

## Auto immunity and fragmented Germ Cells

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**Abstract:** Background: Autoimmune diseases` incidence had increased significantly by 1995-as compared to 1983, by when tubectomy, contraception was being steadily implemented; hence an altruistic correlation was sought after.

Methods: Data of 64 people with varied autoimmune diseases spread over 1989 -2012 from 7 geographical locations, each separated by ~500 km distance, was tabulated into 3 age groups, namely 20-35 years, 35-50 years, >50 years and association with contraception status, consumption of fish without scales, gills, shell fish, was analyzed by bio informatics, retrospectively in 2012.

In 2002, 2003 data of 105 patients from the community and hospital was analyzed for association of contraception status, prevalent diseases and estrogen levels.

Results: Contraceptive users demonstrated 15 fold increase in auto-immune diseases among 20-35 years [ $p < 0.0005$ ]; 40 fold increase in auto-immune diseases among 35-50 years [ $p < 0.0005$ ]; 5 fold increase in autoimmune diseases were seen with consumption of fish without scales and gills in non contraceptive users also.

Endogenous estrogen was reduced below normal in 61% of patients using contraception [ $p < 0.0005$ ].

Conclusion: The concept is contraception results in smashed fragmentation of Germ Cells, to a centric fragments, ring chromosomes, chromatid breaks, being identified by immune surveillance as foreign, leading to auto immunity; associated reduced endogenous estrogen or androgen, results in defaulted cell cycle, cell metabolism of differentiation, growth, controlled multiplication, degeneration, apoptosis, regeneration, genomic repertoire, leading to impaired immunity; auto-immunity is also produced by consumption of fish without scales and gills due to its toxins mediated cytotoxicity, by molecular mimicry, in non contraceptive users also. Abstinence for 7 days after last menstrual period, prevents exposure of raw endometrial surface to germ cells; abstinence for 45 days after male baby delivery, 90 days after girl baby delivery prevents germ cells exposure to raw placental detached surface and reduces auto immunity.

**Key Words:** Era of Contraception; smashed fragmentation of germ cells; autologous germ cell replant; subsets of population with, without contraception.

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### I. Introduction

As contraception was effectively, increasingly, implemented by 2000, increased incidence of dreadful autoimmune diseases like systemic lupus erythematosus, rheumatoid arthritis, demyelination, poly radiculopathies, transverse myelitis, multiple sclerosis, thyroiditis, auto immune hepatitis, purpuras, hemolytic anemia, with crippling disabilities, morbidity, mortality, were noticed by ~1994 [era of contraception-20<sup>th</sup>, 21<sup>st</sup> centuries]; increase in auto-immune diseases in reproductive age group was obvious; people were attributing onset of, for e.g. polyarthritis to after tubectomy, [implemented as family welfare schemes, without evidence base i.e. no prior or post studies for safety or therapeutic indication]though ignored by medical professionals, since the procedures as such were uneventful; hence a retrospective analysis to detect, any possible correlation with contraception [if any], as etiology for increasing autoimmune diseases was planned.

### II. Methods:

Data of 64 people with various auto immune diseases namely systemic lupus erythematosus, angioneurotic edema, demyelination, polyradiculopathy, tranverse myelitis, neuromyelitis optica, multiple sclerosis, nephritis, progressive systemic sclerosis, primary pulmonary hypertension, mixed connective tissue disease, rheumatoid arthritis, who were cared for, by the corresponding author, spanning over 1989-2012, from 7 geographical locations, separated by ~500Km. distance, was tabulated, to correlate with contraception status of the individual, their parents, consumption of fish without scales, gills .The data was stratified into 3 age groups i.e. 20-35 years, 35-50 years, >50 years and retrospective bioinformatics analysis was undertaken in 2012.

Correlation of consumption of fish without scales and gills, contraception status, with acute kidney disease, demyelination, pancreatic cancer, gastro enteritis, angio neurotic edema systemic sclerosis, systemic lupus erythematosus and urticaria were also analyzed retrospectively from data of 403 patients having presented with corresponding illnesses from 1989-2012 clinical practice of the corresponding author; of them 97 patients had nephritis, 33 patients were diagnosed to have progressive systemic sclerosis or systemic lupus erythematosus, 31 patients had manifested with angioneurotic edema, and 58 patients had demyelination. These patients also were divided into the 3 age groups.

