



## EVIDENCES - THREE PRONGED DEFENSE OF BODY AGAINST CANCER CELLS RESULTING IN CARDIAC, METABOLIC AND AUTO-IMMUNE DISORDERS

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### ABSTRACT

In depth study of thousands of articles in various international journals and information from text books is collected to conceive and compile evidences in favour of this theory. This paper contains evidences that cancer cells (CCs) are present in the body of every individual, they manifest as diabetes simultaneously causing other symptoms of metabolic syndrome. After they grow beyond a particular threshold, in presence of insulin resistance (IR), CCs in the body cause hyperinsulinemia and hyperglycemia. Hyperinsulinemia in presence of IR, aid quick proliferation causing increased incidence of cancer. High LDL requirement and ability to recruit a food supply cause dyslipidemia. This deadly combination results into diverse complications; body needs to fight these CCs. Evidences support THREE ways adopted by the body to control them, hypertension, increased androgen levels and macrophage activity, resulting in cardiac disorders, PCOS and autoimmune disorders; dyslipidemia is a common feature. The only way to safely control the activity of these CCs is to reduce glucose availability, and starve them by improving insulin sensitization. Insulin sensitization can be achieved through physical exercise and insulin sensitizing agents (ISA). We can conclude that CCs are the cause of syndrome X and not the result of it. CCs may be responsible for degenerative and autoimmune disorders, besides syndrome X and cancer. Insulin sensitization through physical exercise or ISA should be effective in the treatment and prevention of Syndrome X. ISA should be able to inhibit tumor growth.

**Keywords:** Diabetes, Insulin resistance, Hyperinsulinemia, Autoimmune diseases, hormone disorders, cardiac disorders, cancer.

### INTRODUCTION

Striking coincidence of cause and effect is noticed when syndrome X is viewed in light of characteristics of cancer cells. It is an eye opener and points the arrow of suspicion towards cancer cells as the cause of diabetes, hypertension and PCOS. An in depth review of vast data revealed this to be true and is supported by unbeatable evidences including reasons for the association of dyslipidemia and all the other symptoms of Syndrome X.

The strongest evidence in support of this hypothesis is that:

Besides explaining the nexus of symptoms of syndrome X, it also provides answers and explanation to several unanswered questions like:

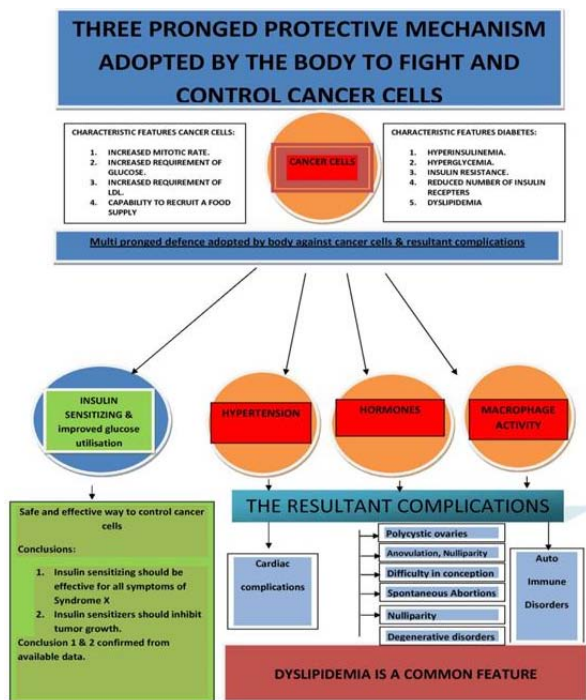
- Why and what is diabetes, hypertension and PCOS, including their causes?
- Why and what causes hypertension and hyperandrogenism?
- Why and how dyslipidemia is associated with diabetes, hypertension, PCOS & cancer?
- Why and how there is a higher incidence of cancer in diabetic, hypertensive & PCOS patients?
- Why and how giving insulin directly or drugs improving insulin secretion are carcinogenic in diabetic patients?

- Why hypertension seems to be protective from cancer during the initial few years?
- Why all antihypertensive drugs seem to be carcinogenic?
- Why and how Metformin seems to attenuate hypertension and is effective in PCOS, anovulation, nulliparity and cancer?
- Why and how drugs that improve glucose utilization help in controlling blood pressure and reduce the incidence of cancer?
- Why and how physical exercise helps in controlling diabetes, hypertension and dyslipidemia?
- What are the yet unknown causes for spontaneous abortions?

