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Original Antigenic Sin

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I have been asked to talk about immunisation today. The core of my argument relates to a concept called original antigenic sin. The "doctrine", as written in 1960[1] said:

"The antibody of childhood is largely a response to dominant antigen of the virus causing the first type A influenza infection of the lifetime. The antibody forming mechanisms are highly conditioned by the first stimulus, so that later infections with strains of the same type successfully enhance the original antibody to maintain it at the highest level at all times in that age group. The imprint established by the original virus infection governs the antibody response thereafter. This we have called the Doctrine of the original Antigenic Sin."

The part of this doctrine I wish to concentrate on is the PROCESS by which immunity happens, and how it can be affected.

One example is related to the immunity process created by the whooping cough vaccine and its abnormal immunity pathway (See page 506, Cherry 04.pdf/ and chapter 82 in FOPTA for detailed explanation) that is different from that of natural disease and likely to result in carrier state. If it indeed is determined by how the infant experiences the disease, (and or other epigenetic effects), then why do we risk vaccinating babies at birth for no right reason?

To put the vaccination "event" into context, this presentation will look at the factors that determine which babies are most likely to suffer; the which, what, why, how, where and it what order it all happens.

My central theme, as the quote below infers, is outlining the specific time frames within the neonatal developmental process… during which, any assault on the immune system learning process will ultimately cost some children a huge price.

[1] Francis T Jr., 1960. "On the doctrine of Original Antigenic Sin." *Proc Am Philos Soc* 104:572.

Caveat: Much of the research related to the immune system is done on mice or rats even though they are so different; some has also been replicated in human subjects.

It should also be stressed that damage is not limited to the neonatal period. I am living proof of that, as are others like me. The immune system and blood brain barrier of a child or an adolescent are different from those of an adult, and vaccines hold risks for them all. Humans are not identical clones and the developmental processes are such that in my opinion, it is never a time to dive in with needles, thick and fast.

If vaccines cause damage, then why don't they trash every baby they are given to? That is what I'd like to talk about tonight.

The vulnerability of the neonatal immune system of any species is an irrefutable biological fact.

> ***"I would challenge any colleague, clinician or research scientist to claim that we have a basic understanding of the human newborn immune system. It is well established in studies in animal models that the newborn immune system is very distinct from the adolescent or adult. In fact, the immune system of newborns in animal models can easily be perturbed to ensure that it cannot respond properly later in life."***
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> ***May 12, 1999, Verbal testimony: USA Senate Dr Bonnie Dunbar.***

Dr Bonnie Dunbar, Professor of Immunobiology spent over 25 years of her career working in vaccine development and autoimmunity, mostly at Baylor University, USA. When her brother and two of her laboratory assistants sustained serious permanent damage following their work-required Hepatitis B vaccination, she woke up to the reality of "vaccine damage".

In terms of the human baby, such a quote needs to be put within the whole context of physical and immunological development during gestation, around birth and through the first few years of life.

Also essential, is a careful look at the difference between dogma and what is known and not yet known. The word "science" is often not synonymous with "established accurate fact". One of my caveats in regards to this discussion is that I'm all too well aware of how much the medical profession doesn't know, and how much that affects, alters or makes a monkey of what they do know and what I might say today.

GENES

First I want to talk about genes, because they are the "in thing". "Vaccinomics" is partly about finding out which genes cause people *not* to develop immunity to vaccines (and diseases). We are discovering, as we learn more, that the action of genes often depends on diet: Poor diet leading to faulty gene expression and resulting in inadequate immunity… exactly what anecdotal literature of old told you about malnutrition but using fancy words. One of the USA's foremost proponents of vaccinomics is Gregory Poland, the ardent vaccine defender (See FOPTA for discussion of vaccinomics).

Some geneticists are finally realising that it's not the ***genes*** per se that determine disease susceptibility and orchestrate the development of immunity, but the environmental impact on gene expression and ultimate function:

http://www.telegraph.co.uk/scienceandtechnology/science/sciencenews/5190914/Genetic-magic-bullet-cures-have-proven-a-false-dawn.html

Professor Steve Jones, a geneticist, said the belief that a few genes held the key to ridding the world of conditions such as cancer and diabetes had proved to be "plain wrong". …

Scientists embarked on a search for rogue genes responsible for just about every modern malady, hoping such conditions could be blamed on a small set of genes - which could then lead to a cure.

But the more they investigated, the more complicated they realized finding a cure would be. Many individual genes say little about the real risk of illness, and they found ***diet and the environment had a significant influence*** *on the development of disease.*

In other words, because genes are not static and pre-recorded automatons, the real question that must be asked is: ***"what are those factors that 'alter' genes and cause gene expression to go haywire?"***

Everyone knows ***or should know*** that the foundation of a healthy baby's life is laid during pregnancy, but how many pregnant women and their partners really appreciate how crucial the weeks of gestation are for the rest of the child's life? And how many realize that proper nutrition and optimal health must start even before pregnancy, during the all important adolescent years? How many young mothers really understand the amazing changes that do occur inside their bodies and very candidly how many health professionals are truly able to explain all that to them? Not too many I would dare say!

PREGNANCY

In 1989, Kerstin Uvnäs-Moberg wrote "The Gastrointestinal Tract in Growth and Reproduction"[2] after carefully studying her own four pregnancies and described how polypeptides[3] "***exert profound effects not only on the process of digestion itself but also on the metabolism of ingested nutrients and even on the emotions and behaviour. At no stage of life are these physiological functions more critical than during growth and reproduction."***

The normal activity of the gastrointestinal tract clearly changes during pregnancy in order to orchestrate the all important changes in the mother's body that will result in specific weight gain for specific purposes.

Cholecystokinin inhibits the transit of food out of the stomach, enhancing digestion and absorption of nutrients into the circulation. It also stimulates the release of bile from the gallbladder and the secretion of pancreatic enzymes. Its higher levels during the first trimester of pregnancy leads to the nausea, intense hunger, vertigo, and fatigue that are common during that period and are aimed at reducing physical activity and allowing the body to function more properly. Working without let-up during pregnancy is therefore counterproductive to the purpose and function of the physiologically increased cholecystokinin production. After the third month, the levels of cholecystokinin gradually decrease but remain elevated up to delivery, optimizing digestion and facilitating anabolic metabolism and weight gain.

Secretin stimulates the secretion of bicarbonate to neutralize gastric acidity and both ***thicken the gut mucosa and*** acting as growth hormones.

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[2] Uvnäs-Moberg, K. 1989. "The Gastrointestinal Tract in Growth and Reproduction" *Sci Am*. July; 261 (1) 78-83 PMID 2568686

[3] Polypeptides: short protein chains of from 10 to 100 amino acids.

Somatostatin decreases gastrointestinal motility and blocks the secretion of hydrochloric acid in the stomach and of bile from gallbladder thus inhibiting the uptake of nutrients and moderating cholecystokinin and gastrin.

The Peyer's patches in the mother's gut double in size in order to later establish a gut/breast connection and seed the newborn with essential bacterial fragments encased inside mononuclear cells. A pregnant woman's bone turn-over changes markedly. Her immune system changes, and suppresses the innate arm in order not to reject the "graft" that is her baby. How her body functions is radically altered. Many women can also relate to "brain mush" of pregnancy. It's all part of a process.

The baby is trained for digestion by regularly swallowing amniotic fluid since the first month of gestation. This results in the secretion of foetal gastrin, and somatostatin, which are released in a time pattern resembling that seen after breastfeeding.

I wonder if this is also intended to keep the amniotic fluid always "clean".

The absence or serious decrease in the intake of nutrients during pregnancy and or any interference with their absorption can and do compromise intra-uterine growth and health.

Examples of ***nutrient absence*** or deficiency are:

- Maternal folic acid deficiency resulting in neural tube defects: DNA cannot make accurate copies of itself without folic acid resulting in incorrect gene replication/expression
- Maternal selenium and magnesium deficiency hampering he ability of the cervix to open during labour. This seems to be only well known by veterinarians.

As so well stated[4] : ***"The maternal nutrition and metabolic environment is critical in determining not only reproduction but also long term health and viability."*** Data from Holland looking at famine in World War II found that famine in the first trimester led to an increased risk of adult coronary heart disease; second trimester famine led to an increase in renal disease, and late gestation famine led to low birth weight for the length of gestation with glucose-insult homeostasis being most affected."

[4] Symonds M.E., 2007 "Long-term effects of nutritional programming of the embryo and fetus: mechanisms and critical windows." *Reprod Fertil Devl* 19(1):53-63. PMID: 17389135.

There is a huge body of work looking at what happens in utero and later, ***when macro and micronutrients are lacking.*** Unfortunately most of the focus is on what can be done in early childhood in order to mitigate the damage incurred during pregnancy. It would seem that the first priority should be to teach pregnant women proper nutrition at the right time.

Two different examples of interference are:

1) That caused by certain antidepressants[5] which can lead to an increase in atrial septal defects, and the combinations of certain SRI's with benzodiazapines that sometimes result in an increase in cardiac anomalies.
2) Prenatal depression[6] of itself, and without drug interference, adversely affects fetal growth and is a potential risk factor for a number of pregnancy complications including miscarriage, premature delivery, low birth weight and a smaller head circumference. Infants born to seriously depressed mothers are also more likely to exhibit growth retardation through the first year of life, as well as increased morbidity, mortality, adverse neurodevelopmental outcomes, cardiovascular disorders and diabetes. ***A threefold increase in maternal cortisol levels*** can impact the foetus by the second trimester.

The study revealed that **prenatal depression was associated with poorer diet and eating habits.** Although the authors **did NOT collect information about the mothers' nutrition** they nevertheless stated that "***Future research should evaluate maternal nutrition as a potential moderator for the effects of maternal depression on fetal development***"!

Better maternal education will help ensure that a woman will start a pregnancy in good health and on an excellent diet, so that at least her nutrition will not be a trigger for depression.

An ongoing study reported in the Sunday Star Times[7], revealed that ***stress hormones in pregnancy created timid, anxious and temperamental children***. Professor Michael Meaney also stated that attention deficit disorder, fear, anxiety, acute shyness, social phobias and schizophrenia could all be linked back to poor foetal development and

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[5] Oberlander, T.F., 2008 **"**Major congenital malformations following prenatal exposure to serotonin reuptake inhibitors and benzodiazepines using population-based health data." *Birth Defects Res B Dev Reprod Toxicol.* Feb;83(1):68-76. PMID:18293409.

[6] Diego M.A., 2009. "Prenatal depression restricts fetal growth" *Early mum Dev.* Jan;85(1):65-70 PMIX: 18723301.

[7] Chisholm D. 2008. "Anxious mothers make timid babies" *Sunday Star Times* August 10, Page A5.

maternal stress. His study was looking at where these problems can be offset by good parenting skills and better upbringing.

Maybe we should be dealing with the reasons that make mothers so often anxious and stressed and particularly those created by the demands resulting from the so-called "obstetric best practice".

3) Mother's anxiety during pregnancy is sometimes associated[8] with asthma in their children. The study said there was causal evidence for a dose response relationship, but its mechanism remains speculative. Two pathways have been proposed: ***direct epigenetic effects and neuroendocrine dysregulation***: that prenatal stress alters the hypothalamo-pituitary-adrenal axis regulation leading to programmed alteration of stress responses after birth, altered cytokine patterns or epigenetic regulation of the glucocorticoid gene, and altered methylation of genes of relevance to asthma.
4) The use of anti acids to stop heartburn[9] [10], or for any other reason, at any time during pregnancy, enhances the production of food-specific IgE antibodies.

In other words, gene expression is a direct response to signals from the environment.

The influence of anti acids is not surprising when one understands the careful nutrition/ immunological/ph balance of the gut. The article stated that "***maternal acid-suppressive drug use significantly increased the risk for developing childhood asthma***." The mechanism for preventing food allergy is that gastric acid suppression interferes with normal digestion of peptides in the stomach, changes the ph, which will change the gut flora and lead to increased IgE sensitization and increases Th2-bias in the offspring, with a significant increased chance of developing asthma.

After birth, adult ph levels are not reached until the age of 2 on average, forcing skeptics to wonder whether the use of drugs such as Zantac in babies presumably to control hyperacidity and gastro-oesophageal reflux might also cause allergy. One can't mess with things at the wrong time and not expect negative consequences.

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[8] Cookson, H. 2009. "Mothers' anxiety during pregnancy is associated with asthma in their children." *J Allergy Clin Immunol.*IApril 123(4):847-853. PMID: 19348924.

[9] Kemp A.S., 2009. "Allergy and gastric acid suppression." *Clin Exp Allergy* Feb; 39(2):176-8. PMID :19068100

[10] Dehlink E, et al., 2009. "First evidence of a possible association between gastric acid suppression during pregnancy and childhood asthma: a population-based register study." *Clin Exp Allergy* Feb; 39(2):246-53 PMID: 19134022

5) Antibiotics during pregnancy.
6) Acetaminophen during pregnancy,

Other interferences, which are less obvious, are estrogen mimickers, lead, and toxins. In fact any drug or vaccine administered during pregnancy can cause problems.

The only reliable immunological protection a newborn receives before birth is from IgG antibodies to bacteria and viruses transmitted through the placenta.

Birth.

Birth is ***the absolute lynch pin***, for healthy immune development, even for "healthy" babies.

How a baby is born, makes a huge difference to what happens in the first 12 months of life, yet many doctors and mothers consider ***caesarians to be a matter of "choice".***

Vaginal Delivery

Vaginal birth is the newborn's first experience of sustained stress where a whole series of important events occur which can deeply influence the infant for a long time.

Catacholamines triggered in labour result in absorption of lung liquid and improve lung compliance. *The excretion of catecholamines, which make a baby absorb lung fluid during labour so that once the baby is ready his chest expands and oxygen transfer happens unimpeded by "wet lung" dysfunction.*

Catacholamines dilate bronchioles; increase blood flow to vital organs, mobilize fuel to break down normal fat into fatty acids for mitochondrial use, and protect the babies from levels of hypoxia that later in life could seriously compromise an adult. Research[11] shows that this up-regulation combined with the rapid colonization of mucosal and skin surfaces during birth, triggers the release of IL-6 in the newborn, with effects on the immune system, temperature regulation and behaviour.

[11] Marchini G., 2000. "The birth process initiates an acute phase reaction in the fetus-newborn infant." *Acta Paediatr.* Sep;89(9):1082-6. PMID: 11071089.

But most importantly from the perspective of this presentation, ***the process of labour up-regulates the innate immune system***[12] of newborns, (in particular to gram –ve and gram +ve bacteria), in order to safeguard them when they first become exposed to the environment, and starts the process of immune system education.

Caesarian delivery:

Elective caesarian without labour can result in:

1. "Wet lung" which can lead to transient tachypnea, and breathing issues for days and dangerous colonization with infectious bacteria leading to infection.
2. Colonization of the gut flora with a different mix of bacteria, primarily from nurses and doctors hands, incubators or nursery surroundings; the results of which can be seen for up to a year, ***whether or not the mother breastfeeds*** later. This can predispose the baby to diarrhoea, and asthma/allergic sensitization and allergic rhinitis.
3. Lack of stimulus and immune priming to protect the baby from sepsis and other infections.
4. Bonding issues with the mother, particularly if the caesarian leaves the mother debilitated, and the baby flat.

But the critical factor for immune development is the LACK of bacterial flora colonisation because the baby did not come down the vagina.

Importance of bacterial colonisation intra-vaginally.

The journey down the upper vaginal canal starts the vital seeding of the gastrointestinal system with the right flora.

Because there are more than 170 strains of bacteria[13] and yeasts in the vagina of women at a reproductive age, this issue is not something of "little consequence" yet for some reason most obstetricians and paediatricians seem to be oblivious to.

The bacteria picked up during the descent through the vagina creates an environment called ***Colonization resistance***, which is reinforced by putting the baby to the breast

[12] Shen C.M., 2009. "Labour increases the surface expression of two toll-like receptors in the cord blood monocytes of healthy term newborns."*Acta Paediatr*. Apr 14. [Epub ahead of print] PMID 19397538.

[13] Stencel-Gabriel K, et al., 2009. "Prenatal priming of cord blood T lymphocytes by microbiota in the maternal vagina." *Am J Reprod Immunol*. Mar;61(3):246-52. PMID: 19239427.

immediately. The clear fluid the baby swallows in the first few hours, helps spread the bacteria, and start peristalsis. *(How many doctors or mothers realize that that clear fluid is quite abundant, and has a purpose?)* The mother's direct enteromammaric link creates secretory IgA to bacteria, viruses and foods in *her* gut and transfers them to her breast milk (more later).

As Hanson et al reported very recently[14] , "***the combination in a neonate of a not yet established diverse, stable and protective intestinal microflora and an immune system which is yet largely undeveloped is potentially hazardous***."