In 2003 house to house survey in the community, spread over 3 weeks, was conducted by the corresponding author, to collect data of prevalent diseases of 100 people; the people who were present during the survey were included at random, by convenient sampling into the 3 age groups namely 20-35 years, 35-50 years, >50 years, to include a minimum of 30 people in each age group; serum estrogen estimation was done for 12 people as per their request; the reduced estrogen levels [5-8pg] found in young contraceptive users, was the eye opener, leading to further data analysis.

In 2004 data of 93 hospital patients was collected over a period of 6 months, including diseases prevalent, contraception status, life style, nutrition, type of oil ingested, level of hemoglobin and were assigned to the 3 age groups by stratified random sampling with a minimum of 30 patients in each age group; serum estrogen estimation was done for all 93 patients; the data was tabulated matching diseases against status of contraception and other variables; one patient was a foreign national.

### **III. Results:**

Among 20-35 years, 15 fold increase in auto immunity with a p value of <0.0005, was noticed in contraceptive users for e.g. systemic lupus erythematosus, multiple sclerosis, neuro myelitis optica, poly arthritis, hashimoto's thyroiditis, transverse myelitis, poly radiculopathies, nephritis progressing to renal failure, demyelination presenting as myoclonus, myasthenia gravis, hemolytic anemia Figure 1.

People of 35-50 years exhibited 40 fold increases in auto-immunity [as portrayed earlier] amongst contraceptive users with a p value of <0.0005.

~70 years were only non contraceptive users; auto immunity with its mortality, had probably resulted in early agonizing demise in contraceptive users.

2 fold increase in auto immunity [ p<0.025] namely angio neurotic edema, urticaria, lupus nephritis, systemic sclerosis, renal failure, myoclonus secondary to demyelination was seen in people without contraception specially in the coastal areas, where fond consumption of fish without scales, gills (shell fish, crabs, prawns) is existing Figure3.

Contraception combined with consumption of fish without scales and gills increased the risk of systemic lupus erythematosus, progressive systemic sclerosis by 5 fold among 15-35 years[p<0.0005], among 36-50 years 20 fold increase was seen[p<0.0005]; angioneurotic edema increased among 15-35 years by 5 fold[p<0.0005], among 36-50 years 10 fold increase was seen[p<0.0005]; demyelination was increased by 10 fold among 15-35 years [p<0.0005], 35 fold increase in demyelination was seen among 35-50 years[p<0.0005]; immune mediated nephritis was seen in 16 fold rise among 15-35 years [p<0.0005] and >20 fold increase in nephritis was seen among >36->50years [p<0.0005] figure 3.

15 years adolescents were also manifesting auto immunity either after fish without scales, gills consumption, or born to parents who had used contraception or did not observe abstinence during raw endometrial surface, prior (copper-t, condoms attempted medical termination etc.) to the corresponding pregnancy or were fed on cholesterol deprived diet e.g. progressive systemic sclerosis, multiple sclerosis, angio neurotic edema, nephritis, demyelination, urticaria.

Contraception reversal, recommendation to observe abstinence during raw endometrial surface, with consumption of essential fatty acids rich diet, avoiding consumption of fish without scales, gills as a cause and effect phenomena, regressed autoimmunity(neuro myelitis optica, radiculopathy, multiple sclerosis, reactive arthritis, demyelination, myoclonus, rheumatoid arthritis, nephritis) which were relentlessly progressing, in spite of immune suppressants, prior. There was steady improvement to near complete recovery with no remissions, exacerbations figure 2

61% of people using contraception had below normal estrogen [p<0.0005]; 25% of people using contraception had low normal estrogen-supplementary figure.

Young adolescents, people without contraception improved with corresponding therapies including intravenous immunoglobulin, steroids and essential fatty acids rich diet, avoidance of harmful ingestion of fish without scales, gills.