This paper is divided into sections containing evidences from diabetes, hypertension, PCOS which is much more than what we have conceived till now; it includes spontaneous abortions and nulliparity along with the Polycystic ovaries and anovulation. The next section contains evidences from arthritis.

Besides explaining the etiology of syndrome X with strong unbeatable evidences, it replies to all the unanswered questions with extreme ease and eliminates the unpredictability of Syndrome X and Cancer, making them predictable. I suggest to the readers to kindly go through one section at a time and verify and analyze the logic and the authenticity of the evidences.





**Figure 1:** Evidences - three pronged defense of body against cancer cells resulting in cardiac, metabolic & auto-immune disorders

**Findings:**

Diabetes & Cancer - The Missing Link.

There are reports which suggest a link between Type II Diabetes and Cancer.<sup>1-6</sup> I took an in depth study topic wise, hereunder are the findings of my research on diabetes.

Data reviewed:

Characteristic features of Diabetes Mellitus.

Characteristic features of Cancer cells.

The controversy

- ❖ There is a controversy on that cancer cells are present in the body of every human being, however some reports confirm that cancer cells are present in everybody but the immune system controls them hence disease is not manifested.
- ❖ Patients with diabetes were 1.5-2.5 times more likely to get cancer<sup>1-6</sup>. The reasons for this association are yet unknown.

**Characteristics of Cancer cells<sup>7</sup>**

We shall consider the characteristics which are relevant to this study so as to keep it clear and less confusing.

- Quick proliferation of cancer cells: Loss of regulation of mitotic rate<sup>8</sup>
- Cancer cells have increased glucose and amino acid uptake. These cells have high levels of hexokinase increasing their glucose utilization.<sup>8</sup>
- Elevated uptake of LDL by cancer cells.<sup>9</sup>

- Recruiting a food supply: A tumor of cancerous cells typically skirts these systems and independently signals the body to feed it.<sup>10</sup>

**CHARACTERISTICS OF TYPE II DIABETES**

**Syndrome<sup>11</sup>**

- Hyperglycemia.
- Hyperinsulinemia.
- Reduced number of insulin receptors.
- Insulin resistance.
- Dyslipidemia.

**The Hypothesis**

We know that human body is a colony of cells specialized to perform various functions and the brain is the computer responsible for ensuring supply of raw material, nutrients, oxygen and any other requirement of the cells. In the normal circumstances when the level of glucose goes down in the blood, body cells signal the brain for more glucose, the demand is promptly fulfilled by the brain through a signal from the hypothalamus to the liver and the pancreas, on the other hand, on receiving the signal of increased sugar level the hypothalamus signals the pancreas and the liver and the level is maintained. If cancer cells are present in the body, since they have a higher requirement of sugar,<sup>12</sup> cancer cells have the capacity to recruit a food supply for themselves,<sup>13</sup> hence even at normal sugar level they continue to send the message for more sugar to the brain. Till the time the percentage of these cells is below a certain level (in control of the immune system), the brain may not respond to their demand but as soon as the percentage of these cells exceeds this level (but is well below the level where cancer can be manifested), the brain responds and more sugar is released into the system hence hyperglycemia occurs. The normal cells of the body at this stage send the message to the brain that the sugar levels have exceeded the normal range, this is a confusing situation for the brain and hence feeling that the sugar in the system is not being properly utilized, it signals the pancreas to release more insulin hence hyperinsulinemia occurs. The normal cells already have sufficient sugar; hence in response to the increased insulin levels in the blood they reduce the insulin receptors, thus low no. of insulin receptors and insulin resistance arises.

Thus the ideal combination of symptoms of diabetes is achieved i.e. hyperglycemia, hyperinsulinemia along with insulin resistance and reduced number of insulin receptors.

**Inference**

Cancer cells are present in the body of diabetic patients and are responsible for diabetes mellitus.