Hackansson et al[15] stated in 2003 that gastroenteritis was significantly more common in infants born by CS (caesarian section) than in others, and that the number of hospitalisations for asthma and gastroenteritis was also increased. They further commented that, "***VD (vaginally delivered) siblings to CS children showed an overall increased tendency to be hospitalized during childhood as compared to VD children without CS siblings. <u>The mother who has had a CS may be more prone to demand or desire medical intervention not only for herself but also for her children</u>."*** The authors consider <u>that</u> "fact" a serious confounder if studying long-term morbidity in childhood in relation to mode of delivery.

The study also suggested that increased head circumference due to ventouse vacuum extraction may be associated with an increased serum IgE and asthma, ***"generating the hypothesis that during fetal <u>life a 'programming' occurs</u> that could influence future morbidity in the individual".***

The whole process is intricately programmed so that at every point, interference will cause an effect, the degree of which is unpredictable.

<u>After Birth:</u> The birth of a child is the first step in up-regulating the baby's immune system away from the intrauterine immune depression of the innate immune system (a Th2 profile), towards an environmentally focused defence system which is primary cellular and Th1 based[16].

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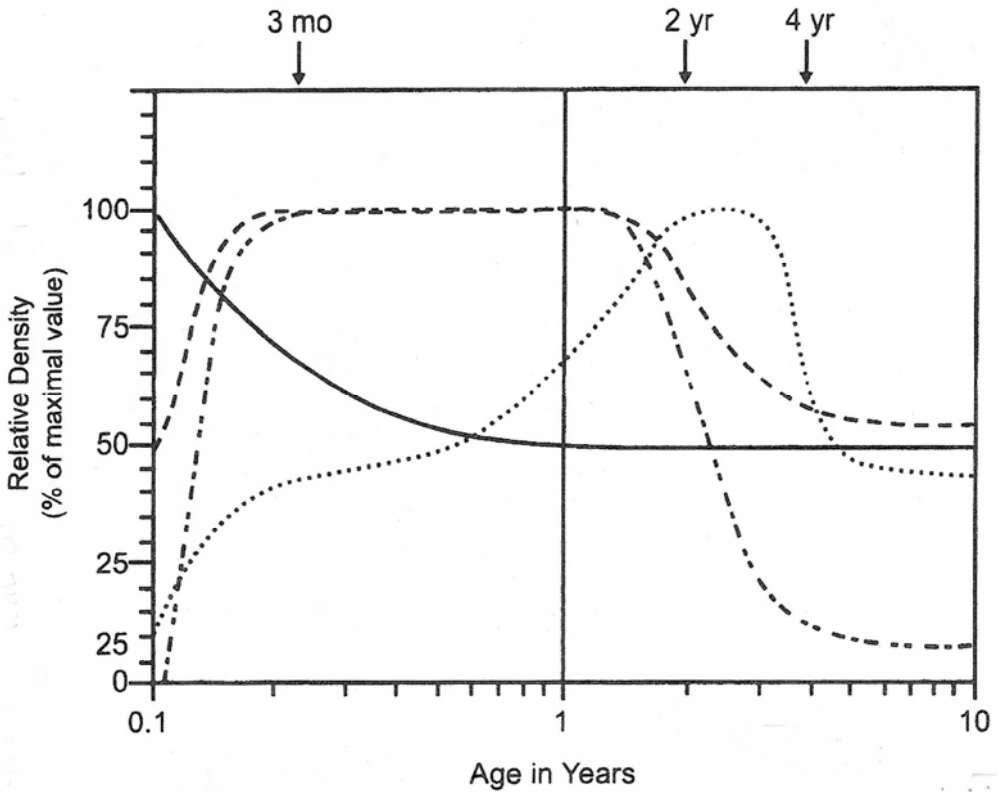
[14] Hanson L.A., et al, 2009. "The mother's immune system is a balanced threat to the foetus, turning to protection of the neonate." *Acta Paediatr.* Feb;98(2):221-8 PMID: 19046342.

[15] Hakansson S, et al. 2003. "Caesarean section increases the risk of hospital care in childhood for asthma and gastroenteritis." *Clin Exp allergy* Jun; 33(6):757-64. PMID: 12801309.

[16] Shen C.M., 2009. "Labour increases the surface expression of two toll-like receptors in the cord blood monocytes of healthy term newborns."*Acta Paediatr*. Apr 14. [Epub ahead of print] PMID 19397538.

Before we go further to look at what epigenetic effects can come after birth, let's take a look at some specific changes to come in the first few years of the baby's life:

Gene expression = where a gene's coded information is translated into building new structures to perform functions operating in cells. It was pointed out to me, that in the first four years of life, with the level of gene expression shown in the graph below, putting high levels of anything which alters gene expression in any way, would, in some children, be like putting a metal pipe into the spokes of a bicycle wheel while travelling at full speed.



——— cholecystokinin-positive neurons

— — — — — spine density on pyramidal neurons.

• — • — • chandelier neuron cartridges.

••••••••• dopamine variscosities.

[No reference. Personal communication by an epigeneticist]

Infants are exposed to a multitude of events and substances which can alter gene expression. Aluminum and thimerasol/thiomersal are very potent gene expression disruptors. So are other chemicals and many innocuous-appearing processed foods.

A baby's brain development.

A baby's brain may contain 100 billion neurons at birth. Later a "synaptic exuberance" quickly occurs and trillions of connections linking those neurons are produced. As the infant starts learning things and adapting to its surroundings, the whole process is

orchestrated by CREB[17] molecules that spin out like a web of wire-like fibres known as axons, attached to amoeboid structures known as dendrites. Those growth cones are equipped with detection units not unlike our radar and sonar units whose job is to locate specific proteins that will ultimately be joined together. Once the axons are connected, nerves begin to fire and the infant's brain forges ahead with literally quadrillions of such connections. Animal experiments have shown that the richer the environment, the more synapses per neuron are produced in the neonate's brain.

Metabolism rates soar, mitochondria go into over-drive and the need for primary nutrients such as minerals, vitamins, and in particular, vitamin C become critical.

At birth, the brain is not myelinated. Myelination starts in the spinal cord and proceeds to the brain stem and the brain with the frontal lobes getting fully myelinated in the 20's. The process is slow in order to allow plasticity and change.

The high pace time period for development of balance, reflexes and posture, is 6 – 12 months. Emotional recognition, translation and response – the limbic system - occur during the first three years of life. During this period, the babies grow and learn at a fast rate and a specific order.

Brain plasticity

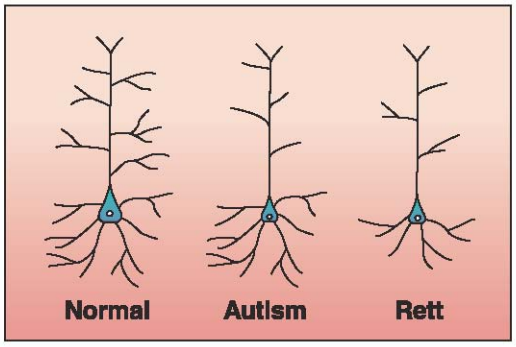


Fig. 2. Schematic representation of pyramidal neurons from control, autism, and Rett brains. In autism, the cell body is small and there is reduced dendritic branching. Similar changes occur in Rett, along with reduction in basilar dendritic branching. The reported changes are subtle and apply to a few neurons in selected brain regions in each disorder (*50, 81*).

Anything that throws a monkey wrench into this particular period of gene expression in the brain could have tragic consequences. Such as, you ask?

In 2003, a viewpoint[18] was expressed that autism and Rett syndrome, resulted from ***"disruption of postnatal or experience-dependent synaptic plasticity***". The author described how in autism mutations in two different neuroligins draw attention to the… postsynaptic cell adhesion molecules, some of which are known to interact with β-neurexin which are encoded by three large genes which give rise to α and β isoforms, depending on the choice of promoter. ***"…α-Neurexins are essential for***

[17] Creb is short for cyclicadenosine monophosphate response element binding protein which looks like an omeba, sitting inside cells and activating genes.

[18] Zoghbi H.Y. 2003. "Postnatal Neurodevelopmental Disorders: Meeting at the Synapse?" *Science* Oct 31; 302(5646):826-30. PMID:14593168.

calcium-triggered neurotransmitter release… neuroligin 1 stimulates presynaptic differentiation and synaptic vesicle recruitment by clustering β-neurexin." The author finished by saying that … ***"some of its targets will directly or indirectly regulate gene products involved in autism. These interactions might occur at the synapse or regulate synaptic functions"***.

There's no surprise in that, when you consider the difficulties children with ASD's have. Two years later, another researcher[19] said "Genetic abnormalities, including point mutations and chromosomal rearrangements, in loci corresponding to the genes for the synaptic proteins neuroligin and PSD95 are associated with autism… variations of neuroligin expression levels, which might occur *in vivo as a result of mutation of* **copy number polymorphism***, might tip the excitation to inhibition balance in the intact brain. Variations in this balance might be sufficient to change, not only local circuit function, but also connectivity patterns between brain regions, leading to developmental and behavioural deficits*…" In other words she was looking at the various molecular and cellular pathways ***that regulate synapse formation, function and maturation.***

Many articles have looked at various ideas, like neurexins[20] which are a key to language related brain structures in a developing brain. The problem is, of course, that often when looking at any one gene[21], ***"microdeletions and microduplications have been found in approximately 1% of autism cases".*** The article goes on to say that genetic findings support the role of neuronal cell-adhesion molecules resulting in ***"underconnectivity"*** in subjects with autism as a result of ***"structural and functional disconnection of brain regions".*** They are looking at specific genetic variants which are involved in shaping the physical structure and functional connectivity of the brain, and say, ***"Together with studies addressing epigenetic modifications and comprehensive analysis of environmental risk factors, these pieces of information can be better integrated to improve our understanding of the molecular basis of ASDs and foster the development of early preventive and corrective strategies."***

[19] Cline H. 2005. "Synaptogenesis: A Balancing Act between Excitation and Inhibition." *Curr Biol.* 15(2005)pp R203-R205. PMID: 15797012.
[20] Alarcon M,. et al., 2008. "Linkage, association, and gene-expression analyses identify CNTNAP2 as an autism-susceptibility gene." *Am J. Hum Genet.* Jan; 82(1):150-9. PMID: 18179893.
[21] Wang K, et al. 2009. "Common genetic variants on 5p14.1 association with autism spectrum disorders." *Nature* Apr 28 [Epub ahead of print] PMID:19404256.

Just recently, geneticists[22] consider they have made great strides by finding several copy number variations on the genes which encode neuronal cell-adhesion molecules,… or ubiquitin degradation, ***"indicating that these two important gene networks expressed within the central nervous system, may contribute to the genetic susceptibility of ASD."***

The authors identified seven genes which had an increase of copy number variations, and which were involved in neuron development; ***"the ubiquitin-proteasome system operates pre- and post- synaptic compartments, regulating synaptic attributes including neurotransmitter release, synaptic vesicle recycling in pre-synaptic terminals and dynamic changes in dendritic spines and the post synaptic density."***

That was beautifully illustrated in the drawing by Zoghbi above.
The author also says, ***"The role of ubiquitin in the turnover of synaptic components such as the neuronal cell-adhesion molecules in a process involving regulation of activity-dependent synaptic plasticity presents a mechanism that links these two major gene networks."***

When you consider the vast number of jobs going on in the brain, you should assume that there are vast numbers of gene expression being orchestrated at any one time. Higher resolution genetic techniques[23] are now supposedly showing that, ***"many different genes contribute, possibly leading by different means to a final common neurodevelopmental pathway that produces the autism phenotype."*** The author says, ***"Neurexins and neuroligins bind to each other across the synaptic cleft, with the neurexin embedded in the presynaptic membrane and the neuroligin embedded in the post-synaptic membrane. This interaction has a dramatic impact on both sides of the synapse …"***

Put crudely, whatever messes with gene expression in the brain, be it chemicals, additives, drugs or vaccines, will be to the child's detriment.

A 2009 study[24] looking at another gene found only 12.5% in that particularly autistic population. But an interesting point was that some of the genes located in the ASD-

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[22] Glessner JT, et al., 2009. "Autism genome-wide copy number variations reveals ubiquitin and neuronal genes." Nature Apr 28 [Epub ahead of print]. PMID: 19404257.
[23] Kim H., et al., 2008. "Disruption of Neurexin 1 Associated with Autism Spectrum Disorder." *Am J Hum Genet.* Jan;82(1):199-207. PMID: 18179900.
[24] Cusco I., et al., 2009. "Autism-specific copy number variants further implicate the phosphatidylinositol signaling pathway and the glutamatergic synapse in the etiology of the disorder." *Hum Mol Genet.* May 15;18(10):1795-804. Epub 2009 Feb 26.. PMID: 19246517.

specific copy number variants are involved in phosphatidylinositol signalling and glutamatergic synapse.

Their work was related to the ***"functional alteration in genes in related neuronal networks."*** Cusco talks about the many different genomic regions, usually found in a small percentage of people, and how diverse they are, ***"the finding of multiple uncommon ASD-related copy number variants, each in a specific patient, further reflects the complexity and multifactorial nature of the ASD phenotype. The search for genetic and genomic variation along the whole genome is still badly needed to better ascertain the genetic background of autistic phenotypes."***

At that rate, they will be looking at genes for the next 50 or so years… which illustrates the importance to geneticists to remain buried in their illusion that it's the gene that causes the disease, rather than the reality something than interference/absence resulting changing the gene, and the instructions the gene generates. Is it easier to continue to blame the gene, rather than looking at what changed the gene? If they looked at what changes gene function, might that mean they have to study maternal mercury burden, amalgams in mouths, antibiotics, nutrition, and vaccines etc? All of which spell "action/absence gene interference".

The smooth synchronised firing of messages and connectivity in brain function, and analysis of a baby's surrounding, is crucial, to babies. The gene expression in the brain as seen on page 11, is literally, supersonic in speed. A neonate's brain is exquisitely sensitive to both nutrient absence and substance interference, because both those situations can result in copy number variants, changed gene expression, with resultant haywire development.

Brain development after five.

Proficiency at most tasks improves between 6 – 10 years of age and later everything else builds on the platform.

Around age 18, the brain's plasticity is markedly reduced by the elimination of connections and synapses that are seldom used. "Use it, or lose it." Babies who are rarely touched and stimulated have a brain 30% smaller than normal for their age. By the age of three, neglected or abused babies develop brains that are highly tuned to danger. A template is formed under such stress and specific brain development follows something often referred to as "hard wiring".

This all takes place in order to facilitate the return of the immune system to a Th1 based immune function with emphasis on the innate arm of defense, the accumulation of nutrients and other "aids" to accomplish the huge multi-tasking job required for optimization of synapsis exuberance.

Development of innate immunity at birth

Immunologists have clever non-threatening ways of admitting that they don't know very much about the innate immune system:

"…***much remains to be elucidated*** ***about how commensal bacteria influence the function of cells of both the innate and adaptive immune systems in health and disease***"[25] and "… ***our understanding of both these systems (human milk and the gut) remains quite incomplete***". [26]

Their knowledge of other aspects of immunology is equally as hampered[27]:

"…vaccination relies on immunological memory, yet our understanding of this fundamental characteristic of the adaptive immune system is incomplete."

What is being discussed with regard to the innate system is primarily work done the last 10 years and no doubt, the tip of the iceberg.

What is known. To discuss this, we must go back to the all important period of pregnancy and its *direct influence on the modulation and education of the immune system.*

During pregnancy, the mother's immune system down-regulates to a Th2 based system, in order to prevent miscarriage of what is in effect a 50% "graft v host" situation. A mother's immune system, after pregnancy, has only been studied in rats.

If you assume rats equate to human ***mothers***, then after birth, what is found[28] is that ***maternal*** immune systems do not return totally to normal. Under the influence of prolactin, and the process of lactation, the immune system seems to be re-adjusted. The

[25] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." Mutation Research Sep 1;622(1-2):58-69. Epub 2007 Apr 6. PMID: 17612575.
[26] Newburg D S et al. 2007. "Protection of the Neonate by the Innate Immune System of Developing gut and of Human Milk." *Ped Research* Jan;61(1):2-8. PMID: 17211132.
[27] Brandtzaeg P. 2007. "Induction of secretory immunity and memory at mucosal surfaces." *Vaccine* Jul 26;25(30):5467-84. Epub 2006 Dec 15. PMID 17227687.
[28] Jaekicke, KI.E., et al 2009. "Lactation modifies stress-induced immune changes in laboratory rats." *Brain Behav. Imm.* Feb 20 epub. PMID: 19232537.

number of phagocytes in the blood is increased in order to enhance the innate immunity in the circulation. High plasma concentrations of prolactin, while inhibiting lymphocyte proliferation at high concentrations, have enhancing effects at lower concentrations. There are decreased B-cell numbers, and reduced IL-2 production. However, lymphocyte activity is increased in the mesenteric lymph nodes in order to provide large amounts of secretory IgA in breast milk.