#### **IV. Discussion:**

Autoimmunity can be defined as immune responses against self tissue and is to some extent ubiquitous; often harmless phenomenon is identified by the presence of low titer auto antibodies or auto reactive T cells; auto immune diseases occur if these auto immune responses cause significant organ damage; <sup>1</sup> major cause of morbidity and disability affecting 1 in 30 adults.

Organ specific autoimmunity is seen in Graves disease, autoimmune hemolytic anemia, Good Pasture's syndrome, Myasthenia Gravis, pemphigus vulgaris, purpuras, primary biliary cirrhosis, primary antiphospholipid syndrome, rheumatoid arthritis, type 1 diabetes mellitus, pernicious anemia; multisystem involvement is seen in systemic lupus erythematosus, mixed connective tissue disease, systemic sclerosis

Immunological tolerance in immune response, identifying self from foreign, failure of which results in auto immune disease;

Central tolerance occurs during lymphocytes development and this operates in thymus, bone marrow; T, B lymphocytes that identify self antigens are eliminated, this is active in fetal life, continues throughout life as immature lymphocytes are generated; some auto reactive cells escape deletion and enter circulation.

These are controlled by peripheral tolerance mechanisms; suppression of auto reactive cells by regulatory T cells and the generation of hypo responsiveness [anergy] in lymphocytes which encounter antigen, in the absence of the co stimulatory signals that accompany inflammation. Antigens within the eye are not normally patrolled by lymphocytes, antigens within these 'immunologically privileged' sites are inaccessible to auto reactive cells; when the cells or components of cells that are not exposed to immune response as self antigen, gets exposed after cell, tissue damage, auto immunity can develop.

Literature mentions both genetic, environmental factors contribute; auto immune diseases are more common in women than men the reason is unclear; determinants of auto immune susceptibility are HLA genes, responsible for shaping lymphocyte responses. Other susceptibility genes include cytokine activity, co-stimulation and cell death. Several environmental factors trigger auto immunity, in genetically predisposed individuals, common is infection for e.g. rheumatic fever after streptococcal infection, reactive arthritis after bacterial infection; one of the mechanisms postulated is cross reactivity between infectious pathogen and self determinants [molecular mimicry] and release of sequestered antigens not visible to the immune system, from damaged tissue, alternatively infection leads to production of inflammatory cytokines, overwhelming the control mechanisms, that prevent bystander damage.

Gell and Coomb's classification of hypersensitivity diseases: type-1: immunoglobulin E mediated mast cell degranulation, allergic disease, not autoimmune; type-2: antibody mediated binding of Immunoglobulin G, M, to antigens on cell surface and cell killing; type3: immunoglobulin G and M bind to soluble antigens, form immune complexes which trigger complement pathway; type4: mediated by activated T cells, phagocytes, natural killer cells;

Susceptibility genes for autoimmunity comes from family studies-15-30% of pairs of monozygotic twins <sup>2</sup> show disease concordance, compared with 5% of dizygotic twins in rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, type-1 diabetes mellitus; gene coding PTPN22 is associated with multiple auto-immune diseases; its product is a phosphatase, expressed by a variety of hemopoietic cells, that down regulates, antigen receptor mediated, stimulation of T and B cells; mechanism of tissue injury in auto immune diseases is divided into antibody mediated and cell mediated processes; auto antibodies bind to alpha 3 chain of type -4 collagen in the basement membrane, in systemic lupus erythematosus; immune response to self antigen, causes the pathology in auto-immune diseases.

90% of patients with systemic lupus erythematosus <sup>3</sup> are in reproductive age group, incidence is 10-400 /lakh population; estradiol of oral contraceptive pills, hormone replacement therapy increases risk of systemic lupus erythematosus. ultra violet light increases flares by 70% increasing apoptosis in skin cells, altering Deoxy ribonucleic acid, intercellular proteins to make them antigenic; infections induce a normal immune response that matures to contain T and B cells that recognize self antigen, such cells are not appropriately regulated, Epstein Barre virus can trigger systemic lupus erythematosus, in susceptible individuals; Epstein barre virus amino acid sequences mimic sequences on human splicesomes-ribonucleic acid, protein antigens often recognized by auto antibodies. Tobacco smoking, prolonged exposure to silica increase the risk.