**Table 1: Evidences from diabetes**

1.	As per this theory diabetes is caused by increasing no. of cancer cells and is manifested when the percentage of cancer cells exceeds a certain level, this means: - Such patients should manifest cancer more frequently.	Exactly this trend is manifested in diabetic patients. Diabetic patients are 1.5 -2.5 times more prone to various types of cancer <sup>14</sup> of liver, pancreas, endometrium, colon/rectum, breast and bladders <sup>15-17</sup> .
2.	Cancer cells show a higher uptake of LDL. <sup>18</sup> Since cancer cells possess the capacity to direct the body and recruit food supply for them, they should also disturb the cholesterol levels of the body.	Close association of dyslipidemia with type II diabetes confirms this.
3.	Interestingly, several antidiabetic therapies, including the biguanides and the peroxisome proliferator-activated receptor ligands may also have activity against breast cancer <sup>19-21</sup> and are being tested in clinical trials.	Those anti diabetic drugs which work to improve insulin resistance will bring down the blood glucose level by improving the uptake of glucose by normal cells, hence reduce the availability of glucose for the cancer cells and thus will restrict the growth of cancer cells. Other drugs which reduce the blood glucose levels by increasing insulin secretion will improve the uptake of glucose by both cancer cells and the normal cells hence will boost growth of cancer cells.
4.	Exogenous insulin is associated with an increased risk. <sup>22</sup>	Giving exogenous insulin would increase the insulin levels and hence the uptake of glucose, both by the cancer cells as well as the normal cells. Hence in spite of bringing the blood glucose level to normal, it will be associated with a faster growth of cancer cells and thus a higher incidence of cancer.

## EVIDENCES FROM HYPERTENSION

### Characteristic features of hypertension

- Heightened proliferation, characterized by higher organ to body weight ratio, has been observed early in hypertension, at least in genetic models, even at birth<sup>23-28</sup>
- Insulin resistance and hyperinsulinemia.<sup>29</sup>
- Hyperlipidemia is prevalent in hypertension but the cause of this association is unknown.<sup>30,31</sup>

### The controversy & questions

There is a controversy on effects of antihypertensive drugs on cancer; some reports suggest that almost all antihypertensive drugs are carcinogenic.<sup>32-34</sup>

### The hypothesis

To prove our point let us begin with a presumption. Let us evaluate, in light of the characteristic features of cancer cells, what will be the picture if cancer cells are present in the body of a hypertensive patient. Will they lead to the situation as seen in hypertensive?

- 1) Heightened proliferation: They would lead to an increased rate of proliferation of cells in certain parts where they are present and active.

- 2) Increased glucose and amino acid uptake: Should lead to Hyperglycemia, hyperinsulinaemia and insulin resistance.
- 3) Elevated uptake of LDL by cancer cells: Should lead to dyslipidaemia.

### Confirmation of the presumption

Heightened proliferation:- The heightened proliferation activates the immune system to control the cancer cells, which probably is only partly successful.<sup>35-37</sup>

Brain raises the blood pressure: Hypertension seems to be protective against cancer for initial five years. If cancer cells are present in the vascular smooth muscles, just like the rise of body temperature i.e. pyrexia is a symptom of underlying infection, the hypothalamus instructs an increase in the blood pressure as a symptom of quick proliferation of vascular smooth muscle cells to prevent the lumen from being reduced and to aid the immune system, this may arrest the growth rate of the cancer cells at least for some time.

Reducing the blood pressure for long duration increases the risk of cancer<sup>38-40</sup>:- Reducing the blood pressure for long term will reduce the control of the body on the growth of cancer cells and thus they grow at a faster rate creating the impression that most of/all anti hypertensive drugs are carcinogenic.

Increased amino acid and glucose uptake<sup>41</sup>:- We know that human body is a colony of cells specialized to perform various functions and the brain is the computer responsible for ensuring supply of raw material, nutrients, oxygen and any other requirement of the cells. In the normal circumstances when the level of glucose goes down in the blood, body cells signal the brain for more glucose, the demand is promptly fulfilled by the brain through a signal to the liver and the pancreas, on the other hand when the sugar level rises the brain signals to the pancreas and the liver and the level is maintained. If cancer cells are present in the body, since they have a higher requirement of sugar,<sup>41</sup> cancer cells have the capacity to recruit a food supply for themselves,<sup>41</sup> hence even at normal sugar level they continue to send the message for more sugar to the brain. Till the time the percentage of these cells is below a certain level (in control of the immune system), the brain may not respond to their demand but as soon as the percentage of these cells exceeds this level (but is well below the level where cancer can be manifested), the brain responds and more sugar is released into the system hence hyperglycemia occurs. The normal cells of the body at this stage send the message to the brain that the sugar levels have exceeded the normal range, this is a confusing situation for the brain and hence feeling that the sugar in the system is not being properly utilized by the cells, it signals the pancreas to release more insulin hence hyperinsulinemia<sup>42</sup> occurs. The normal cells already have sufficient sugar; hence in response to the increased insulin levels in the blood they reduce the insulin



receptors, thus low no. of insulin receptors and insulin resistance arises.