During pregnancy, the fetal focus is on preparing the intestinal tract[29] which ***"is not only an organ for digestion and absorption of nutrients; it also performs major endocrine, neural and immunologic functions":***

"The intestine undergoes tremendous growth during fetal life. It elongates 1000 fold from 5 – 40 weeks. The length doubles in the last 15 weeks of gestation reaching a mean length at birth of 275 cm. In the small intestine, fingerlike projections, the villi, are already formed at 16 weeks gestation. Microvilli begin to cover the apical surface of the small intestinal epithelium so that by adulthood, the intestinal surface provides the largest interface between the outside environment and the internal milieu (approximately 2,000,000 cm^2, which is about the size of a tennis court. The increase in surface area during development has significant implications in terms of nutrient absorptive capacity."

Immunologically, the mucus membranes are all set to go even before birth. Peyer's patches, which are hundreds of little "stations" in the intestine are ready with associated lymphoid patches and colonic follicles. Everything is covered with meconium, even though, for the last month, the foetus has been swallowing down up to 450 mls of amniotic fluid[30] every 24 hours. Imagine, if you will, a new, live innate "computer" with all the bits in place, but without the software and necessary regular updates over time, to make the hardware work correctly.

During that period, what the mother eats is all important[31] :"…***the composition of the host's diet is responsible for the metabolic activities and species composition of the microbiota, as different species grow better on different substrates."***

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[29] Neu, J. 2007. "Gastrointestinal maturation and implications for infant feeding." Dec;83(12):767-75. Epub 2007 Oct 29. PMID: 17913404.

[30] Neu J. 2007 "Gastrointestinal maturation and implications for infant feeding" Early Hum Dev. Dec;83(12):767-75. Epub 2007 Oct 29. PMID 17913404.

[31] Noverr, M C et al., 2004. "Does the microbiota regulate immune responses outside the gut?" *Trends in Microbiology* Dec;12(12):562-8. PMID 15539116.

Other factors also have a considerable bearing on the developing fetal immune system during pregnancy[32]:

"The variations might be induced by multi-factors such as gene and race, environment and region, dietetic habits of mothers, components of each mother's breast milk".

Expectant mothers living on a farm have children with a decreased risk of allergic disorders later in life[33]. ***"Treg cells, comprehensively assessed in number, gene expression, epigenetic regulation, and function were mainly at higher levels and more efficient in offspring of farming compared with non-farming mothers…maternal exposure to this natural model of allergy protection can modulate Treg cells already before birth, indirectly reflecting early immune development."***

Mothers who were occasionally exposed to farm animals (and farm milk), showed higher immune stimulation than exclusively non-farming mothers.

Researchers [34] have commented how seaweed taken in a traditional Japanese diet of vegetables, fruit, antioxidants, fibre and minerals, independently of everything else, resulted in a decreased rate of allergic rhinitis in pregnant women. Calcium, phosphorus and magnesium also decreased allergic disorders and fish and fish oil decreased eczema and atopic dermatitis in high risk children for a year. The study mentions a study in which grandmaternal smoking influences asthma in 5 year old grandchildren, and maternal smoking significantly affected the developing baby's immune system.

The authors also pointed out the significant effects of alcohol, smoking, environmental epigenetic influences such as road traffic and diesel exhaust, wood smoke, xenobiotic chemicals, endocrine disruptors, heavy metals, low dose radiation and even anti-acids in pregnancy.

Not surprisingly, they don't mention vaccines.

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[32] Chen, J, et al., 2007. "Development of intestinal bifidobacteria and lactobacilli in breastfed neonates." *Clin Nutr* Oct;26(5):559-66. Epub 2007 May 15. PMID 17507117.

[33] Schaub, B., et al. 2009. "Maternal farm exposure modulates neonatal immune mechanisms through regulatory T cells." *J Allergy Clin Immunol.* Apr;123(4):774-82.e.5. PMID 19348917.

[34] Pali-Schöll, I. 2009. "Update on allergies in pregnancy, lactation, and early childhood."*J Allergy Clin Immunol.* May;123(5):1012-21. Epub 2009 Feb 26. PMID: 19249083

Immune Development during the Neonatal Period

After birth, there is rapid development of the baby's innate system. The non-allergic normal mother's prenatal Th2 immune system also reverts towards Th1 but with subtle differences as she gets ready to provide an innate system for two people.

So why does the baby's immune system need to focus on the Th1 (innate system) quickly? Mostly because this is the part of the immune system that will constantly be in use as a "first receiver".

As some have written[35] : ***"The vast majority of infections involve the mucosae with regard to initial microbial colonization and/or entry into the body…"*** This is how immune system development takes place, with the body having in place a learned program which follows a logical step-by-step process in order to protect itself. This requires ongoing programming in the baby's gut, in concert with the environment, with the ***lynch pin being breastfeeding***.

> ***"Breastmilk contains factors that are capable of programming the infant's developing immune system and metabolism into a health-promoting model."***
>
> "In addition to a near-optimal combination of nutrients for the growing infant, breastmilk contains a wide array of bioactive molecules that are known to protect the infant against infectious disease and modulate the composition of the indigenous intestinal microbiota… We suggest that this early immunomodulation via breastmilk is vital for infant health and may explain the epidemiological data indicating that breastmilk reduces the risk of immunoinflammatory conditions in infancy and also later in life. The body of scientific data regarding the role of transforming growth factor-β in breastmilk in enhancing healthy immune maturation and reducing the risk of disease is reviewed in this article."[36] (continued…)

[35] Brandtzaeg P. 2007. "Induction of secretory immunity and memory at mucosal surfaces." *Vaccine* Jul 26;25(30):5467-84. Epub 2006 Dec 15. PMID 17227687.

[36] Rautava S, Walker WA., 2009. "Academy of Breastfeeding Medicine founder's lecture 2008: breastfeeding—an extrauterine link between mother and child." Breastfeed Med. Mar;4(1):3-10. PMID: 19292608.

"Consumption of breastmilk significantly reduces the incidence of NEC in neonates."

"Breastfeeding may have more long-term consequences regarding child health by having an impact on the development of chronic ailments such as asthma and atopic disease or obesity… (and) may also confer protection against celiac disease."

"Intriguingly, breastfed infants display increased weight gain during the first 6 months of life but appear to have a reduced risk of obesity in later life. This effect is demonstrated in a cohort study of more than 15,000 children in the United States, in which breastfeeding protected against obesity in adolescence. A similar conclusion of an inverse association between breastfeeding and obesity in later life was drawn in a meta-analysis of 28 studies…. Lower blood cholesterol concentrations in adulthood … "

"… individuals who had been breastfed had a significantly lower risk of developing type 2 diabetes in later life."

Factors in breastmilk may prime the infant's immune system and metabolism during infancy in a way that promotes health decades later. Immunologists know[37] that; ***"the gut mucosa contains at least 80% of the body's plasma cells, and some 90% of these activated B-cells produce pIgA[38]"***

When it comes to the immune system, the gut is all important. ***It is a dual-function organ intended to absorb nutrients while supporting and re-enforcing the immune system[39]:***

"**A particularly interesting location with respect to the induction of tolerance is the intestine, as *this tissue facilitates the absorption of essential nutrients and at the same***

[37] Brandtzaeg P. 2007. "Induction of secretory immunity and memory at mucosal surfaces." *Vaccine* Jul 26;25(30):5467-84. Epub 2006 Dec 15. PMID 17227687.

[38] pIgA = polymeric immunoglobulin A is a secretory IgA which has a specific job to move through the epithelial cell walls.

[39] Lee, Je-Wook et al, 2007. "Peripheral antigen display by lymph node stroma promotes T cell tolerance to intestinal self." *Nat Immunol* Feb 8(2):181-90. PMID: 17195844.

time protects the body from invasive and resident microbes, which are potential immune stimulants."

During the baby's first two years of life, specific functions swing into place aimed at dampening the immune system. In the early days/weeks/months, other parts of the immune system are set-up to start functioning. The most notable are the lymphoid tissues. The first two listed below are extra, and hard-working immune defences that disappear in late adolescence (or at least become hard to find!):

1) The nasopharygeal lymphoid tissue (NALT) includes at least five different types of dendritic or antigen presenting cells and produces IgM and IgA

2) The bronchial lymphoid tissue (BALT) that performs similar functions in the bronchial tree [40]

Both immune centers are intricately linked to the gut and influenced by breast milk. They provide added protection to the Waldeyer's ring formed by the palatine and lingual tonsils to effectively stand as a total fortress resisting the entry of pathogens into the stomach and lungs.

But the key factor to orchestrate the overall development of the immune system of the baby is actually the very first one to come into play: ***the bacterial colonisation during birth by the mother's commensal[41] bacteria.***

Two years ago, a researcher surprisingly oblivious to history, wrote[42]: ***"The concept that bacteria might have a pivotal role in early human development is relatively new, and may seem at first absurd."*** Had he paid attention to the multiple treatises in my possession and the vast numbers I don't possess, he would not have declared:

"Previously the microbial flora was largely ignored or understood in terms of a more or less continuous battle between humans and bacteria, with occasional areas of apparent truce such as the gastrointestinal tract where large numbers of bacteria appeared to coexist with the host to no apparent detriment."

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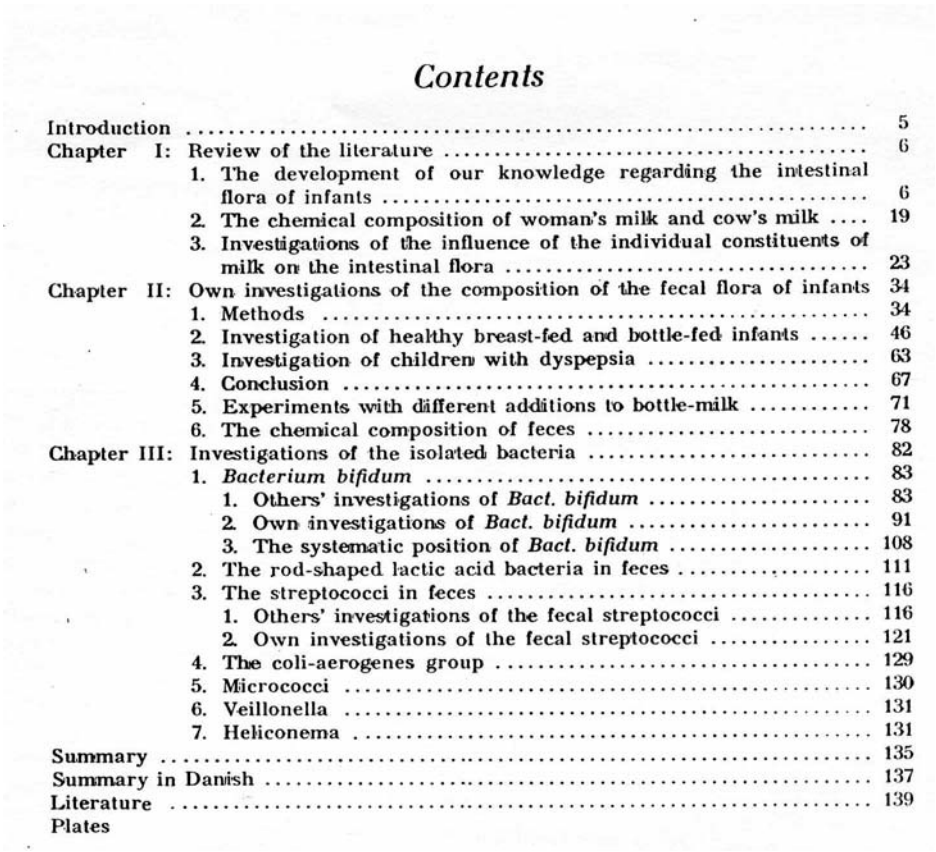
[40] Cerutti A et al, 2008. "The Biology of Intestinal Immunoglobulin A Responses." *Immunity* Jun;28(6):740-50. PMID: 18549797.

[41] Commensal means "sharing the table", so these bacteria are the ones constantly resident, sharing space in the mother's body.

[42] Wilks, M. 2007. "Bacteria and Early human development." *Early Human Development* 83, 165-170. PMID: 17289307.

Nothing could have been further from the truth! Because of his unfamiliarity with the literature written on the role of bacteria in and on the gut, he consigned to oblivion, with one fell swoop Escherich (1886) and the huge body of work before him.

The first paper[43] I have that compared the gut flora of bottle versus breastfed baby, was written in 1905 and in French. In recent months or years I have only seen it referenced once. The next major monograph[44] in my possession is dated 1946 and fortunately in English. The list of contents speaks for itself and shows the great lengths Olsen went to.



Contents

I have never seen this remarkable document referenced in modern writings, yet it details some of the huge amount of work done before antibiotics were around to mess gut flora up, and compares formula fed and breastfed babies. The authors lament the fact that most of the autopsies were on bottle fed babies, since they rarely saw deaths among breastfed babies. They really wanted to look at what also happened to breastfed babies but those never seemed to die and come to autopsy the way bottle fed babies did, which tells you something!

The historical work had a great advantage over the work of today, because sampling was done from day one while today's studies often do not begin until day three.

This is what Olsen wrote on page 17: "***the oral flora of the child first of all depends on the vaginal flora of the mother, to a less degree on the flora of the breast of the mother, the bathing water and the hands of the nurse***."

[43] Tissier, H. 1905. "Repartition des microbes dans l'intestin du nourrisson." *Ann Inst. Past. 19, 109-123.*

[44] Olsen, Erik. "Studies on The Intestinal Flora of Infants." Ejnar Munksgaard, Copenhagen 1949.

Right from 1900, the concept that "good" bacteria protected, and "bad" bacteria injured the infant, was very well advanced. This monograph should be compulsory reading for paediatric gastroenterologists and researchers, because within the limits of the crude technology available, the monograph gave as clear a picture as one could get from pre-antibiotic days. It also says many of the things researchers are still saying today, but without the *mysterious and* unintelligible science or the geek-speak today's medical literature has become famous for.

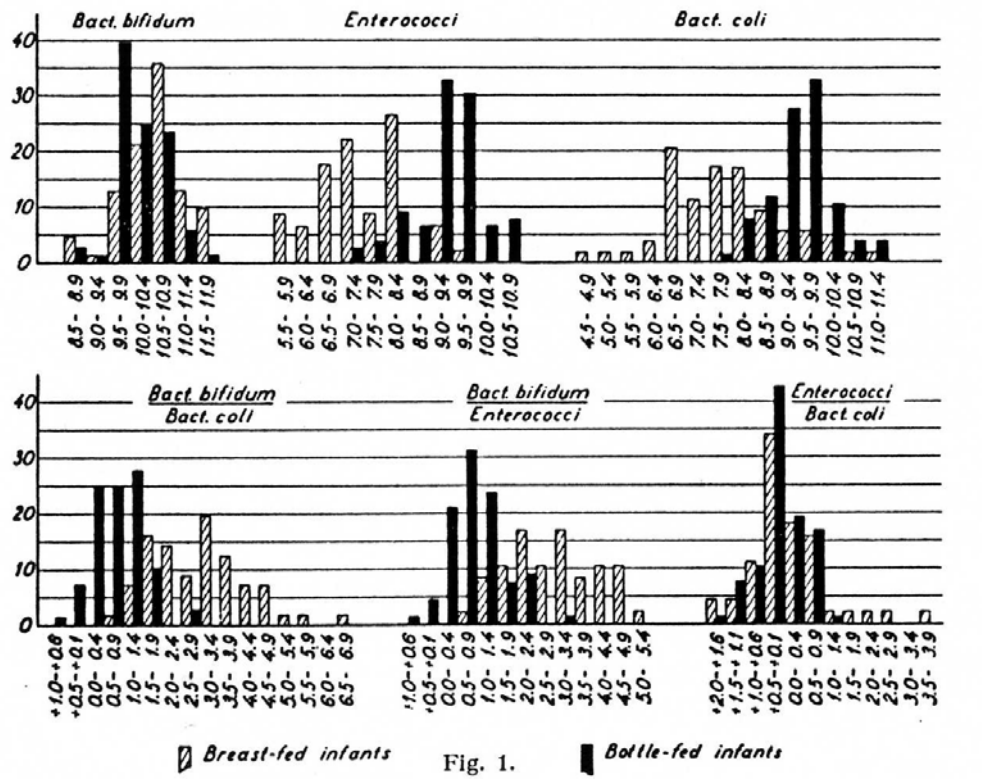


Fig. 1.

One type of testing the authors did, which modern investigators rarely do is testing the stool ph. Studies have shown that the gut ph in breast-fed babies varied from 4.7 – 5.1 while the ph in bottle-fed babies was between 8.3 and 9.6. That significant ph difference definitely influenced bacterial colonisation.

Today's researchers should not be surprised to read that Clostridia pretty much disappeared from the bowels of breastfed babies while flourishing in bottle fed babies precisely and only because clostridia prefers the more alkaline environment which formula creates.

In earlier days, doctors saw what happened to babies with gut dysbiosis and went to extreme lengths to study it. The huge excess of deaths in ***bottle fed babies*** was solely because those babies were deprived of protective commensal bacteria; the gut ph was very alkaline, favouring E.coli and other pathogenic bacteria; and they were deprived of the outstanding immunity that comes in breast milk specifically teaching, and helping the immune system to work.

