolution of the higher organisms from the lower. The lower ones have very clear-cut virulence-enhancing paths to traverse while the higher ones have rather diffuse goals to achieve due to greater complexity of the more evolved psyche in relation to their more complex physiology and the ecology. Meta-evolution alone can explain evolution in its true colors in which direction contemporary biology is heading.

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