**Table 2: Evidences from hypertension**

	As per this theory hypertension is a protective measure by the body to arrest the growth of cancer cells, this means	
1.	Lowering the Blood pressure should increase the rate of proliferation and thus the incidence of cancer.	Actually this has been the controversy with antihypertensive therapy. The antihypertensive drugs reduce the blood pressure thus the cancer cells get an opportunity to grow faster, increasing the incidence of cancer in patients taking antihypertensive treatment. Thus creating the false impression that all antihypertensive drugs are carcinogenic. <sup>43-45</sup>
2.	Hyperinsulinemia and insulin resistance should be associated with hypertension. If cancer cells are present in the body, since they have a higher requirement of glucose, cancer cells have the capacity to recruit a food supply for themselves <sup>46</sup> , Hyperinsulinemia and insulin resistance should be associated with hypertension.	Essential hypertension is an insulin resistant state. <sup>46</sup>
3.	Cancer cells show a higher uptake of LDL <sup>47</sup> and they also possess the capacity to direct the body and recruit food supply for them, they should also disturb the cholesterol levels of the body.	Close association of dyslipidemia with hypertension confirms this once again. <sup>48,49</sup>
4.	Why insulin sensitizing agents help reduce blood pressure?	Growth of cancer cells can be harnessed if glucose availability is reduced. Insulin sensitizing agents reduce the availability of glucose by improving insulin resistance, thus control the proliferation of cancer cells, hence hypertension is eased. Insulin sensitizing agents help reduce blood pressure. <sup>50-54</sup>
5.	Metformin should be effective in controlling cancer.	Metformin is effective in cancer and induces apoptosis in cancer cells. <sup>55-57</sup>
6.	Why and how physical exercise has positive effect on hypertension and cancer?	Insulin sensitivity and utilization of glucose by normal cells improves with physical exercise <sup>58</sup> , thus reducing the availability of glucose for cancer cells controlling the proliferation - the benefits of physical exercise in hypertension is known to all of us.
7.	Cancer cells show a higher requirement of LDL hence statins by reducing the availability of LDL should retard the growth and induce apoptosis in cancer cells. Hence they should help in reducing blood pressure.	Statins induce apoptosis and cell growth arrest in prostate cancer cells. <sup>59,60</sup> Taking statins leads to modest but significant reduction in blood pressure. <sup>59,60</sup>
8.	Statins should be effective in controlling cancer.	Statins induce apoptosis and inhibit cancer cell growth. <sup>60</sup>

If this compensatory hyperinsulinemia is able to control the hyperglycemia only hypertension is manifested, and if it is unable to control the hyperglycemia diabetes with hypertension is manifested. Thus the ideal combination of symptoms of hypertension or hypertension with diabetes is achieved i.e. increased blood pressure along with hyperinsulinemia and insulin resistance, and hyperglycemia in case of hypertension with diabetes.

#### Inference

- Cancer cells are present in the body of hypertensive patients.
- Just like pyrexia, hypertension is a symptom of the underlying cause i.e. quick proliferation of cancer cells in the vascular smooth muscles. It is a protective measure by the body to arrest the growth of cancer cells.

#### Conclusions

This confirms the following:-

- Cancer cells are present in the body of diabetic as well as hypertensive patients and manifest their presence in the form of hyperglycemia and are a cause for hyperinsulinemia, reduced number of insulin receptors and insulin resistance.
- Quick proliferation of cancer cells in the vascular smooth muscles leads the brain to signal increase in blood pressure. Thus, just like pyrexia, hypertension is a symptom of the underlying cause i.e. quick proliferation of cancer cells.
- Hypertension is a protective measure by the body against cancer rather than being a risk factor in cancer.

#### EVIDENCES FROM PCOS

#### Characteristics of PCOS<sup>61</sup>

- Several cysts on the surface of the ovaries.
- Irregular menstrual cycles.
- Thickened endometrium.
- Hyperandrogenism.
- Hirsutism.
- Infertility.
- Hyperinsulinemia.
- Insulin resistance.
- Dyslipidemia.

#### The Hypothesis

The female reproductive system incorporates a controlled cell proliferation simultaneously at three sites – the endometrium, the ovaries and the mammary glands and this it does under a strict balance of male and female hormones. The male hormones tend to retard the



proliferation<sup>62</sup> and the female hormones tend to increase it<sup>63</sup>. A disciplined balance of these hormones provides optimum circumstances for a well controlled proliferation. This balance of the male and the female hormones is maintained by the hypothalamus of the brain through the FSH and LH released from the pituitary gland stimulating the ovaries to produce estrogens, progesterone and testosterone.