The purpose of bacterial colonisation.

"***Commensal bacteria might provide instruction for the development of the host immune system. If this is the case, then the developmental signals provided might be crucial for establishing immunological health in mammals***."[45]

"***The effects of the commensal microbiota may be more profound; influencing process as complex as lipid metabolism of the host, predisposition to obesity, immune development and homeostasis, inflammation, repair and angiogenesis***."[46]

The polysaccharide of one particular gut commensal appears to be very important: "***The vertebrate brain and immune system are the only organs that require environmental interactions for development. We report here that maturation of the mammalian immune system requires the specific direction of an immunomodulatory molecule provided by symbiotic bacteria. B. fragilis, a ubiquitous constituent of the mammalian lower gastrointestinal microflora, elaborates a polysaccharide that directs the development of CD4+ T cells…"***[47]

Compared to Olsen's days:

1) "***The gradual colonization depends on the mother's microbiota, mode of delivery and environment***[48]" What a mother does not possess, she can not give. If her diet is such that a healthy commensal flora is not supportable, then she can never give her baby a strong and healthy flora. This particular study took a group of women, and administered Lactobacillus rhamnosus probiotics to half of them for four weeks prior to delivery continuing until the last samples for both groups were obtained. The group of women on the probiotics had more diverse bifidobacterium microbiota than the controls.
2) The mode of delivery had a deep impact on the composition of the intestinal microbiota at the very beginning of life. ***"…the primary gut flora in infants born by cesarean delivery may be disturbed for up to 6 months after the birth. The clinical***

[45] Mazmanian S K., et al, 2006. "The love-hate relationship between bacterial polysaccharides and the host immune system" *Nature Rev Immunol* Nov;6(11): 849 -858. PMID: 17024229.
[46] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." Mutation Research Sep 1;622(1-2):58-69. Epub 2007 Apr 6. PMID: 17612575.
[47] Mazmanian S.K. et al, 2005. "An immunomodulatory Molecule of Symbiotic Bacteria Directs Maturation of the Host Immune System." *Cell*. Jul 15;122(1):107-18 PMID 16009137.
[48] Gueimonde M., et al 2006. Effect of Maternal Consumption of Lactobacillus GG on Transfer and Establishment of Fecal Bifidobacterial Microbiota in Neonates." *J Pediatr Gastroenterol Nutr*. Feb; 42(2):166-70. PMID: 16456409.

relevance of these changes is unknown…" Infants born through caesarian had lower numbers of bifidobacteria and Bacteroides, and were more often colonized with C. difficile[49].

3) ***"…the immune system must be programmed to respond only to threatening microbes and not to the body's own tissues, foods, and other harmless material. On the other hand, it must develop tolerance to such factors. The process is not fully understood, but obviously exposure to the normal intestinal microbial flora has a central role in the normal development of oral tolerance and builds on the appearance of regulatory T lymphocytes…the ongoing increase in allergic diseases in recent decades may be linked to inefficient development of oral tolerance."***[50]
4) "***Early microbial exposure of the gut is thought to dramatically reduce the incidence of inflammatory, autoimmune and atopic diseases… microbial colonization plays an important role in regulating and fine-tuning the immune system throughout life***…"[51]
5) "***Babies who develop allergy, are less often colonized by bifidobacteria but more often with Staphylococcus aureus and have higher counts of clostridia"***[52] One study[53] says, "***Interestingly, probiotic supplementation of mothers pregnant with at-risk babies also prevents subsequent atopic disease***."

But another says "***The use of probiotics in infant nutrition can only be justified once we have derived a detailed understanding of their action in the longer term***."[54]

This is truly an extraordinary statement.

If such a comment was applied to vaccines and other drugs, how many would arrive on the market … so quickly?

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[49] Penders, J. et al, 2006. "Factors influencing the composition of the intestinal microbiota in Early Infancy"*Pediatrics* Aug;118(20:511-21. PMID 16882802.
[50] Hanson, L.A. 2007. "Session 1: Feeding and infant development Breast-feeding and immune function." *Proc Nutr Soc* 66, 382-396. PMID: 17637091.
[51] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.
[52] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.
[53] Noverr, M C et al., 2004. "Does the microbiota regulate immune responses outside the gut?" *Trends in Microbiology* Dec;12(12):562-8. PMID 15539116
[54] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.

Another study[55] points out how several epidemiological studies show that the composition of gut flora differs between atopic individuals and non-atopic individuals, and that anthroposophical children (who refrain from antibiotics, vaccines and eat a lot of fermented foods and a much more natural diet) have significantly lower allergy rates than "normal" children at the same schools.

But it is a fact that caesarian delivery is not the only factor responsible for the ruining of a healthy, established "first and all important" commensal bacterial flora.

Antibiotics.

"***Antibiotics can have the most profound impact on an individual's GI microbiota and antibiotic use in industrialized countries is significantly greater than in developing countries***.[56]" Antibiotics are pretty much standard with caesarian deliveries, so the baby with get a double whammy. It will be colonized by the operative theatre environment, the nurses and doctors' hands and perhaps the NICU as well, AND in addition it will receive antibiotics in NICU, as well as those from the mother.

The most crucial step to colonize the gut, may just have been defoliated by antibiotics, which continue to affect the process for not just the next week, but for months to come.

What's worse[57] is that, ***"Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome."***

Even under normal circumstances however, changes in society can alter bacterial commensal balance. A Swedish study[58]comparing the colonization of new born babies and infants in the 1970s and 1980, with now, found that *Coagulase-negative staphylococci*, not previously regarded as a commensal has now become ubiquitous in the first year. The same was mentioned for *S epidermidis*, and *clostridium difficile*. The article also commented on the reduction in Sweden of colonisation by hospital bacteria, which is a good thing. However, the article mentioned that *bacteroides*, a very important part of

[55] Mazmanian S K., et al, 2006. "The love-hate relationship between bacterial polysaccharides and the host immune system" *Nature Reviews* Vol 6 Nov. 849 -858. PMID: 17024229.

[56] Noverr, M C et al., 2004. "Does the microbiota regulate immune responses outside the gut?" *Trends in Microbiology* Dec;12(12):562-8. PMID 15539116.

[57] Schumann, A., et al., 2005. "Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome." *Physiol Genomics* Oct 17;23(2):235-45. Epub 2005. Aug 30. PMID: 16131529.

[58] Adlerberth, I., et al 2006. "Reduced Enterobacterial and Increased Staphylococcal Colonisation of the Infantile Bowel: An Effect of Hygienic Lifestyle?" *Pediatric Research* 59:96-101. PMID: 16380405.

commensal, often didn't appear in the bowels of Swedish caesarian babies until a year of age. In discussing these changes, the author says, ***"Inasmuch as Gram-positive and Gram-negative bacteria induce partly different mediators when interacting with the innate immune system, a changed colonization pattern caused by increased hygiene may have global effects on the developing infantile immune system."***

Is it increased hygiene,… or active bacterial deprivation and destruction at birth and thereafter, inside a society estranged from nature, shunning traditional lactic acid fermented type foods, not eating the probiotics of yesteryear, and now eating a SAD[59] diet?

In the early postnatal period, just after the baby is born whether by caesarian or vaginally, only traces of SIgA and SIgM can be detected in the baby. Some IgG is even present on mucosal surfaces as early as 34 weeks gestation because of placental transfer.

BREAST MILK

So, the gut of the adult and baby has this dual function of food, and immune system. It should not then come as a surprise that ***breast-milk*** has molecules in it which are ***not just food but an immune system as well***.

As Newberg et al[60] so aptly put it: "***Human milk accelerates maturation of the gut barrier function, but formula does not***."

Stem Cells.

Breastmilk contains stem cells which are a crucial orchestrator of development and repair.

"It was Dr Cregan's interest in infant health that led him to investigate the complex cellular components of human milk. "I was looking at this vast complexity of cells and I thought, 'No one knows anything about them'."

His hunch was that if breast milk contains all these cells, surely it has their precursors, too?

[59] SAD = Standard American diet. Perhaps Swedish Average Diet ☺

[60] Newburg D S et al. 2007. "Protection of the Neonate by the Innate Immune System of Developing gut and of Human Milk." *Ped Research* Jan;61(1):2-8. PMID: 17211132

His team cultured cells from human breast milk and found a population that tested positive for the stem cell marker, nestin. Further analysis showed that a side population of the stem cells were of multiple lineages with the potential to differentiate into multiple cell types. This means the cells could potentially be "reprogrammed" to form many types of human tissue.

He believes that it not only meets all the nutritional needs of a growing infant but contains key markers that guide his or her development into adulthood.

"We already know how breast milk provides for the baby's nutritional needs, but we are only just beginning to understand that it probably performs many other functions," says Dr Cregan, a molecular biologist at The University of Western Australia.

He says that, in essence, a new mother's mammary glands take over from the placenta to provide the development guidance to ensure a baby's genetic destiny is fulfilled.

"It is setting the baby up for the perfect development," he says." [61]

Dr Cregan also said in another press release[62], that, "***For the mother, choosing not to breastfeed increases her risk of breast and ovarian cancer, osteoporosis and heart disease and her body takes longer to return to its pre-pregnancy state."***

Hi work showed that breastmilk contains differentiated epithelial and putative stem cells, undifferentiated and differentiated, and that cells testing positive to nestin[63] are, ***"multipotent stem cells in bone marrow, in neural, pancreatic and epithelial tissues***." Since this work is so new, the consequences of depriving babies of these sorts of stem cells by choosing to use formula, is obviously unknown.

Colostrum: As any farmer can tell you, the most crucial step towards good animal health in any mammal is that the animal receives colostrum as quickly as possible. In humans, pre-colostrum fluid is clear, and relatively plentiful. Constant nursing allows this clear fluid to help sweep the colonised bacteria down through the gut system.

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[61] Madden C., 2008. "Breast milk contains stem cells." *Science Alert* 10 February 2008. http://www.sciencealert.com.au/news/20081102-16879.html

[62] PR. 2008. "Stem cell discovery: another reason why breast is best." *The university of Western Australia* 17 January. http://www.news.uwa.edu.au/node/121

[63] Cregan MD, et al., 2007. "Identification of nestin-positive putative mammary stem cells in human breastmilk." *Cell Tissue Res.* July;329(1):129-36. PMID: 17440749.

Colostrum[64] provides the baby with a massive bolus dose of very high concentrations of anti-inflammatory interferons, transforming growth factors, antioxidants, protease inhibitors, prostaglandins etc. Colostrum provides protective macromolecules at a time when the gut can absorb them and when the gut priming and maturation start. In addition, Colostrum and breast milk contain high levels of soluble CD 14, which helps activate phagocytes in the gut to deal with gram negative and positive bacteria which may follow soon after.

The mother's immune system starts to revert back to a Th1 base when her breast-milk comes in, in order to provide not only nutrition but also an immune barrier to fend off infection, and various molecules to start further maturation of that system[65]: "***The maturation of the intestinal barrier is the consequence of morphological and functional changes of the mucosa which occur under genetic and endocrine control***."

The number one local player in this day to day teaching manual is ***Secretory IgA***: ***"…an adequate mucosal barrier function of neonates depends on a supply of SIgA antibodies from breast milk"*** [66] The proof of that is that, ***"epidemiological data suggest that the risk of dying from diarrhoea is reduced 14 – 24 times in breast-fed babies."***

In contrast to an adult, who produces 40 mg/kg/day secretory IgA a breastfed baby of one month will receive 125 mg/kg/day and a 4 month old 500 – 1,000 mg/kg/day ***from breast-milk***. Secretory IgA is an anti-adherin and anti-inflammatory.

"IgA shields the commensal flora from both the innate and the systemic immune system… very critical in early life when mechanisms of immune regulation are not fully operational.. "[67]

"Secretory IgA… entraps dietary antigens and microorganisms in the mucus; downmodulates the expression of proinflammatory bacterial epitopes on commensal bacteria and in general promotes the maintenance of appropriate bacterial communities

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[64] Newburg D S et al. 2007. "Protection of the Neonate by the Innate Immune System of Developing gut and of Human Milk." *Ped Research* Jan;61(1):2-8. PMID: 17211132.

[65] Schumann, A., et al., 2005. "Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome." *Physiol Genomics* Oct 17;23(2):235-45. Epub 2005. Aug 30. PMID: 16131529.

[66] Brandtzaeg P. 2007. "Induction of secretory immunity and memory at mucosal surfaces." *Vaccine* Jul 26;25(30):5467-84. Epub 2006 Dec 15. PMID 17227687.

[67] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.

with specific intestinal segments."[68] It blocks bacteria from attaching to the epithelial cells, mediates removal of pathogens from inside cells; attached to microfold cells (part of the Peyer's patches system) to help with antigen capturing, in order that the M-cells present them to circulating B cells priming the body to make antibodies against nasty bacteria.

IgA is the main "dampener downer", controlling bad bacteria, orchestrating food antigen acceptance, providing innate immunity, and keeping the commensal colonies where they should be.

Fatty Acids

The 4% fat (triglycerides) in human milk is a major source of calories that when mixed with mouth and stomach lipases are digested into free fatty acids able to inhibit viruses, bacteria and protozoans. Monoglycerides act like soap and break the surface tension on pathogenic membranes. Fatty acids - linoleic and lauric acid - are especially high in breast milk.

Anti-cancer cells.

While breast milk is food it would be more accurate to describe it as[69] the "optimum gene expression conductor".

"Apha-lactalbumin …. In its completely folded state it helps produce lactose and nourishes babies, but when it's partially unfolded, it forces cancer cells to burst open and die. These proteins, and a few others, offer evidence that a standard dogma in biology must fall. According to the old view, one DNA sequence produces one amino acid sequence that produces a particular structure that performs one function. But now biologists must recognize the existence of proteins with more than one structure that perform more than one function."

"The accepted scientific rule has been, 'one structure, one function,' " says Svanborg. "But having multiple functions would be a very energy-saving, economical way for a protein to operate." It's altogether too practical for nature to pass up…studies explain how transformed alpha-lac snuffs out cancer and other risky cells, and characterizes the

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[68] Cerutti A et al, 2008. "The Biology of Intestinal Immunoglobulin A Responses." *Immunity* Jun;28(6):740-50. PMID: 18549797.

[69] http://www.discover.com/issues/jun-99/features/featcancer/ **Got Cancer Killers?** By Peter Radetsky Photographs by Thomas Wester DISCOVER Vol. 20 No. 06 | June 1999

protein down to the molecular level. And they announced that not only does it kill cells, it eliminates pneumococcus bacteria, too."

Breastfeeding decreases the risk of cancer, infection allergy and autoimmunity in infants[70].

Some other breast milk constituents:

Breast milk provides bacterial adhesins which help bifidus and other commensals attach to the mucosa to remain and multiply[71]. ***Oligosaccharides*** in mother's milk[72] acts as fermentation nutrients for commensals, (in particularly that promoting the growth of bifidobacteria), while the ***lactose*** which produces short chain fatty acids plays a postbiotic role, particularly butyrate, which is a major fuel for colonocytes, and anti-apoptotic, pro-proliferative agent, which aids in strengthening intercellular right junctions.

"***The major milk protein lactoferrin can destroy microbes and reduce inflammatory responses… promotes growth of bifidobacteria, as well as cleaving colonization factors on Haemophilus influenzae and E. coli. Lactoferrin has antiviral effects, and acts against fungi like candida albicans, and decreases the risk of infections caused by bacteria, viruses and fungi without the use of inflammatory mechanisms. It also actively blocks interleukins and prevents pro-inflammatory mechanisms from being initiated. The non-absorbed milk oligosaccharides block attachment of microbes to the infant's mucosae, preventing infections***." This article[73] also points out additional components in breast milk with protect against neonatal septicaemia and meningitis and says, "***It is therefore important to start breast-feeding immediately***."

"Lysozyme, an enzyme capable of destroying Gram-negative bacteria by disrupting their cell walls is found in significant quantities in breastmilk and also in the stool of breastfed infant. Additional directly antimicrobial innate immune molecules found in breastmilk include α- and ß-defensins. Non digestible glycans, most importantly oligosaccharides, may act as specific decoy receptor molecules for pathogenic microbes. Bacteria binding to breastmilk oligosaccharides are prevented from binding to intestinal epithelial cells,

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[70] Hanson, L.A. 2007. "Session 1: Feeding and infant development Breast-feeding and immune function." *Proc Nutr Soc* 66, 382-396. PMID: 17637091.
[71] Hanson, L.A. 2007. "Session 1: Feeding and infant development Breast-feeding and immune function." *Proc Nutr Soc* 66, 382-396. PMID: 17637091.
[72] Neu J. 2007 "Gastrointestinal maturation and implications for infant feeding PMID 17913404
[73] Hanson, L.A. 2007. "Session 1: Feeding and infant development Breast-feeding and immune function." *Proc Nutr Soc* 66, 382-396. PMID: 17637091.

which is a crucial early step in bacterial attachment and pathogenesis of infectious disease."[74]

"In addition to innate immune receptors such as sCD14 and Toll-like receptors, breastmilk contains cytokines, cytokine receptors, growth factors, and functional maternal immune cells that may modulate immune responses and intestinal maturation of the infant. Colostrum contains high concentrations of epidermal growth factor, which has been shown to enter the systemic circulation in the infant and therefore may play a role in inducing maturation in the infant intestine and other tissues. Interestingly, the concentration of epidermal growth factor is particularly high in breastmilk from mothers whose infants have been born prematurely."[75]

Tranforming growth factor (TGF)-β a cytokine found abundantly in breastmilk has a wide variety of effects extending from regulation of cell proliferation and differentiation to modulation of immune responses.