Multiple sclerosis, demyelination disorders <sup>4</sup> are immune mediated characterized by destruction of central nervous system, peripheral nervous system is spared; multiple sclerosis is the most common disease, second only to trauma as a cause of neurological disability, beginning in early to middle adult hood; 3,50,000 individuals in United States of America, 25 million in the world, rapidly evolving incapacitating disease.

Rheumatoid arthritis <sup>5</sup> is a chronic inflammatory disease of unknown etiology marked by symmetric poly arthritis, it's a systemic disease; serum antibodies to cyclic citrullinated peptides are now recognized as a valuable biomarker, with high specificity.

Urticaria involves superficial portion of the dermis <sup>6</sup> presenting as well circumscribed wheals with erythematosus raised serpiginous borders, blanched centers that may coalesce to form giant wheals; angio

edema is a well demarcated localized edema involving deeper layers of the skin including the subcutaneous tissue and are disorders of immune mediated injury including allergies, anaphylaxis. Shell fish, fresh fruits, fish, milk products, legumes including peanuts, various drugs, pollens, animal dander, mold spores, microfilaria in the lymphatic, chocolate, legumes can produce wheals, angio neurotic edema and dermatographism.

The concept is contraception (condoms, copper-t, vasectomy, tubectomy, abortions)–guillotine protocol based-(without therapeutic indication, without evidence based i.e. no studies prior or post contraception for necessity, safety in medical practice, as against the principles, practice of medicine) implemented, permitted by Life Sciences –unaware results in definite, smashed destruction<sup>7</sup> of extremely fragile germ cells-[slender chromatids with minimal collagen, life in them-moves, respire, metabolizes-(marvel God ordained physiology,)which would have liquefied to disappear within a minute, as in the case of 20 million sperms; in 24-48 hours the oocyte after release, if not fertilized, will go out as blighted ovum;] which are fragmented to<sup>7</sup> chromatid breaks, a centric fragments, ring chromosomes in uterus, peritoneal cavity, urogenital pathways of life partners(by the barricades of contraception, offered during high neurohumoral mediation to gush out sperms ).

Associated reduced endogenous estrogen mediated by hypothalamic-pituitary axis governed by feedbacks from fragmented nuclear materials, collagen of slender chromatids is also detected; these fragmented nuclear materials, components of chromatids, collagen of germ cells are recognized by immune system as foreign( not present in non contraception -normal physiology) auto antibodies namely anti nuclear, anti histone, anti smooth muscle , antimicrosomal, anti thyro peroxidase antibodies; since zygote's genetic information is present identically in all cells,<sup>8</sup> auto antibodies developed against chromatids' components of germ cells can destroy every cell, any system – organ specific, multisystem diseases, increases with age, present during reproductive age group, more in women.

Reduced endogenous estrogen secondary to artificially acquired contraception results in neoplastic changes, degenerative cell changes due to genomic repertoire<sup>8</sup> default i.e. cell differentiation, controlled multiplication, metabolism, growth nurture requires this hormonal surveillance without which the degenerative diseases namely diabetes mellitus, systemic hypertension, renal, liver failure, hypothyroidism, obesity, epilepsies, depression, psychiatry disorders, divorces suicides , sexual promiscuities acute coronary syndrome, stroke occur with 275% increase after contraception, 500% increase after hysterectomy.

Cholesterol deprived diet results in decreased endogenous hormones synthesis since low density lipoprotein is converted to endogenous estrogen, steroid hormones; with resultant increase in degenerative diseases<sup>9, 9a</sup>

The concept is germ cells traverse the lumen of genital tract lined by mucosa, physiologically; raw bloody, incompletely regenerated endometrial surface exposure to germ cells, also can initiate auto antibodies, i.e. 7 days abstinence after last menstrual period {3 days shedding+4 days regrowth of endometrium}, 45 days abstinence after boy baby delivery, 90 days abstinence after girl baby delivery(raw detached placental surface is double for girl baby with double x, more estrogen synthesis which is 2-3 steps later in synthesis than androgen, hence longer duration of lochia i.e. 25 days for male baby delivery, 45-50 days for girl baby delivery, so double the time of abstinence allowing time for the shed endometrium to re grow) if not observed by fathers, life partners, then raw endometrial surface exposure to germ cells can initiate auto immune processes or auto reactive cells endangering mother's life peripartum by e.g. vasculitis and can be transmitted in low titer exposures to the next child born leading to collagen vascular diseases in the child by teen age since the immune multiplication increases with age.