A particular level of Androgens and estrogens maintains the optimum proliferation at all the three sites, but if cancer cells are present at any one of these sites this balance is disturbed as below:

**The cancer cells are present at the endometrium:** The cancer cells have a characteristic feature to proliferate quickly<sup>64</sup>, hence at normal level of the hormones the normal cells will proliferate at a normal speed suppose  $n$  proliferations/unit time while the cancer cells will proliferate  $x$  times faster. Thus the speed of proliferation in the mammary glands and the ovaries will be  $n$  proliferations/unit time while there will be a dual rate of proliferation at the endometrium, the normal cells proliferating at the rate of  $n$  proliferations/unit time and the cancer cells proliferating at the rate of  $n \times x = nx$  proliferations/unit time. Hence there will be a difference in the rate of proliferation in the three sites. This difference can be calculated as per the equation\*:

$$D = \frac{n - n(1+x)}{y+z} *$$

Where,

$D$  is the difference in the rate of proliferation between the endometrium and the other two sites,

$n$  is the rate of proliferation of normal cells,

$x$  is the difference in the rate of proliferation of cancer cells and the normal cells,

$y$  and  $z$  are the number of cancer cells and the number of normal cell in the endometrium.

NOTE: Currently we do not have the technology to count the cancer cells in very small tumors. Hence this calculation shall be hypothetical.

\*Equation Contributed by Niharika Dosaj [Written permission has been obtained from her for publishing this on 15<sup>th</sup> September 2011]

The hypothalamus of the brain perceives this difference and instructs an increase in the androgens to control this hyperplasia.

This increase in the androgen level achieves the optimum rate of proliferation at the endometrium on the one hand, but on the other it retards the proliferation at the ovaries hence failing to mature the ovum leading to formation of several cysts. These "cysts" are actually immature follicles, not cysts ("polyfollicular ovary syndrome" would have been a more accurate name). The follicles have developed from primordial follicles, but the

development has stopped ("arrested") at an early antral stage due to the disturbed ovarian function<sup>65</sup>. On the other hand this hormonal imbalance leads to irregular menstrual cycles, increase in the thickness of endometrium, hirsutism and other symptoms of PCOS<sup>65</sup>.

Other characteristic features of cancer cells are higher requirement of glucose and LDL and recruiting a food supply for them, this leads to hyperinsulinaemia and dyslipidaemia in PCOS patients<sup>66</sup>. Thus we see that an ideal combination of the syndrome is achieved i.e. a polycystic ovary, hyperinsulinaemia, dyslipidaemia and hyperandrogenism resulting in infertility, hirsutism, thickening of the endometrium and irregular menstrual cycles.

**Cancer cells in the breast:** The increased rate of proliferation in this case is in the breasts. Brain instructs an increase in the androgen level to control this hyperplasia. Increased androgen level controls the proliferation in the breasts but retards the proliferation in the ovaries resulting in PCOS and on the other hand retarding the proliferation in the endometrium results in an under prepared endometrium which in case of a pregnancy may not be able to sustain the implant and result into an early miscarriage or nulliparity. Nulliparity is expected in this case because it will prevent pregnancy in two ways, firstly, by delaying the maturity of the ovum or causing anovulation and secondly by an under prepared endometrium, in case of a successful ovulation and fertilization the implanting of the zygote may fail and the patient or the clinician may not even come to know about the success achieved in fertilization. On the other hand this hyperandrogenism is going to persist during the pregnancy and retard the development of the endometrium throughout, thus may result in a miscarriage early or delayed<sup>67</sup>.

**Cancer cells in the ovaries:** The hyperplasia in this case is in the ovaries. Brain instructs an increase in the androgen level to control the hyperplasia. Hence ovulation is normal, multiple cysts in the ovaries are absent in this case, but other symptoms of hyperandrogenism without a poly cystic ovary will be seen. In case of a pregnancy an early miscarriage within 4-8 weeks, till placental progesterone is produced, may occur due to an under prepared endometrium. Late miscarriage may not be expected in this case because during pregnancy there is no ovulation hence no proliferation in the ovaries the increased level of progesterone inhibits pituitary gonadotropins and hence inhibits ovulation<sup>68</sup>. Thus in absence of favorable circumstances the proliferation in the ovaries is automatically controlled, this will allow a normal development of the endometrium later during the pregnancy.