TGf-β is essential for healthy immune maturation in mammals. There are three TGF-β forms so far identified which are all encoded by separate genes. TGf-β is produced by immune cells and enhances the induction and function of regulatory T cells and barrier function by inducing IgA antibody production, but interestingly, it's TGF-β2 is most abundant in breastmilk.

"Responsiveness to TGF-2 is developmentally regulated … the neonate may be … adapted to immunoregulation by TGF-β2 in breastmilk… (and) intestinal responsiveness is confined to the neonatal period when the intestine is exposed to TGF-β2 in breastmilk."

TGF-β is also known to be vital in preventing the development of allergic airway disease in mice, and when TGFβ's are removed allergy followed. Breastmilk, ***"inhibits systemic allergic responses…"*** However, this appears to apply primarily, to any allergen introduced via the mucosal surfaces. Anecdotally, the automatic protection of TGF-β does not appear extend to something injected into the breastfed baby, given that some fully breastfed babies have had serious reactions to vaccines including anaphylaxis.

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[74] Rautava S, Walker WA., 2009. "Academy of Breastfeeding Medicine founder's lecture 2008: breastfeeding—an extrauterine link between mother and child." Breastfeed Med. Mar;4(1):3-10. PMID: 19292608.

[75] Rautava S, Walker WA., 2009. "Academy of Breastfeeding Medicine founder's lecture 2008: breastfeeding—an extrauterine link between mother and child." Breastfeed Med. Mar;4(1):3-10. PMID: 19292608.

The dose of TGF-β in breastmilk is crucial. Allergic mothers have been reported to be lower in allergic mothers than in healthy mothers. If a mother has lower levels, then the baby may be at risk of allergic development.

What is CD14? CD 14 is a protein which directly triggers the development of particular cells which crank out antibodies.[76]

That just scratches the surface… the more they look, the more they find.

Post-birth Nutrition.

If "mother and baby" nutrition from conception to age 2 is inadequate, the result is low birth weight and slow linear growth during infancy. Liver development is hampered, as is the learning process for lipid metabolism[77]. Breast milk with its high levels of cholesterol is crucial for future lipid metabolism patterning.

After birth, babies normally double their birth weight in four to six months, and to do this, they require an energy intake of calories per kg of body weight, four times that of an adult. When babies breastfeed, their gastrin, cholecystokinin and insulin levels rise to a similar level to that seen when sucking on a pacifier. Both activities result in "sleepiness".

When babies are sick, or stressed, the levels of somatostatin increase, mobilizing energy reserves, inhibiting the gastrointestinal tract and retarding growth.

For the baby, from a physiological and immunological point of view, lactation is a continuation of pregnancy with the mother storing energy in the breast by an increase in prolactin, which decreases the number of insulin receptors in maternal fat stores (reducing nutrient uptake there). At the same time, the number of receptors in the mammary glands increase, leading to the formation of breast milk that will take over the transfer of nutrients from the umbilical cord.

A woman's caloric requirement is higher while breastfeeding than during pregnancy by at least 25%. Fat (lipoprotein lipase) is laid down in the buttock and thigh fat area in pregnancy, specifically to be used during breast feeding. If a mother doesn't lose this fat by breastfeeding, it comes hard to move.

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[76] Filipp D, et al. 2001. "Soluble CD14 inn colostrum and milk induces B cell growth and differentiation." *Proc Natl Acad Sci USA.* Jan 16;98(2):603-8. PMID: 11209057.

[77] Kajantie E, et al, 2008. "Growth before 2 years of age and serum lipids 60 years later: the Helsinki Birth Cohort study" *Int J Epidemiol* Apr;37(2):280-9.Epub 2008 Feb 11. PMID: 18267964.

Changes in the mother continue during breastfeeding. The digestive process is optimized and the mucosa of the entire gut is thickened in order to meet the increased metabolic needs of breastfeeding. Peyer's patches double in size to process bacterial particles for transfer to breast-milk, and osteoprotegerin patterns change to start "teaching and rewiring" nutritional and immunological processes in the baby.

Women tend to feel sleepy when breastfeeding, because cholecystokinin is released from the gastrointestinal tract in response to the baby's suckling. This serves two purposes. It saves energy, and keeps the mother with her offspring. Breastfeeding, through regulating gastrointestinal function, synchronizes the mother and baby's metabolisms, so that they become symbiotic both physiologically and psychologically.

Much more is known about breast milk and nutritional optimization but time does not allow more elaboration yet it is also a fact that we have to date only scratched the surface and that there is so much more to learn about the subject

BACTERIA IN BREASTMILK AS AN IMMUNE SYSTEM 'TEACHER':

The mother[78] also provides some bacteria from her gut through her breast milk:
"Intestinally derived bacterial components are transported to the lactating breast within mononuclear cells. This programs the neonatal immune system to recognise specific bacterial molecular patterns and to respond appropriately to pathogens and commensal organisms."

These are sent from the Peyer's patches in the mothers gut to the breast milk, and to the baby. Breast milk is therefore not innately sterile.

Complex bacteria combinations transfer via breast milk, including lactose degrading lactic acid producing bacteria like S thermophilus, S epidermidis and b longum. The most common bacteria transferred are staphylococci and streptococci. Also enterococci, peptostreptococci, corynebacterium, escheria, bacteroides, clostridium, eubacteriaum and s. thermophilus species.

"The observation that microbial components pass into the circulation of healthy individuals, albeit within an intracellular compartment, is potentially controversial and challenges the dogma that translocation of such material occurs only during sepsis.

[78] Perez PF, et al 2007. "Bacterial imprinting of the neonatal immune system: lessons from maternal cells?" *Pediatrics* Mar;119(3):e724-32. PMID 17332189. (Key article)

Such a transfer of bacteria through milk may be a means by which maternal microbes colonize the neonatal gut. Such a mechanism may provide a colonization advantage to bacteria of the mother's intestinal microbiota at a time when the low bacterial diversity in the neonatal intestine is permissive to colonization.

<u>This phenomenon represents an education of the neonatal immune system by maternally derived bacterial molecular motifs</u>.

Neonatal immune cells must learn to differentiate between self-antigens, dietary antigens, commensal organisms and pathogens"

These bacterial components are delivered prepackaged with adhesins, which stick the good bacteria to the gut walls and help them colonize and multiply efficiently.

However again, a mother can only give what she has got if her gut flora has been trashed by a poor diet or by several rounds of antibiotics during a hospital delivery.

<u>Baby Gut Immune Conductor: B. fragilis.</u>

"***A single bacterial polysaccharide from a commensal bacterium, Bacteroides fragilis, is capable of directing the cellular and physical maturation of the developing immune system. Other non cultivated bacteria have been shown to direct immune development… accumulating evidence demonstrates that the commensal gut microbiota can influence epithelial and stromal cell biology, the function of dendritic cells (DC's) T and B cells suggesting that at the level of the mucosal immune system, their effects are likely to be profound***."[79]

"***Difference in the neonatal gut microflora precede the development of atopy, suggesting a crucial role of the balance of indigenous intestinal bacteria for the maturation of human immunity to nonatopic mode….the successful maturation of the gut mucosal immune system requires constant microbial stimulus from the developing gastrointestinal microflora***"[80]

[79] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.

[80] Kalliomaki M et al, 2001. "Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing." *J Allergy Clin Immunol* Jan;107(1):129-34. PMID: 11150002.

Antibiotics and the wrecking of the neonatal gut flora:

"Neonatal antibiotic treatment has been shown to reduce the biodiversity of the fecal microbiota, to delay the colonization by beneficial species such as Bifidobacteria or Lactobacilli, and to induce colonization by antibiotic-resistant or opportunistic strains."[81]

Oral use of antibiotics (mainly amoxicillin) ***by the infant during the first 1 month of life***, resulted in decreased numbers of bifidobacteria and B fragilis-group. Lower counts of bifidobacteria were also observed after oral administration of the antimycotic miconazole.[82]

But this is not all antibiotics do[83]: "***We observed that several genes related to host defense and antigen presentation were downregulated after the antibiotic treatment, whereas genes related to mast cell activation were upregulated. These results suggest that early antibiotic treatment may disrupt the normal process of antigen presentation and handling in a period that is related to a massive penetration of novel food antigens in the gut***."

"It is possible that the widespread antibiotic use and vaccination of children that occur in developed countries together with improved sanitation, lead to the clearance of symbiotic bacteria such as B. fragilis at an essential time in immune development, results in the absence of molecules such as polysaccharides. The aberrant development of the immune system that occurs without specific direction of this class of immunomodulatory molecule might lead to the overproduction of TH2 cytokines and the onset of atopic and asthmatic disorders." [84] B. fragilis corrects the system Th2 bias found in the absence of bacterial colonisation of mice.

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[81] Schumann, A., et al., 2005. "Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome." *Physiol Genomics* Oct 17;23(2):235-45. Epub 2005. Aug 30. PMID: 16131529.

[82] Penders, J. et al,2006. "Factors influencing the composition of the intestinal microbiota in Early Infancy" *Pediatrics*. Aug;118(2):511-21. PMID 16882802.

[83] Schumann, A., et al., 2005. "Neonatal antibiotic treatment alters gastrointestinal tract developmental gene expression and intestinal barrier transcriptome." *Physiol Genomics* Oct 17;23(2):235-45. Epub 2005. Aug 30. PMID: 16131529.

[84] Mazmanian S K., et al, 2006. "The love-hate relationship between bacterial polysaccharides and the host immune system" *Nature Rev Immunol.* Nov;6(11):849 -858. PMID: 17024229.

"The significance of polysaccharide's role in immune homeostasis lies in its ability to mediate establishment of a proper TH1/TH2 balance for the host, a fundamental aspect of healthy immunologic function." [85]

Some authors have been asking questions[86] about antibiotics: ***"If bacteria are important in early human development <u>then this has obvious implications</u> for the use of antibiotics and probiotics. The use of peripartum antibiotics has become prevalent in modern obstetric and neonatal practice, mainly aimed at reducing the incidence of gp B streptococcal infection. Whilst this aim has been achieved, there was a doubling in the rate of E.coli early onset sepsis in very low birth weight infants in a decade. Similarly, in a recent case control study, intrapartum antibiotic use was associated with an increase in late onset serious bacterial infections."***

"In a recent large study of over 1000 infants at one month of age, antibiotic usage was associated with decreased numbers of bifidobacteria and Bacteroides."

<u>Osteoprotegerin: Another example of nutrient and immune system modulation.</u>

Osteoprotegerin (OPG) is a naturally occurring member of the tumor necrosis factor receptor family. Osteoprotegerin ***orchestrates good bone development,*** prevents osteoporosis, regulates B cell maturation and helps develop efficient antibody response.

In breast milk, OPG is found at concentrations 1,000-fold higher than in human serum[87].

The neonatal period is critical for the processes which govern normal bone remodeling and the development of the immune system responses. Because osteogenesis is an exceedingly rapid process in babyhood, to ensure that bone formation keeps up with the rapid growth in size, and weight, and that the baby learns to tolerate self antigens, differentiate the succession of bacterial species that constitute normal intestinal flora, but

[85] Mazmanian S.K. et al, 2005. "An immunomodulatory Molecule of Symbiotic Bacteria Directs Maturation of the Host Immune System." *Cell*. Jul 15;122(1):107-18 PMID 16009137.
[86] Wilks, M. 2007. "Bacteria and Early human development." *Early Human Development* 83, 165-170. PMID: 17289307.
[87] Vidal K, et al. 2004 "Osteoprotegerin in human milk: a potential role in the regulation of bone metabolism and immune development. *Pediatr Res.* Jun;55(6):1001-8. PMID 15155868.

remain alert to harmful pathogens, breast milk OPG is one of the key orchestrators of both processes. OPG may also regulate the Th1/Th2 balance.

Breast milk actively "teaches" and orchestrates all nutritional processes, and primes the immune system of healthy infants, in a progressive manner, almost like following a "developmental manual". Its influence isn't just short term, but it also has a long term immune-modulating effect on the developing cellular immune system.

The basis for good bone formation is laid in pregnancy, and developed during breastfeeding. The mother's diet must contain all the various minerals associated with bone development. I don't believe that it's a coincidence that in the last three decades, childhood fractures have increased by 30%. How a baby is formed in utero, and fed in the first few years of life, sets the pattern for what will then follow.

For more bone information, see Bone 101.

The thymus and its role in adaptive immunity.

Smoking during pregnancy[88] adversely affects both the baby's size and thymus size.

The thymus of a breastfed baby is ***twice the size*** of formula fed infants[89]. This is orchestrated by maternal nutrition and the quantity of IL-7 in the breast milk. Anything which interrupts the development and function of the thymus, at any time has potentially serious consequences:

"It is possible that such early variations may represent a permanent programming of thymic development which in turn could influence adult T cell function through differences in T cell pool size, repertoire, or both. The accumulated effects of these events, is predicted to precipitate premature immune senescence by inducing accelerated T cell division with age ***as a response to the disproportionate pressure on an immune system that is fundamentally inhibited by early-life events****."*

But what do vaccines do to thymic size and function? Sadly no one seems to know and there does not seem to be a single study that asked the question and looked at the subject.

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[88] Zeyrek D, et al. 2008. "Decreased thymus size in full-term newborn infants of smoking mothers." *Med Sci Monit.* Aug; 14(8):CR423-6. PMID: 18668000.

[89] Jeppesen DL, et al, 2004. "T-lymphocyte subsets, thymic size and breastfeeding in infancy." *Pediatr Allergy Immunol* Apr;15(2):127-132. PMID: 15059188.

Collinson et al [90] stated in 2003: **"Restriction of thymic activity during its establishment of the T-cell repertoire may alternatively lead to defective immunological memory or premature immunosenescence."**

Could that be happening in all those babies on formula with smaller thymuses?

Breast milk continues to orchestrate the thymus as long as the baby is breastfed, and the absolute numbers of both CD4+ and CD8+ cells increase between 8 and 10 months of age with continued breastfeeding. Studies in Africa[91] have shown that thymic size varied with the season and was smaller during the "hungry" season. If a mother did not have it, the baby did not get it and that applied to both under nutrition and malnutrition

EXPLOSION OF ALLERGY in WESTERN CHILDREN: The HYGIENE HYPOTHESIS

Before we go further, let's look at the historic round up of how immunologists saw, and see, the Hygiene Hypothesis[92]. Originally the "refusal" of the immune system to revert from Th2 to Th1 was thought to be due to a reduced microbial burden in early childhood. After the discovery of regulatory T cells, it became clear that their decreased activity (i.e., reduced immune suppression) was the simpler explanation, and immunologists preferred talking about "immune deviation".

After more "discoveries", ***"a new paradigm was erected, and an impressive amount of previously reported in vitro and in vivo data showing the existence of a process of immune deviation was fully discarded, as in a sort of iconoclastic fury."*** The increase in Th1 nephropathies in comparison to Th2-mediated nephropathies in developed countries suggested that immune deviation due to reduced microbial burden may have played a role.

Now the politically correct opinion appears to be that atopic subjects don't have an ***immune deviation***, but have a ***differently polarized***, T-cell effector response to common environmental allergens.

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[90] Collinson AC, et al. 2003. Birth season and environment influences on patterns of thymic growth in rural Gambain infants." *Acta Paediatra* Sep;92(9):1014-20. PMID: 14599061. (KEY STUDY)

[91] Jeppenson DL. 2003. "The size of the thymus: an important immunological diagnostic tool?" *Acta Paediatr.* Sep;92(9):994-6. PMID: 14599055.

[92] Romagnani, S. 2007. "Coming back to a missing immune deviation as the main explanatory mechanism for the hygiene hypothesis." *J. Allergy Clin Immunol* 119:1511-3. PMID 17556059.

Where do vaccines fit into all this?

For all his ignorance about historical work on gut flora, Wilks asked an interesting question[93]: ***"If the development of mammalian intestinal structure, immune system and metabolism are mediated by the presence of a bacterial flora, what other mammalian systems might be dependent in the same way? Might this process actually begin in utero?"***

I would venture to answer "Most mammalian systems" and "Yes." I believe that correct bacterial orchestration of the immune system, and the gene expression maturation of the immune system via TGF-β2 in breastmilk, is far more profound than immunologists have stopped to consider.