Shell fish, fish without scales, gills, on ingestion [their cells with their proteins-(flesh) initiate] auto antibodies either by molecular mimicry or hap ten mediated mechanisms by their toxins or proteins ; consumption of fish without scales, gills is seen to be associated with pancreatic cancers, painful diverticulitis requiring hemicolectomy, angioneurotic edema, myoclonus, demyelination with transverse myelopathies, poly radiculopathies, nephritis, urticaria, gastro enteritis, gastrointestinal neoplasm.

When a mother wears copper-T or uses some contraception in between pregnancies ,auto antibodies developed by smashed fragmentation of germ cells are transmitted to the progeny through the placenta and the child born after contraception, as they grow in age they increasingly manifest auto immune diseases as the autoimmunity multiplies with age; in addition, placenta accrete like complications can develop during pregnancy following contraception, secondary to chronic endometriosis, fibrosis of endometrium. A teen ager without practicing contraception( generally in India, premarital sex is still prohibited) can develop auto immune diseases by this above portrayed mechanism-interim contraception between pregnancies by the parents and trans placental transmission or by consuming fish without scales, gills.

Contraception reversal leads to halt of germ cells destruction, restoration of endogenous estrogen or androgen, cell cycle, cell metabolism, auto immune diseases regress-79.9% and does not progress to multisystem involvement or end stage diseases-figure 2

## V. Conclusion:

The concept is contraception, abortion, with smashed fragmentation of germ cells, to a centric fragments, ring chromosomes, chromatid breaks, identified by immune surveillance as foreign, results in autoimmunity; since genetic information in every cell is identical to that of zygote, auto immunity to any loci of genes can develop involving multisystem closely present in the loci of chromatid breaks; associated decreased endogenous estrogen, androgen surveillance for cell metabolism, cell cycle, cell immunity, tolerance, has resulted in enhanced auto antibody production, auto reactive cells, increase in auto immune diseases by 15 fold among 20-35 years, 40 fold increase in auto immune diseases among 35-50 years [p <0.0005]targeting multiple systems, namely nephritis, poly radiculopathy, demyelination, multiple sclerosis, neuro myelitis optica, transverse myelitis.

Non contraceptive users also manifest 5 fold increase in auto immune diseases with a p value of <0.0005 probably because of consumption of cholesterol deprived diet, fish without scales and gills, exposure of germ cells to raw bloody endometrial surface instead of abstinence during first 7 days after last menstrual period, 45 days after male baby delivery, 90 days after girl baby delivery.

Adolescents manifest auto immune diseases probably by trans placental transmission of auto antibodies from the mother who had used interim contraception in between prior pregnancies and by consumption of fish without scales, gills; cholesterol deprived diet, resultant reduced endogenous estrogen, androgen, genetic acquired defects, increased gene susceptibility to auto antibodies.

Contraception reversal, halts germ cells destruction, retrieves normal path transport of germ cells, restores endogenous estrogen, androgen[similar to autologous germ cell replant effect] and 79.9% diseases regress including autoimmune diseases without exacerbations; defaulted genomic repertoire under hormonal surveillance is restored.