### Inference

Cancer cells are present in any of the three sites of proliferation in the reproductive system of PCOS patients and are responsible for the symptoms of the syndrome and this they do by increased proliferation resulting into



protective hyperandrogenism. Hence the anatomical changes and the physiological symptoms are achieved.

**Table 3: Evidences from hyperandronism**

1.	As per this theory hyperandrogenism in PCOS is caused by quick proliferation of cancer cells in the endometrium, this means that these patients should manifest a thickened endometrium and a higher incidence of cancer of the endometrium.	PCOS patients manifest a precancer hyperplasia and are at a greater risk of getting cancer of the endometrium <sup>69</sup> .
2.	As per this theory hyperandrogenism in PCOS is caused by quick proliferation of cancer cells in the breast, due to ovulation failure and under prepared endometrium it should lead to nulliparity. Thus nulliparous patients should have a higher incidence of breast cancer.	The conclusions of the present study do not contradict the association of nulliparity and age at first birth with breast cancer incidence. <sup>70</sup>
3.	Cancer cells have a higher requirement of glucose and they have the capacity to recruit a food supply for themselves, hence PCOS should be associated with hyperglycemia and hyperinsulinemia.	Hyperinsulinemia is present in PCOS patients and they are at a higher risk of getting diabetes. <sup>71</sup>
4.	Insulin sensitizing agents reduce the availability of glucose for cancer cells <sup>71</sup> , hence reduce the activity of cancer cells and bring down androgen levels. Hence metformin should be effective in both PCOS and endometrial cancer.	Metformin is found to be effective in PCOS and endometrial cancer. <sup>71</sup>
5.	Physical exercise corrects insulin resistance and reduces hyperinsulinemia thus reducing the availability of glucose for cancer cells, hence reducing their activity. Thus physical exercise should reduce the androgen levels by reducing the proliferation of cancer cells and should be an effective remedy for PCOS.	All women with PCOS who are overweight would benefit from a regime of diet reform and exercise. <sup>71</sup>
6.	Metformin should be effective in cancer and what is the dose?	Effective dose of metformin in endometrial cancer may be 850mg twice daily. <sup>72</sup>
7.	Cancer cells show a higher uptake of LDL and they possess the capacity to recruit food supply for themselves, they should also disturb the cholesterol levels of the body.	Close association of dyslipidemia with PCOS confirms this. <sup>73</sup>
8.	PCOS is caused by cancer cells and hyperandrogenism is a protective measure by the body, hence suppressing androgen should increase the risk of cancer in PCOS patients.	Suppressing androgen with spironolactone is carcinogenic. <sup>74</sup> Narsesyan et al attribute the carcinogenic activity of spironolactone to its antiandrogenic activity. Carcinogenic activity of this compound (Spironolactone) in chronic experiments in rats is possibly connected with its influence on metabolism and antiandrogenic activity. <sup>75</sup>
9.	Since androgen and estrogen work in a balance increasing estrogen means suppressing androgen. Thus estrogen therapy should be carcinogenic.	Estrogen therapy for PCOS is carcinogenic. <sup>76</sup> It's disconcerting to think that a natural hormone circulating in significant amounts through the bodies of half the world's population is a carcinogen, but it's now official. In December the National Institute of Environmental Health Sciences (NIEHS) added estrogen to its list of known cancer-causing agents. <sup>77</sup>

Just like pyrexia hyperandrogenism is a symptom of the underlying cause i.e. quick proliferation of cancer cells in the endometrium, breasts or the ovaries and is a

protective measure adopted by the body to restrict the growth of cancer cells. However, the imbalance of hormones thus created is responsible for the symptoms and complications of PCOS.

### Conclusions

This confirms the following:-

- (1) Cancer cells are present in the body of the PCOS patients and are a cause for hyperinsulinemia and hyperandrogenism.
- (2) Syndrome X and PCOS are children of the same parents i.e. the root cause behind both is the same. Presence of cancer cells in the body is manifested as diabetes while hypertension and PCOS are the result of body's attempt to control them.
- (3) Although it is responsible for the symptoms of PCOS, hyperandrogenism is a defensive measure of the body in response to quick proliferation of cancer cells and thus protects the patient from cancer of the endometrium, breasts or ovaries.