Wilks also asked ***"Whilst inflammatory bowel diseases may well have their origins in early host-microbe interactions when the host is learning to react appropriately to its developing microbial flora, clinical manifestations may not be apparent for many years. This makes applying the new approaches and findings described above extremely difficult."***

I agree that doctors might not connect something years on, to something else they didn't take into account in the first year of life. I disagree that this fact makes new approaches extremely difficult. The medical profession has had no problem interfering at every possible turn. So what is so difficult about respecting the way a body is designed to work, given the right conditions? Shouldn't the default position be that unless a baby's life is threatened, a caesarean section doesn't happen? That unless a mother has a bilateral mastectomy, breast-feeding happens, long term?

If some classify a decision to let a baby develop its immune system under the direction of breast milk and not to vaccinate as "child abuse" then it's hard to see why elective caesareans, formula feeding, over-use of antibiotics and even the unnecessary use of anti-acids during pregnancy, are not also considered "child abuse."

[93] Wilks, M. 2007. "Bacteria and Early human development." *Early Human Development* 83, 165-170. PMID: 17289307.

However, given the current politically correct position where it's a mother's "right" to chose to have a caesarean, and it's a mother's right to chose to bottle-feed, and a mother's right to demand antibiotics for the merest sneeze, my pick is that ***the only use for*** information such as I am bringing you today, will be :

- to try to make formula "better"
- to patent some unique at-caesarean-birth bacterial inoculum to swab into a baby's mouth before it's lifted from inside it's mother's stomach
- and to make new vaccines using the mucosal tract as entry portal, instead of injections.

Can we agree on the following point: ***that prenatal and antenatal events rely on correct gene expression as a result of an environment to support the correct working of the master plan, and that anything that impacts on that, can cause a change with profound long lasting consequences?***

"What is an immunologist supposed to know about the intricacies of the complete immune system?"

Immunology exists to study the way the immune system works as a whole to confer protection against disease."[94]

Note the words, "***as a whole***." However, when you consider the fact that the medical profession has only taken the innate immune system seriously in the last decade the next sentence is very revealing:

"Broad and conceptually profound, it is understandably difficult for the field to devote equivalent attention to the cellular mechanisms involved."

"***Equivalent attention***"… in comparison to what?

Most research regarding vaccines and any involvement with the immune system, has previously concentrated on humoral antibodies …the "end point" of the process.

[94] Mellman I. 2007. "Private Lives: reflections and challenges in understanding the cell biology of the immune system." *Science* Aug 3; 317(5838):625-7. PMID: 17673653.

"***The cellular mechanisms involved***" are fundamental to human existence, yet immunologists have such a limited understanding of those processes, or how a baby's immune system matures.

They certainly cannot possibly know all the potential consequences of administering multiple vaccines to the specific baby they are about to needle. They know bits about what can go wrong when vaccinating mice, a model which they claim is totally relevant to humans. Yet when something goes wrong with the vaccinated mice, the language changes, and suddenly the implications are not so relevant to humans anymore.

What do immunologists now know about the development of a baby's immune system?

"It is acknowledged that early childhood is characterized by an increased susceptibility to infectious diseases, and this has been attributed both to ***immaturity of the immune system*** *at birth and to the* ***sluggish development*** *of immune competence in the postnatal and early childhood years****… considerable gaps still exist in current understanding of the mechanisms underlying immune maturation in healthy children****."*

These authors[95] go on to say, ***"There is also a paucity of knowledge concerning the rate at which IL-12 production develops between infancy and adulthood, an issue with fundamental implications for our understanding of host defense and immunoregulation during childhood… the capacity to synthesise adult levels of IL-12 does not appear to develop until well into adolescence, and the factors that regulate the ontogeny of IL-12 remain poorly defined…other than cord blood studies there have been no studies to our knowledge of IL-12 production by healthy children in the postnatal period."***

"neonatal APC's lack the capacity to deliver important TH1 polarizing signals to T cells… neonatal monocyte derived dendritic cells also have a specific defect in IL-12 p35 gene expression though this can be corrected by the addition of exogenous IFN-γ to cultures. The exact nature of the signals required to induce neonatal cells to synthesise adults levels of bioactive IL-12 remains poorly understood at present.

[95] Upham J.W. et al., 2002. "Development of Interleukin-12-Producing Capacity throughout Childhood." *Infect Immun.* Dec;70(12):6583-8. PMID: 12438328.

The above article suggests two things: First that immunologists do not know what they are looking at and yet refuse to say "I don't know". They hedge instead (see words in blue) and never consider that drugs and vaccines might affect the immune system in ways that they do not yet understand.

Second, the language betrays a fundamental belief by immunologists that a baby's immune system is ***"defective",*** and that they need to introduce ***"exogenous"*** compounds and vaccines into it to force it to perform at an adult capacity.

Marodi wrote in 2002 article[96]: ***"To define the molecular mechanisms involved in these regulatory pathways in newborns vs. adults, and the anatomic sites that are critical to type 2 bias in neonates will be a major task for future research."***

- Who, in the face of these facts, is asking the fundamental questions:

- WHAT is the purpose of the slowness of a baby's immune system?
- HOW is that controlled in terms of gene expression?
- WHAT RELATIONSHIP does breastfeeding have to the step-wise processes of gradual immune system maturation?

Where are rational minds considering the point that ***if*** a baby SHOULD have an adult's immune system to function appropriately for it's age, it WOULD have?

- ***WHAT is the significance of the slow maturation of a baby's immune system in terms of appropriate adaptation to the environment, and short and long term survival of the human race?***
- ***COULD IT BE POSSIBLE that by ignoring the principles of slow maturation, and instead attempting to change it, that the whole master plan crashes in some children, in some form or other?***

Many medical publications show immunologists fixated on "fixing it". Apart from a few articles questioning whether current vaccines are the best teacher, most immunologists write with utter confidence about a future where they will get into a baby's nose and gut with various chemical and vaccine compounds to make a baby's immune system work "as it should"…

[96] Marodi L.2002."Down-regulation of Th1 responses in human neonates? *Clin Exp Immunol* 128:1-2. PMID: 11982583.

Let us look at some of the functions that the medical profession[97] considers *"**inadequate**"* in the human neonate:

"T***he different responses of neonatal B cells and immature B cells from adults marrow might reflect developmental regulation of crucial nuclear signals… essential for antigen-driven responses*** … "***altered threshold of responsiveness of neonatal T cells primarily results from their developmental immaturity*** … "***in humans… germinal centres are not observed until several weeks after birth. In addition the phenotype of the cells that are found in the marginal zone remains immature until around two years of age. The lack of these structures is likely to be an important contributor to the relative immunodeficiency of neonates*** … "***experiments that examine Th polarization under various conditions of antigen presentation provide evidence that low MHC-peptide density, as probably occurs in neonates, favours priming of Th2-type CD4 cells***"…"***the inability of neonatal B cells to upregulate key molecules that are involved in their interaction with T cells might also create conditions in which antigen encounter results in tolerance***."… "***the T-cell compartment is also functionally compromised with neonatal cells showing a greater requirement than adult cells for costimulatory signals***" … "***human neonates are particularly deficient in their responses to bacterial capsular polysaccharides, resulting in significant infant morbidity and mortality from infections diseases***.." … "***the estimated 1.8 million deaths annually from infection during the first year of life, predominantly in the developing world***" … "***A full understanding of the neonatal immune system .. will be required***.."

[98]***"The development of mature plasma cells in the bone marrow is incomplete at birth. Isotype switching is defective, with simultaneous surface expression of different isotypes and immunoglobuline production is low. Again, deficiencies in cytokine networks likely play an important role in diminished functionality of the humoral response. Decreased responsiveness to antigen stimulation, particularly to nonprotein 'T cell-independent' antigens (i.e. carbohydrate antigens) continues well into the second year of life. Examples of this deficiency are well recognized clinically, such as the inability of the newborn to mount an immune response to Streptococcus pneumoniae, and haemophilus influenza, leading to increased susceptibility of newborn to infection with these pathogens…"***

[97] Marshall-Clarke, S et al. 2000. "Neonatal immunity: how well has it grown up?" *Immunol Today* Jan;21(1):35-41. PMID: 10637557.

[98] West L.J. 2002. "Defining critical windows in the development of the human immune system." *Human & Experimental Toxicology* 21, 499-505. PMID: 12458907.

A 1999 medical article showed that long term breastfeeding[99] can develop immunity in babies, against haemophilus which lasts 10 years. Dr Katerina Svanborg proved that breast-milk neutralises streptococcus pneumoniae. So if a mother breastfeeds, is a baby unable to mount an effective immune response to those, or other pathogens?

In 2009, another medical article showed that long term breastfeeding also provides some immunity against viral diseases, like measles,[100] yet medical writers have reported that anecdotally, for nearly a century.

Why are immunologists always insisting that a baby's immune system is "fatally defective"? Is their word use dictated by a belief that vaccination is the ONLY way to go in order to correct all these "defects" and force the maturation of a baby's immune system in a rush.

Why also does it not occur to these people, that a baby's immune system might ***NOT*** be "deficient", or "functionally compromised" or "unable"……***but might actually be DIFFERENT, and developmentally appropriate for its gene expression, age and immunological needs?***

If a very unusual mother thought to ask you how much you know about how her newborn baby's immune system will mature, and/or react to vaccines; and why the difference between a baby's and an adult's response to infection, would you answer: "We don't know that information"? (But we can tell you a bit about mice.)

Any doctor who knows what breast milk does, should be able to answer that mother and to assure her that her baby's immune system needs more than formula and vaccines.

What immunologists DO know about a baby's immune system.

One of the key cells in the innate immune system are the CD4+ T-cells from the large thymus of breastfed babies. These cells grab antigens presented by dentritic cells and release cytokines.

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[99] Silfverdal, S, et al. 1999. "Protective effect of breastfeeding: an ecologic study of Haemophilus influenzae meningitis and breastfeeding in a Swedish population." *Int J. Epidemiol.* Feb; 28(1): 152-6. PMID: 10195681.

[100] Silfverdal, S, et al. 2009. "Breast-feeding and a subsequent diagnosis of measles." *Acta Paediatr.* Apr;98(4): 715-9. Epub 2008 Dec 24. PMID: 19133867.

This year (2009) CD4+ cells from adult and neonatal mice were compared for the ***first*** time and found[101] that ***adult and neonatal*** T-cells ***"are phenotypically and functionally distinct…. Which may at least partially explain the diverse responses that are elicited in vivo in neonates in response to different conditions of antigen exposure."***

Now that we know about "diverse responses", will that fact ever be taken into account when vaccine trials or uses are considered?

Does a baby under the protection of breast milk follow a plan dictated by gene expression? Is that how the baby adapts correctly to its environment? Is this perhaps the reason why: "***many studies in both humans and mice have shown that newborn immune cells are*** qualitatively distinct ***from adult cells***"[102]?

If the concept of ***stage specific, appropriate immune development*** has validity, then what might happen if an event is forced too soon, changing the game plan?

Adkins et al[103] point to the answer: ***"Notably, mice initially immunized as neonates mounted Th2-type-dominant memory responses when re-exposed to the same antigen as adults."***

Yet they go on to say ***"It is important to emphasize that the clear skewing towards TH2-type responses that can be observed in mice is not readily apparent in humans."***

One must ask "Did they look for it?" It certainly seems they did not.

Maybe saying "we don't know" would have been easier?

So what do immunologists know about how vaccines work?

Here are some sandwich[104] quotes. Good news first[105]. "***Despite the success of many vaccines, there is presently little knowledge of the immunological mechanisms that***

[101] Opieta SJ et al 2009. Murine neonatal recent thymic emigrants (RTE) are phenotypically and functionally distinct from adults RTE. *Blood* Jan 23. [Epub ahead of print]. PMID 19168791. (abstract only)
[102] Adkins, B et al., 2004. "Neonatal Adaptive Immunity comes of Age." *Nature Reviews"* Jul;4(7):553-64. PMID 15229474.
[103] Adkins, B et al., 2004. "Neonatal Adaptive Immunity comes of Age." *Nature Reviews"* Jul;4(7):553-64. PMID 15229474.
[104] Wrapping bad news in some feel good fuzzies.

mediate their efficacy…. Furthermore the most commonly used empirical adjuvants in clinical practice, alum and the oil based formulation MF59, while useful for enhancing antibody responses, have no discernible effect on the cellular immune responses."

"Commonly used vaccines promote antibody responses but have little impact on the cellular immune response and hence their use in the developing immune system may not be optimal or provide appropriate education."[106]

Vaccines seem to suffer from an "urgency" clause and paediatricians constantly argue that early vaccination is necessary because of the "immaturity of the baby's immune system" and the risk of serious infection. Yet, if the job is really done properly, (no caesarean, no antibiotics and a well-nourished breastfeeding mother) doesn't the urgency disappear?

In 2001, Adkins wrote in another article[107]: "***Immunisation during the neonatal period often results in Th2-biased secondary responses….these experiments demonstrated that neonates are selectively impaired in the development of Th1 memory effector function. Together, these results indicate that neonates are biased to Th2 function at all phases on an immune response. Siegrist and his colleague observed Th2 skewing in neonatal mice immunized with a variety of Ags precipitated with aluminium,… Bona and colleagues reported Th2 responses in neonates immunized with live or attenuated virus while comparably immunized adults developed Th1 responses… we have also found that animals initially immunized as neonates show Th2 dominant memory responses. … thus under many conditions, neonates appear to be biased to Th2 lineage function.***"

In 2002 we were told[108], ***"It is clear that antigen-specific responses to diphtheria, tetanus, and pertussis vaccination in infancy are Th2 skewed. It therefore appears that the functional deficiencies of neonatal APC's are not intrinsic to these cells, as they can be induced to mature to adult-equivalent functional competence via the provision of appropriate microenvironmental signals."***

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[105] Pulendran, B et al., 2006. "Translating Innate Immunity into Immunological Memory: Implications for Vaccine Development." *Cell* 124, 849 – 863. PMID 16497593.

[106] Kelly D., et al., 2007. "Importance of microbial colonization of the gut in early life to the development of immunity." *Mutation Research* 622: 58-69. PMID: 17612575.

[107] Adkins, B, et al. 2001. "The Generation of Th Memory in Neonates Versus Adults: Prolonged Primary Th2 Effector Function and Impaired Development of Th1 Memory Effector function in Murine Neonates." *J. Immunol* Jan 15;166(2):918-25. PMID: 11145668.

[108] Upham J.W. et al., 2002. "Development of Interleukin-12-Producing Capacity throughout Childhood." *Infect Immun.* Dec;70(12):6583-8. PMID: 12438328.

By injecting interferons, and other substances, they claim they can "mature" an immune system to deliver "appropriate" signals. But who knows what is "appropriate" … and doesn't a baby already have an "appropriate" immune system?

"Of further interest, we demonstrated that for children immunized at 2, 4 and 6 months of age, in vitro IFN-y responses to tetanus toxoid varied markedly in stability over the ensuing year, with vaccine-specific IFN-y reactivity being lost in a substantial subset. Such instability of Th1 function in the early postnatal period is similar to that reported for the mouse."

How might a vaccination inappropriately skew this "defective" baby's immune system to Th2?

Remember this[109]?

"The antibody forming mechanisms are highly conditioned by the first stimulus, so that later infections with strains of the same type successfully enhance the original antibody to maintain it at the highest level at all times in that age group. The imprint established by the original virus infection governs the antibody response thereafter. This we have called the Doctrine of the original Antigenic Sin."

What say a baby has a series of many such first stimuluses inside a "window of vulnerability" when the immune system isn't supposed to be challenged that way? Where:

1) A neonate, who is in the process of a developmental programme where the innate immunity is being educated while under the immunological surveillance of breast-milk, might, like mice, have no option when a "vaccine monkey wrench" is thrown in.

2) Any vaccine which is adjuvanted to aluminium, will usually give a Th2 immunity, particularly in a neonate, and aluminium adjuvants will always result in IgE, a marker of allergy. The very adjuvant used, enforces the bias to that of allergy potential at the first stimulus, and also dictates any subsequent immune response to those antigens. But what about the immune system as a whole?

[109] Francis T Jr., 1960. "On the doctrine of Original Antigenic Sin." *Proc Am Philos Soc* 104:572.

3) Most of the effects of aluminium are unknown, according to an immunologist I discussed this with. But I was also told that 99% of the known effects are bad. As I've dealt with much of that elsewhere, I will solely focus on the point at hand.

When a vaccine is administered intramuscularly, this is what they know happens:

- The needle goes in, piercing the muscle to a depth of around 2 cm or more.

- The plunger is pushed delivering a particulate vaccine consisting of many antigens, as well as the various target microbes, e.g. diphtheria etc. Some of the other antigens are aluminium, polysorbate, antibiotics… the other antigenic constituents can be found on the data sheet at Medsafe. Also injected are unlisted bacterial toxins and extraneous proteins from the vaccine manufacture process. The needle is pulled out.

- Puncturing muscle to that depth causes muscle damage, resulting in necrosis and the release of uric acid which triggers what is known as DAMPS or "Damage associated molecular patterns".