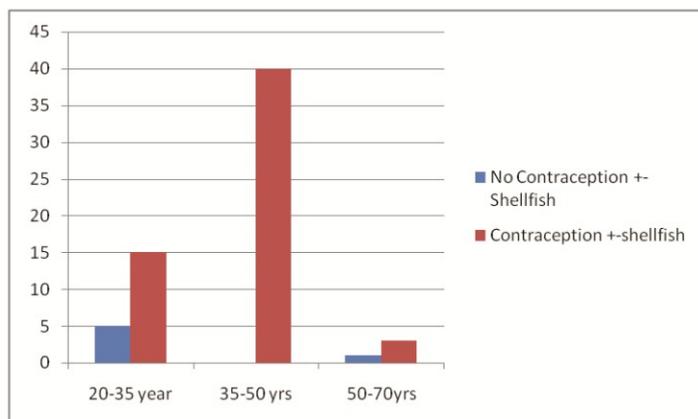
### Key Points:

- Contraception increases auto immune diseases by 15-40 fold increase among 20-50 years [p <0.0005]
- Adolescents manifest auto immune diseases by Tran's placental transfer of auto antibodies from the mother who had used interim contraception between pregnancies.
- Contraception with smashed destruction of germ cells into nuclear fragments results in auto antibodies, auto reactive cells.
- Non contraception also manifests 5 fold increase in auto immune diseases by consuming fish without scales, gills; exposure of germ cells to raw endometrial bloody surface.

### Conflicts Of Interests: None Declared

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Prevalence of autoimmune diseases (1989-2012-clinical practice)

Figure 1

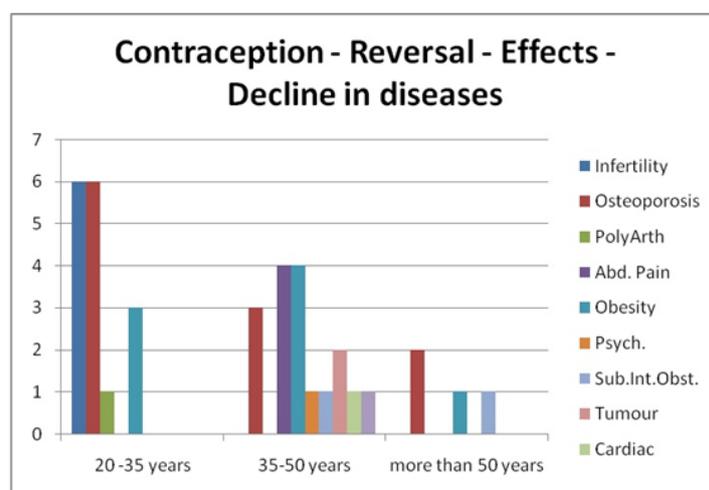


Figure2

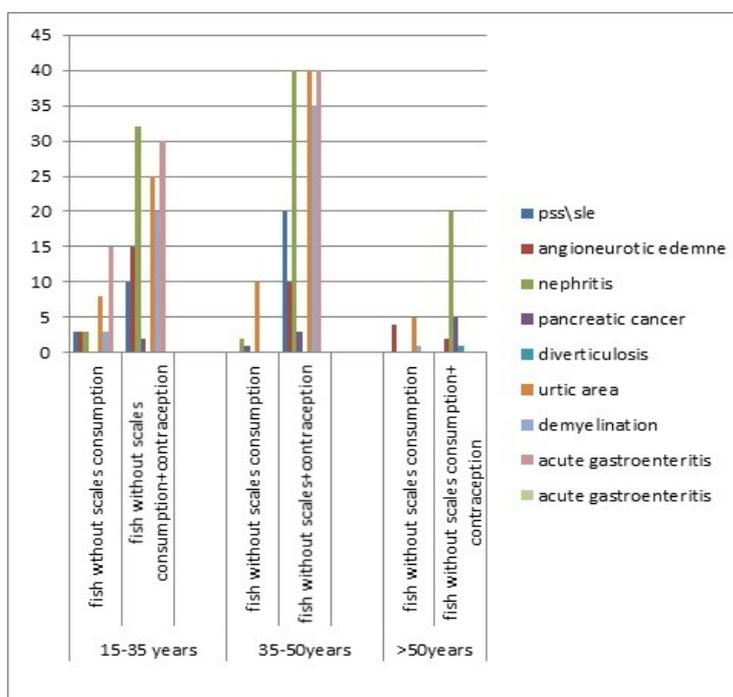


Figure-3 Prevalence of auto immune diseases and contraception