### Discussion

**Polycystic ovaries:** - Hyper proliferation of the cancer cells in the breasts or the endometrium results into hyperandrogenism which retards the development of the ovum leading to polycystic ovaries.

**Irregular menstrual cycles:** - Due to increased androgens, improper development of the ovum and the endometrium; the secretion of progesterone is disturbed leading to disturbed cycles.

**Increased endometrial thickness:** - Women with PCOS are also at risk for endometrial cancer. Irregular menstrual periods and the lack of ovulation cause women to produce the hormone estrogen, but not the hormone progesterone. Progesterone causes the endometrium to shed each month as a menstrual period. Without progesterone, the endometrium becomes thick, which can cause heavy or irregular bleeding. Over time, this can lead to endometrial hyperplasia, when the lining grows too much, and cancer.

**Infertility:-** Anovulation is caused due to hyperandrogenism which is a result of hyperproliferation of cancer cells in the endometrium or the breasts.

**Nulliparity:-** There may be several reasons for nulliparity, which include anovulation, or failure of an implant due to an under prepared endometrium. Primarily, anovulation may occur due to retarded proliferation at the ovaries leading to failure of the ovum to mature, thus leading to polycystic ovaries. This may occur due to the presence and hyperproliferation of the cancer cells in the breasts or the endometrium. Not all patients with polycystic ovaries will be nulliparous because they may sometimes ovulate, but ovulation in such patients will be irregular, hence patients will find difficulty in conceiving. Failure of the endometrium to sustain the implant is another reason for nulliparity. In such cases patient or the clinician may or



may not come to know about the success achieved in ovulation and fertilization, the implant may fail instantaneously, before any test could detect the pregnancy creating an impression of a delayed menstrual cycle.

**Spontaneous abortions:-** An under prepared endometrium or the retarded growth of the endometrium may lead to early or delayed abortions. There may be several sets of circumstances which may lead to such a situation. Firstly, hyperandrogenism due to hyper proliferation of cancer cells in the breasts would retard the proliferation at the endometrium leaving it under prepared at the time of implant which may lead to the failure of the implant,

Or the endometrium may be prepared to such extent as to hold the implant for a few days but continuous hyperandrogenism due to proliferation of the cancer cells in the breasts would lead to continuous retardation of the growth of the endometrium, hence the pregnancy may fail at any time. Thus in this case early or delayed abortions may be expected. On the other hand if hyperandrogenism is caused due to hyperproliferation of the cancer cells in the ovaries, the implant may fail early due to under prepared endometrium but a delayed abortion in this case may not be expected because there is no ovulation during pregnancy, the increased level of progesterone inhibits pituitary gonadotropins and hence inhibits ovulation hence no proliferation of cancer cells, resulting into normal proliferation in the endometrium.

**Controlling these cancer cells:-** Insulin sensitizing agents, by improving the utilization of glucose by normal body cells, reduce the availability of glucose for these cancer cells hence control their rate of proliferation. Thus the androgen levels will be reduced<sup>(84)</sup> resulting in relief from the symptoms of PCOS. This is the reason why Metformin has been found to be effective in PCOS, Cancer of the endometrium, in inducing ovulation and in correcting nulliparity besides controlling the symptoms of hyperandrogenism like hirsutism, acne etc<sup>84</sup>.

Insulin sensitizers are thus effective in the following diseases

- 1) All types of cancers.
- 2) Diseases caused due to diabetes and hyperinsulinemia which include:-
  - ❖ Reduced effectiveness of the body's natural Retinoids.
  - ❖ PCOS
  - ❖ Acne
  - ❖ Myopia
  - ❖ Skin tags
  - ❖ Acanthosis Nigricans
  - ❖ Stature

3) Diseases caused due to dyslipidemia and hypertension which include all cardiovascular problems.

Looking into the above scenario we reach to the conclusion that cancer cells are present in the body of every individual and the body fights back in three major ways

- 1) Hypertension
- 2) Hormonal control of proliferation
- 3) Immune action

This three pronged defense adopted by the body leads to various problems related to hypertension, dyslipidemia, hormonal imbalance, autoimmune diseases aging or age related degenerative diseases as depicted in figure 1.

In presence of insulin resistance, the presence of cancer cells is manifested as diabetes only when their number surpasses a certain threshold. However even otherwise, they are neither silent nor in total control of the body but continue to proliferate either gradually or opportunistically initiating autoimmune action, a persistent increase in the androgen levels, resulting in various autoimmune, hormonal and degenerative disorders. Thus if analyzed we should find more evidences from autoimmune and degenerative disorders. Hence let us now analyze the autoimmune disorders like arthritis wherein we will find that besides other evidences the hypothesis in itself will form evidence.