- The presence of aluminium intensifies DAMPS into danger signals. Aluminium precipitates the formation of depots of the antigen and adjuvant, which continually activate the immune system for years.

- Much of the aluminium is dispersed, but can travel in unusual ways. In mice, under normal physiological conditions, aluminium is transported by transferrin receptors into the brain within half an hour[110] of vaccination: "***the increase in aluminium content of the brains, seen only in mice which received vaccines containing aluminium hydroxide, cannot be due to aluminium in the blood within the brains. Therefore, there must have been an accumulation of aluminium in the brains of the mice which were immunized with aluminium aduvanted vaccines."***

- Aluminium "switches on" monocytes to become dendritic cells.

- Aluminium always produces Th2 immunity responses.

[110] Redhead K. et al. 1992. "Aluminium-Adjuvanted Vaccines Transiently Increase Aluminium Levels in Murine Brain Tissue." *Pharm & Tox* 70; 278-280. PMID: 1608913.

- Aluminium always provokes IgE, a marker of allergy.
- Aluminium, in laboratory mice, seriously interferes with gene expression.
- By creating aluminium depots with residual aluminium, the monocytes which were "switched on" are unable to "switch off" because of continuous DAMP signals sent out by the depot.
- BUT in a child with a TH2 skewed immune system, after receiving a childhood booster shot or vaccine containing aluminium, if that child eats a peanut butter sandwich, or inhales pollen, or something… which happen to pass through the gut into the body and meet an aluminium molecule being excreted, that antigen can be treated as another antigen, therefore provoking another acquired allergy.

Might that explain much of the increase in allergy, atopy and immune related dysfunction seen in the last few decades?

Let's look at the only study which has looked at aluminium levels in babies. The number of vaccines used in this study[111], are fewer than our current schedule: ***Birth*** Hep B (0.25 mg Al); ***2 months*** DPTHepB (.5-1.1 mg); ***4 months*** DPT (.25-.85); ***6 months*** DPTHepB (.5-1.1); ***12 months***, DPT (.25-.85)

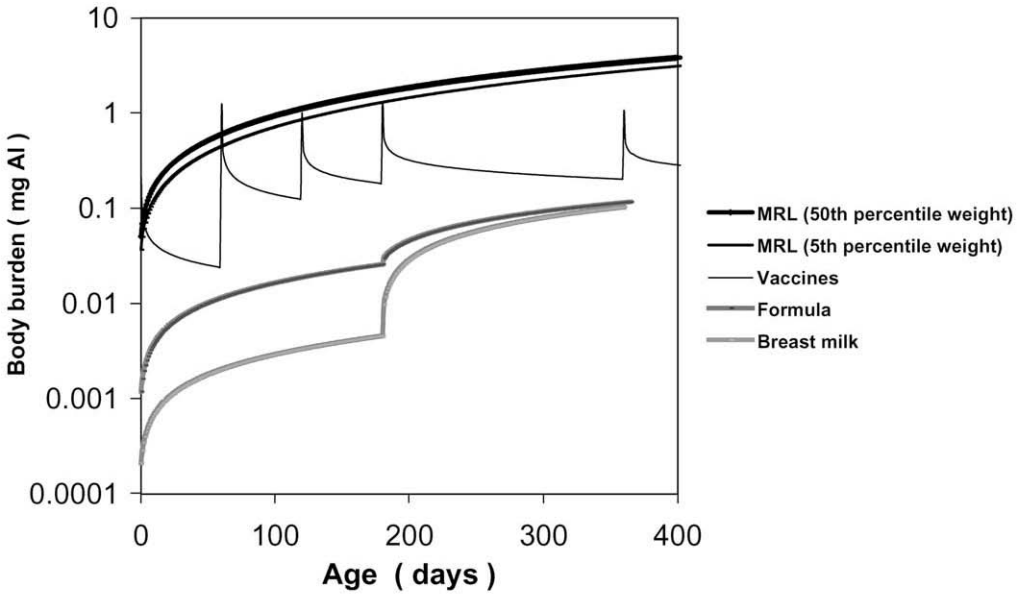

Fig. 1. Aluminum body burden contributions from diet and vaccines relative to MRL level intake.

What might the aluminium spikes going through the maximum recommended level on that graph, look like with New Zealand's vaccination

[111] Keith LS, et al. 2002. "Aluminium toxicokinetics regarding infant diet and vaccinations." *Vaccine* May 31;20 Suppl 3:S13-7. PMID: 12184359.

schedule today? What has been the impact of the aluminium in vaccines on babies up to now? Immunologists don't know, because they've never looked at it in a meaningful way comparing vaccinated and unvaccinated children. Furthermore, aluminium has never been tested for toxicity by injection, in babies or animal neonatal models which theoretically replicate what happens in babies.

One study[112] asks and answers the question:

"***What is the evidence that early childhood immunization promote the development of asthma? An IgE response to vaccine antigens is commonly detectable in the sera of children vaccinated with diphtheria/tetanus, and the IgE response to vaccine antigens is more pronounced among atopic individuals."***

Asthma prevalence rates decreased successively from 13.8 to 5.9 with each month delay in DPT administration… the likelihood of asthma at age 7 years was halved in children who received their first dose of DPT more than 4 months after birth."

***"Delayed administration of the first dose of DPT of more than 2 months from the recommended 2 month period was associated with a reduced risk of childhood asthma by 50% ... However among children with delays in all 3 doses, the likelihood of asthma was further* reduced to 60%."**

I wonder what would have happened if they had waited longer?

A study[113] was performed taking blood samples from five 6 month old babies, who were vaccinated at 3 and 5 months respectively. After 12 hours in vitro re-stimulation of the PBMC with pertussis toxin antigen, *14 immune response pathways, 33 allergy related and 66 asthma-related genes were found activated*.

The authors said, ***"Little is known about the gene expression changes involved in immune responses in adults, and infants after vaccination, even less is known about asthma and allergy associated genes expressed during or after immune responses…the ideal time-point for the expression of immune response genes with an association to asthma and***

[112] McDonald, K.L., et al. 2008. "Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma." *J. Allergy Clin Immunol* Mar;112 (3):626-31. Epub Jan 18. PMID: 18207561.
[113] Lahdenpera A I. 2008. "Kinetics of asthma- and allergy-associated immune response gene expression in peripheral blood mononuclear cells from vaccinated infants after in vitro re-stimulation with vaccine antigen." *Vaccine* 26, 1725-1730. PMID: 18336961.

allergy in peripheral blood mononuclear cells (PBMC) of humans has not yet been determined."

Remember that[114], "***the characteristics of vaccine immunity in infants and young children remain incompletely understood***."

More accurate is this 2008 statement[115]: ***"This review clearly illustrates that knowledge of the development of the immune system in infants has numerous black holes."***

Here's a typical mouthful[116] from an immunologist: "Lymphoid ***development*** is ultimately determined by a ***succession of gene expression programs*** and by ***stage-specific networks*** of classical transcription factors, which act as ***drivers in the progression*** to specific immune cell types." I've highlighted the key phrases.

Isn't that exactly what I'm hypothesising in a different context? Does a baby's immune system learn appropriate responses through a step by step, developmental maturation programme orchestrated by the mother's breast milk and gene expression in the baby?

Here's another massive leap in illogic[117]: "***Maternal T lymphocytes are present at relatively low concentrations in breast milk but their role in the recipient infant is currently unknown. Therefore, young infants are dependent on their own immune system to fight infections caused by intracellular pathogens for which immune defences merely depend on T lymphocytes***."

If the function of breast milk T-lymphocytes in babies is ***unknown***, … if immunologists admit that they have yet to identify all immunological agents in breast milk, isn't there a possibility that there might be something unknown to them, which does the job?

What might happen, in this immunological world consisting of "***numerous black holes***"… if something hijacks the "gene expression message sending programme", before the next

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[114] Kumagai T, et al. 2004. "Poor immune responses to influenza vaccination in infants." *Vaccine* 22:3404-3410. PMID 15308365.

[115] M'Rabet L et al, 2008. "Breast-Feeding and it's Role in Early Development of the Immune system in Infants: Consequences for Health Later in Life *J. Nutr.* 138, 9; Health Module. PMID: 18716187.

[116] Kioussis D, et al. 2007. "Epigenetic flexibility underlying lineage choices in the adaptive immune system." Aug 3;317(5838):620-2. PMID: 17673651.

[117] Marchant A, et al. 2005. "T cell-mediated immune responses in human newborns: ready to learn?" *Clin Exp Immunol* Jul;141(1):10-8 PMID: 15958064.

stage-specific development ***driver*** has a chance to mature the next process? There is obviously some flexibility in an adult, because the article[118] goes on, ***"During lymphocyte development, a certain set of "fixed" transcriptional decisions appears to coexist with flexible changes in gene expression."*** In a transition period, the immune system can do two things at once, allowing room for some cross talk, and errors to be overlooked. ***But*** one thing immunologists haven't worked out is whether this flexibility is less certain in babies.

Why is this important? Because adults are not babies, and when you vaccinate neonates the default response in mice is different to adult's:

"***Secondary exposure to antigen in neonates usually leads to a lack of Th1 cells and a bias toward Th2 Immunity. This unbalanced response may explain the susceptibility of neonates to microbial infections and allergic reactions."***

But might it not be, that the immune system response is only "unbalanced" in the context of the fact that it's being asked to do something that it shouldn't be doing? After all, if the vaccine isn't given at the neonatal stage, the response doesn't happen.

The neonatal mechanism[119] they say is: ***"the lack of secondary Th1 responses stems from the apoptosis of Th1 cells driven by IL-4 produced by their Th2 counterparts."*** But the key statement in the accompanying press release[120], is where Professor Habib Zaghouani says, "***a slowly maturing component of the immune system***" might explain why newborns contract infections easily, and added, ***"Perhaps we should test vaccines at a very early age in animals to establish a regimen with the most effectiveness."*** He also said that in mice, waiting until after a mouse was six days old the immune system had matured, was enough to stop the death of Th1 cells. What's the equivalent age in Human Mice? One year? Two years? Who knows?

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[118] Kioussis D, et al. 2007. "Epigenetic flexibility underlying lineage choices in the adaptive immune system." Aug 3;317(5838):620-2. PMID: 17673651.

[119] Lee, H H et al., 2008. "Delayed maturation of an Il-12-producing dendritic cell subset explains the early Th2 bias in neonatal immunity." J Exp. Med.205:2269-2280. PMID: 18762566.

[120] EurekAlert, 1 April 2009. "New evidence explains poor infant immune response to certain vaccines, says MU researcher." http://www.eurekalert.org/pub_releases/2009-04/uom-nee040109.php

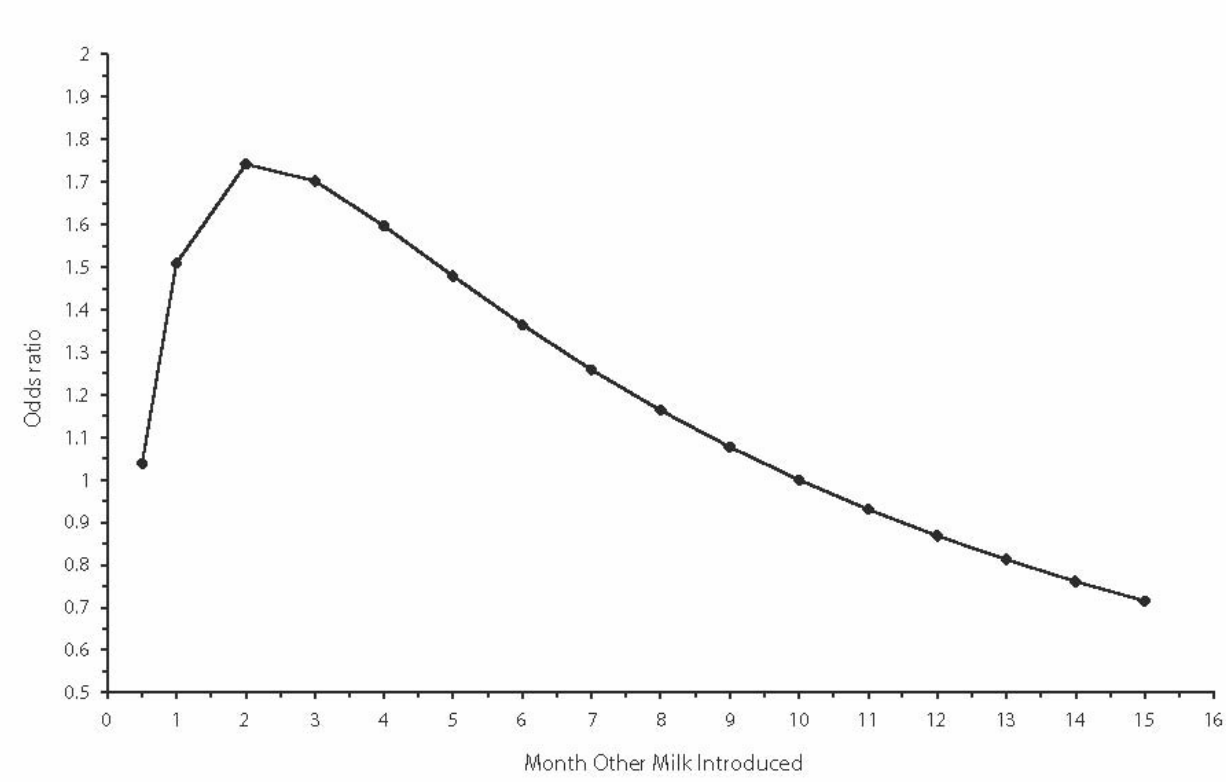

FIGURE 2—Exclusive breastfeeding (i.e., months until other milk was introduced) and risk of asthma in 6-year-old children.

"***We demonstrated that for children immunized at 2, 4 and 6 months of age, in vitro IFN-y responses to tetanus toxoid varied markedly in stability over the ensuing year…"***[121]

Could this immune derangement have a flow down effect for some children?

"The prevalence of atopic disorders has increased dramatically during the second half of the previous century, but explanations for this epidemic are still being sought. Vaccinations having been an element of western lifestyle for decades have been suggested to be involved." [122]

Pertussis has been known to trigger IgE infection, and has been hypothesised to change the risk for atopic disorders. The study authors decided to study the relationship between

[121] Upham J.W. et al., 2002. "Development of Interleukin-12-Producing Capacity throughout Childhood." *Infect Immun.* Dec;70(12):6583-8. PMID: 12438328.

[122] Bernsen RMD, et al, 2008. "Reported pertussis infection and risk of atopy in 8 – 12-yr-old vaccinated and non-vaccinated children." Pediatr Allergy Immunol 19: 46-52. PMID 18086216.

pertussis vaccination in baby hood, and pertussis infection and atopic disorders in 671 unvaccinated and 1033 vaccinated children by use of a questionnaire. After testing 80 of the unvaccinated children they concluded that the vaccination status was ***reliably reported***.

Half of the unvaccinated children's parents reported their children had had pertussis in the last year.

8.9% of the vaccinated children's parents reported the same.

In the unvaccinated children, there were no important associations between pertussis infection and atopic disorders.

"***In group II (vaccinated) however, all prevalences of atopic disorders were higher in the group of children who reportedly had a past pertussis infection, with the associations for asthma, hay fever, the combination of asthma and hay fever and food allergy being statistically significant…. This suggests that the effect of pertussis infection on atopy is restricted to pertussis-vaccinated children, an explanation supported by research in a mouse model"*** which showed that whooping cough induced lung pathology and this induction was stronger after prior pertussis vaccination (both whole cell and acellular).

The authors took serious fright at the ramifications of such a result and started tangled convoluted arguments as to the limitations of this study. They then surmised without evidence that ***perhaps*** the atopic children didn't seroconvert to the vaccine properly. They surmised, (apparently without checking with the parents), that ***maybe*** the diagnosis of pertussis in the vaccinated children was ***spurious and misdiagnosed***. After confounding this, that, and the other, they said, ***"In summary, evidence for a causal association between pertussis infection and atopic disorders is still inconclusive***." A much better prospective study repeatedly assessing immune responses to pertussis as well as positive RASTS was recommended.

In 2009, the results of another study[123] of 14,893 Steiner children who lived on farms came to the stunning conclusion that measles INFECTION may protect against allergic disease in children. While previous studies had shown that measles vaccine was associated with the development of allergic disease, this study did not show that. Of the

[123] Roselund H et al., 2009. "Allergic disease and atopic sensitization in children in relation to measles vaccination and measles infection." *Pediatrics* Mar;123(3):771-8. PMID: 19255001.

children, 9136 (73%) were vaccinated, 2561 (20%) had had measles and 1815 had had neither measles nor vaccine. 11% of the vaccinated children had also had measles. The study found that, "***measles infection was inversely associated with any allergic symptom or physician's diagnosis of allergy, whereas there were no associations with measles vaccination."*** Again, we then read tangled convoluted discussions. There was a positive relationship between the measles vaccine and rhinoconjunctivitis, but that was dismissed as ***"a difference in disease prevalence".*** Another ***"limitation"*** was the low prevalence of allergic disease and atopic sensitization in the unvaccinated anthroposophical children without measles infection! With all the limitations, confoundings and excuses just about everything is dismissed with, you wonder why they even bothered to publish the study. Or the previous pertussis study.

However, another study in Turkey[124] is interesting. Turkey still has high rates of measles despite vaccination, and cannot be considered to be a country constrained by the "hygiene hypothesis". The study found that,

In conclusion, children with a history of measles in our study group had less frequent symptoms of allergic diseases. In children without a history of measles, sensitivity develops, particularly to the house dust mite.

The realisation is now dawning with vaccine defenders, that using vaccines that provide "back end" immunity, isn't the "right" way to get immunity. So even though knowledge of the innate immune system has numerous black holes, researchers[125] have decided that infant nasal associated lymphoid tissue, has promise as the next way to deliver vaccines: "***This constitutes an intriguing structural basis for the current interest in exploiting the nasal route in humans to combat serious health threats in the world."*** So far, disease antigen alone does nothing, so the search is on for new, "potent" adjuvants.

Just about every article on the innate immunity[126] of the newborn, contains comments like these:

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[124] Kucukosmanoglu E et al. 2006. "Frequency of allergic diseases following measles." Allergol Immunopathol (Madr).Jul-Aug;34(4):146-9 full text online: http://www.elsevier.es/revistas/ctl_servlet?_f=7064&ip=203.89.174.146&articuloid=13091040

[125] Brandtzaeg P. 2007. "Induction of secretory immunity and memory at mucosal surfaces." *Vaccine* Jul 26;25(30):5467-84. Epub 2006 Dec 15. PMID 17227687.

[126] Levy O. 2007. "Innate immunity of the newborn: basic mechanisms and clinical correlates." *Nat Rev Immunol.* May;7(5):379-90. PMID: 17457344.

"Finally, as birth is a relatively reliable point of contact with health-care systems worldwide, and therefore vaccines given at birth reach a relatively high proportion of the population, the potential of certain TLR[127] agonists capable of efficiently activating Th1-cell-polarizing responses from neonatal APC's are of substantial interest as novel neonatal vaccine adjuvant."

This concluding paragraph was in the same article as this comment: ***"Overall, the innate immune mechanisms of the neonatal respiratory tract provide protection against microbial infection and prevent over-exuberant inflammation, while mediating the effects of environmental TLR agonists that serve as aeroadjuvants to reduce the atopic potential of aeroallergens."***

What does he think provoking a strong Th1 response to override an immune system designed to prevent over-exuberant responses, might lead to? After all, the authors of a 2008 study[128] reported that ***"consequences of an impaired immune maturation for the onset of autoimmunity are not yet known".***

Interfering specifically to attempt to make a baby's immune system perform like an adult's is diametrically opposed to the programming being followed by neonatal gene expression, which is primarily focussed on inducing tolerance (to stop allergy), and avoiding destructive inflammation. Why does this man, who admits to knowing so little about the immune system, presume it's okay to waltz in there and toss yet another of man's ***"be wise, immunise"*** ideas into a newborn baby?

To me, this is madness. To immunologists, they would like nothing better than to ***"fix all the faults in a baby's immune system"***.

In the meantime, they are ensuring their future jobs with the current generation of highly allergic children, in an era where in comparison with the past, anaphylactic reactions are at almost epidemic proportions. What will the next generation be like?

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[127] TLR = Toll like receptors play an important role in sensing bacterial products and in activating and skewing the immune system.

[128] M'Rabet L et al, 2008. "Breast-Feeding and its Role in Early Development of the Immune system in Infants: Consequences for Health Later in Life *J. Nutr.* 138, 9; Health Module. PMID: 18716187.

In the land of epigenetics, scientists know[129] that: ***"Early negative life events have long been known to have lasting effects on health and disease. Many studies have demonstrated an association between stressful life events in childhood and greater risk for mental illness and other chronic diseases in adulthood."***

How many of you have observed a new generation of children who, the minute they step into a doctor's surgery become frightened, and some of whom have to be literally held down to administer vaccines? Much has been made of parental needle phobia, as a reason some parents don't vaccinate. That never actually occurred to me, for the same reason as it is overlooked by most pro vaccine parents today. After all, what is a moment's hurt, for that supposed "lifetime's peace of mind"?

However, many children and adolescents today, no longer trust the medical profession who are a very real source of fear to them. Might giving vaccines, have serious effects, on both a physiological and stress level? What are the long term ramifications of that? Will needle syndrome result in those children never being able to register a normal blood pressure in a doctor's surgery? Will that then be treated with drugs?

Vaccine defenders will say that the other side of that coin is that sickness (which they say a vaccine might prevent), might do exactly the same thing. That however, is not the norm:

"Studies reported in the last decade demonstrated considerable individual variation in susceptibility to disease. It has been suggested that these individual differences may be at least in part due to predisposition to disease. The origin and nature of these predispositions have not been fully explained. The present data demonstrated that early maternal separation altered the severity and kinetics of the response to influenza viral infection suggesting that environmental conditions during early childhood can serve as a source of vulnerability later in life."[130]

Yet we know predisposition is intimately linked with diet, stress and lifestyle.

[129] Avitsure R, et al., 2006. "Role of early stress in the individual differences in host response to viral infection." *Brain, Behaviour and Immunity* 20. 339-348. PMID 16289758.

[130] Avitsure R, et al., 2006. "Role of early stress in the individual differences in host response to viral infection." *Brain, Behaviour and Immunity* 20. 339-348. PMID 16289758.

At the beginning of this presentation, I quoted Dr Dunbar, the famed American vaccine developer who became a serious vaccine sceptic. Here is a similar quote from 2008[131]:

"…it should be realised that the induction of an immune response against non-harmful common environmental antigens, such as food antigens and particular commensals (bacteria), has to be inhibited lest it give rise to undesirable, excessive, and destructive inflammatory and allergic reactions. It appears that the development of the immune system in neonates and young infants is reflected in the enhancement of "specific" immune responses to danger signals and the induction of tolerance toward common non-harmful environmental antigens such as food components as well as the microbiota of the infant gut. It should be realised that the human immune system can be modulated easily during the first months of life, when it can be affected not only positively but, unfortunately, also negatively.

Today, mothers are told, for instance, that the REASON they must vaccinate their children against measles, is because measles is such a dangerous disease and can maim and kill their children if they don't. That's the mantra of today.

But I would like to end this presentation with comments from the father[132] of the measles vaccine:

Those epidemiologists, and there are many, who tend to revere the biological balance, have long argued that the ecological equilibrium of measles is solidly based, that it cannot readily be disrupted and that therefore we must learn to live with this parasite rather than hope to eradicate it. This speaker, not so long ago, was counted among this group and waxed eloquent on this subject in print….

He went on to talk about the comparative mildness of the disease, with the highest mortality in the 6 to eleven month old (probably bottle fed …) and added:

"Thus in the United States, measles is a disease whose importance is not to be measured by total days disability or number of deaths, but rather by human values and by the fact that tools are becoming available which promise effective control and early eradication.

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[131] M'Rabet L et al, 2008. "Breast-Feeding and It's Role in Early Development of the Immune system in Infants: Consequences for Health Later in Life *J. Nutr.* 138, 9; Health Module. PMID: 18716187.

[132] Langmuir AD, et al. 1962. "The importance of measles as a health problem." *Am J Public Health Nations Health.* Feb;52(2)Suppl:1-4. PMID 14462171.

To those who ask me, "Why do you wish to eradicate measles?," I reply with the same answer that Hillary used when asked why he wished to climb Mt. Everest. He said, "Because it is there."

To this may be added, "... and it can be done."

So I ask you tonight, just because something ***can*** be done, ***should*** it be done?

And should parents be treated like criminals if they decide, after serious deliberation, that their babies are better off remaining vaccine free?

A Cautionary tale.

For many years, a 2002 New Zealand article utilising data from the Dunedin based long term study on children bugged me, and it still does to this day. The children in the 2002 study were born at Queen Mary Hospital Dunedin, between April 1972 and March 1973.

The study[133] discussion said, ***"…breastfeeding for 4 weeks or longer increased the likelihood of skin test responses to common allergens at age 13 years, and more than doubled the risk of diagnosed asthma in mid-childhood, with effects persisting into adulthood…Results of longer-term studies consistently show increased atopy and asthma associated with breastfeeding, even after showing protection in the short term."***

Naturally, this article was used by both medical and lay people to justify the use of formula. There was one thing that no-one in the lay media ever mentioned with regard to this study, even though it was stated in the body of the article:

"***Although many newborns who were breastfed received a nightly formula feed while in hospital to allow the mother to sleep, most had hospital stays of only 3 – 4 days."*** The author went on to say, ***"In our study, most infants were exposed to cow's milk formula in maternity hospital. However, such exposure should not bias our findings, since we recorded more atopy and asthma in those breastfed than in those not."***

[133] Sears, M R et al. 2002. "Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study." *Lancet* 360:901-07. PMID: 12354471.

Nowhere in the references in Sear's 2002 article was an 1988 study[134], which showed that all the children who developed cow's milk allergy during exclusive breast-feeding had been exposed to cow's milk at maternity hospital.

Neither did he mention a 1999 study[135] in which, "***the feeding of CM at maternity hospital increases the risk of CMA when compared with the feeding of other supplements but exclusive breast-feeding does not eliminate the risk."*** In the body of the article it expands on the hospital giving newborn babies formula, and says, ***"…supplementary feeding, most of which contain cow's milk (CM) proteins, may provide an immune reaction and retard gut closure to macromolecules."***

Had he gone further back still to 1978, he would have found a study[136] showing that of babies with circulating immune complexes, only one of the 24 had been breastfed. The study didn't say is hospital staff graciously gave the baby formula. While the study hypothesis that breastfeeding should eliminate resorption of cow's protein, in reality they found that mixed fed babies had as many antibodies to cow's milk as formula fed babies did. The article also suggested that long-term, the result of circulating allergy to cow's milk, could be damage to arterial endothelium, with the result of deposition of lipids and formation of atheroma plate, and arteriosclerosis.
The question needs to be asked, ***"What comes home to roost, when man in his 'wisdom' decides that interference will cause no harm"?***

More recently, a Spanish study again showed that, ***"The consumption of one or two bottles of AF (artificial formula) during the first few days of life is related to the development of IgE-mediated CMA (cow's milk allergy)".***

Remember the study which showed[137] that, ***"Delayed administration of the first dose of DPT of more than 2 months from the recommended 2 month period was associated with***

[134] Host A, et al. 1988. A prospective study of cow's milk allergy in exclusively breast-fed infants, incidence, pathogenetic role of early inadvertent exposure to cow's milk formula and characterization of bovine milk protein in human milk." *Acta Paediatr Scand.* Sep;77(5):663-70. PMID 3201972.
[135] Saarinen, K.D. et al, 1999. "Supplementary feeding in maternity hospitals and the risk of cow's milk allergy: A prospective study of 6209 infants."J Allergy Clin Immunol. Aug;104(2 Pt 1):457-61. PMID: 10452771.
[136] Delire M et al, 1978 "Circulating immune complexes in infants fed on cow's milk." *Nature.* April 13;272(5654)632. PMID 565472.
[137] McDonald, K.L., et al. 2008. "Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma." *J. Allergy Clin Immunol* Mar;112 (3):626-31. Epub Jan 18. PMID: 18207561

a reduced risk of childhood asthma <u>by 50%</u> ... However among children with delays in all 3 doses, the likelihood of asthma was further <u>reduced to 60%."</u> ?

The explanation as to why breastfed babies who receive formula in the first few days of life can go on to develop that allergy has to do with that specific "window" in the immune system, and that child individual epigenetic susceptibility.

If you give a baby cow's milk at the start, "exclusively" breastfeed for a few months, and THEN give cow's milk again, the body may react with an "allergy".

Why don't ***all*** babies fed formula from day one, develop cow's milk allergy?

Because having been given it constantly over that window of vulnerability, they have developed "tolerance" to it.

However, some do develop milk allergy. Why? No one seems to know and no one seems to be in the same hurry to find out, as they are in pointing the finger at breastfeeding.

The function of the gut immune system in the first few months of life is a systematic regular programming which allows a child constant early exposure to those antigens which it must learn will not hurt it, and must develop the ability to tolerate it.

Some might then say that if a baby received supplementary feeds at birth, it must then receive supplementary feeds every day in order that it become tolerant to the cow's milk in that window of time.

I could not find a study which looked at using that method as a corrective treatment to fix the intervention which caused the problem.

Another factor which wasn't known about in the 1970's and is still underappreciated today, is the fact that ***maternal and neonatal zinc deficiency*** will impact seriously on the possibility of any allergy development in both prenatal and neonatal development periods, because, ***"zinc deficiency alters the membrane barrier permeability of endothelial and lung epithelial cells and causes ulcerations of the small intestine… patients with chronic intestinal permeability have been shown to have a reduced level of mucosal zinc… zinc deficiency impairs the membrane permeability, the integrity of the apical junction complexes, and the cytoskeleton organization of the intestinal cells, favoring neutrophil migration through the para cellular spaces."***

I believe that zinc deficiency, as well as other macro and micronutrient deficiencies are very common in New Zealand pregnant women, and probably breastfeeding women as well. Both major and minor nutrient deficiencies can have a serious impact on many aspects of cellular integrity and immunological functioning.

In 2000, an article[138] about foetal and infant immunology said, "***Our current understanding of the postnatal maturation of immune function in man is restricted mainly to comparisons between cells taken from cord blood, as representative of fetal/neonatal life, and those from adults. Knowledge of the kinetics of the changes occurring postnatally, and associated qualitative/ quantitative changes in individual cellular functions is exceedingly sparse.***"

The question that needs to be answered is:

"What happens with regard to asthma susceptibility, when the immune system of a baby is regulated longterm by breast milk the way it should be, without any interference by formula?"

That question has been answered (without reference to vaccines), and the graph[139] below shows the result. Presumably, the sooner a mother stops breastfeeding, or introduces milk, the more likely the child to be susceptible to asthma.

Every month a mother delays introducing any other milk, the risk of asthma reduced yet more.

If a mother wants to lay solid structural and immunological foundations for their child, the essentials are:

1) A good diet, with all macro and micronutrients, pre-pregnancy, during pregnancy, and through lactation.

2) A natural birth with no interference.

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[138] Holt P.G.,et al, 2000. "Allergy Review Series VI: The immunology of fetuses and infants. The development of the immune system during pregnancy and early life." *Allergy* 55: 688-697. PMID: 10955693.

[139] Oddy, W. H.et al, 2004. "The Relation of Breastfeeding and Body mass index to Asthma and Atopy in Children: A Prospective Cohort Study to Age 6 years." *Am J Pub Health.* Sep;94(9):1531-7. PMID: 15333310.

3) Baby straight to breast and a total symbiotic relationship from that point on for at the very least 12 months.

4) And in my opinion, no vaccines.

By that time, the gut will have had a decent chance to assist antigens being processed, the gut processing system will have matured, and the baby will be better prepared to start meeting the real world. Of all the people who have studied breastfeeding, I like Wendy Oddy's work the best. Not because she's a woman but because she asked the right questions, did her homework and designed her studies the right way.

Most other studies that consider breast milk an ecological hazard, appear to have been looking for simple solutions, (or a reason to interfere) and in doing so, miss key confounders, ask the wrong questions and come up with answers which just look very strange. Here is one such comment from the same author[140] who wrote up the Dunedin study:

"The hygiene hypothesis may provide a plausible hypothesis for increased asthma and allergy associated with breastfeeding. Protection from viral infections by breastfeeding may induce a skew in the immune system to a Th-2 dominated profile increasing the risk of atopic disease. If breastfeeding decreases the rates of viral wheezing but increases rates of atopic wheeze, one would expect a higher risk of asthma in later childhood when the atopic phenotype is commonest."

Every article I've read by Sears, comes across to me as passive aggressive double-mindedness. I get the feeling that he doesn't like the current breastfeeding policies and that he'd really like to stop women breastfeeding.

But if his assertions were indeed true, the rates of asthma and allergy in breastfed babies, in the days when there was absolutely no bottle formula, would have been huge, and they were not. Furthermore, in the first half of the 20th century, as shown by Olsen's 1949 monograph, the death rate in bottle fed babies was very high allowing them plenty of autopsy and study material, yet by contrast they had a paucity of autopsy material in the breastfed babies.

[140] Duncan JM and Sears MR. 2008. "Breastfeeding and allergies: time for a change in paradigm?" *Curr Opin Allerg Clin Immunol.* Oct;8(5):398-405. PMID: 18769191.

In pregnancy, birth and breast feeding, when everything is done right with no interference unless there is a serious valid cause, I believe that the step-by-step education plan (orchestrated by gene expression) for a baby's efficient survival, works, and works well. It doesn't need improving upon the master design at all. To consider that a baby's immune system is defective is wrong, and ignores the very gene expression which is now the hallowed epigenetic byword.

Interfere with the process … and there could be lifelong consequences.