#### EVIDENCES FROM THE IMMUNE SYSTEM

The defense mechanism of the body recognizes the cancer cells and is activated, it continuously fights and destroys these cancer cells but in many cases it may not prevent the manifestation of diabetes, hypertension or PCOS, sooner or later. This is evident from the facts that: - The macrophages induce apoptosis in the cancer cells by producing the tumor necrosis factor –  $\alpha$ .

#### The Evidence

(1) Tumor necrosis factor –  $\alpha$  is produced by macrophage cells<sup>78</sup>. Tumor necrosis factor –  $\alpha$  has anti-tumor activity<sup>79</sup>. Tumor necrosis factor –  $\alpha$  is present in Diabetes<sup>80</sup>, hypertension<sup>81</sup> and PCOS<sup>82</sup>.

(2) If Tnf–  $\alpha$  is produced by the macrophages to fight the cancer cells manifesting as diabetes, Insulin sensitizers which make the cancer cells lethargic by reducing the availability of glucose should ease the action of macrophages and hence reduce Tnf–  $\alpha$  production.

Metformin suppresses the production of tumor necrosis factor–  $\alpha$ <sup>83</sup>

#### THE HYPOTHESES AS EVIDENCE FROM ARTHRITIS

Looking into the entire scenario we can understand that there can be two hypotheses for the pathogenesis of arthritis, first, autoimmune action should destroy the synovial membrane if cancer cells are present in the membrane and second, if cancer cells are present



elsewhere increased androgen levels should hamper the repairing of the daily wear and tear and cause degeneration, and we know that there are two types of Arthritis:

1. Autoimmune: If the cancer cells are present in the synovial membrane resulting into autoimmune action causing Rheumatoid Arthritis.
2. Hormonal: If the cancer cells are present in any other part of the body, the increased androgen level will retard the regeneration and thus repair of the daily wear and tear of the tissues; this in the long term will result into Osteoarthritis.

**Table 4:** Evidences from arthritis.

1.	If arthritis is caused by cancer cells, these patients should show an increased incidence of cancer.	Patients of Rheumatoid arthritis show an increased incidence of non-hodgkins lymphoma, Hodgkin's disease and lung cancer <sup>85</sup> .
2.	Both the diseases are caused by cancer cells hence there should be a connection between Diabetes and RA and an increased incidence of Diabetes in RA.	"There are tantalizing links between the two diseases," says Daniel Solomon, MD, MPH, an associate professor of medicine at Harvard Medical School and a rheumatologist at Brigham and Women's Hospital in Boston <sup>86</sup> . RA may increase the risk by 50 % <sup>87</sup> .
3.	Dyslipidemia should be associated with Arthritis.	Dyslipidemia is associated with Arthritis <sup>88</sup> .
4.	Arthritis patients should show an increased incidence of hypertension.	About one in five patients with low-active RA displayed rheumatoid cachexia. This condition was associated with high levels of LDL cholesterol, low levels of atheroprotective anti-PC and high frequency of hypertension <sup>88</sup> .
5.	Insulin sensitizing should be an effective treatment for Arthritis.	Physical exercise and insulin sensitizers are effective in reducing the Arthritis <sup>89</sup> .

### FINAL CONCLUSIONS

Finally we reach to the conclusions:

1. Cancer cells are present in the body of every individual.
2. They manifest themselves as Diabetes.
3. Increase in the incidence of cancer with insulin is because in presence of insulin resistance, insulin helps cancer cells to take more glucose and thus proliferate quickly.
4. Increase in cancer on taking antihypertensive therapy is because cancer cells get an opportunity to proliferate quickly due to reduction of blood pressure. It does not prove that antihypertensive drugs are carcinogenic.

5. Insulin sensitizers are the most effective way of controlling these cancer cells and thus best available drugs for the treatment of diabetes, hypertension, cancer and all other related diseases discussed above.
6. Body continuously tries to control/eliminate them adopting all possible means, but they are never in total control of the body.
7. They are responsible for a wide variety of disorders ranging from diabetes to cancer, hypertension to cardiac problems, aging to degenerative disorders, hormone imbalance to metabolic disorders and autoimmune disorders.
8. Best control of these cancer cells is possible only through insulin sensitization achieved through physical exercise.

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