The Prophetic Gift Lesson 6 1Q 2009

Testing the Prophets

What is the purpose of the gift of prophecy? God is trying to break through the darkness in our minds and reach us.

Why does God have prophets?

Is prophecy God's preferred method of communication? Why is it necessary?

Read last paragraph Sabbath's lesson, "Although Mrs. White…"

This is significant, EGW never made the claim, others have felt the need to push this idea. EGW was focused on ministering to others God's love and truth to the best of her ability.

First, before we get into the lesson is it important to believe Ellen White was a prophet?

Does the Bible teach that Spiritual things are Spiritually discerned? What does that mean? Doesn't it mean that our carnal minds, without the aide of the Holy Spirit, cannot comprehend the things of God? Then, wouldn't that mean that whoever writes the truth is only able to do so because the Holy Spirit enlightened their minds?

If Billy Graham speaks or writes the truth who enabled Him? Max Lucado? You, your pastor or Ellen White? To the degree someone presents the truth about God they are only able to do so because of the enlightenment of the Holy Spirit.

Is the truth spoken by a prophet any purer than the truth spoken by a church member, teacher, preacher, lay leader?

So the question as we will see, the only truly important question is, is the person speaking truth?

SUNDAY

How did God speak to prophets? Dreams and visions, was this God's preferred method?

Read second paragraph "During her…"

Thoughts? Some have suggested Ellen White had a seizure disorder called Temporal Lobe Epilepsy and it is this neurological disorder which has accounted for her visions and dreams.

In temporal lobe epilepsy (TLE) the following can occur:

- Often occurs after a head injury
- Alteration of consciousness
- Starring off into space
- Stereotypic movements, lip smacking, posturing, rigidity
- Complete unawareness of surroundings
- Non-responsiveness to any external stimuli including pain
- Hallucinations of various kinds, visual, auditory
- Excessive religious preoccupation
- Hypergraphia – writing profusely
- Often has an aura
- Typically lasts less than two to three minutes
- Breathing may be extremely shallow or even absent, but only for a few seconds or less than a minute
- Several minutes of confusion after the seizure is over

Thoughts?

- Symptoms of TLE vary widely from person to person but the same person only has a few symptoms that repeat over and again with each seizure
- TLE does not increase IQ, creativity, insight, wisdom, or provide any new information. During a seizure neural

circuits of the brain fire and thus one experiences only events, memories or knowledge already contained in their data base. No new information has ever been discovered during a seizure
- The movements in TLE are purposeless and repetitive
- The hypergraphia of TLE is not creative but repetitive and often meaningless, repeating a verse over and over again hundreds of times, long lists of irrelevant items. I had a patient with TLE and she had journals and journals of different material. Her handwriting changed throughout and the subject matter jumped all over the place with no organization or reason.

Thoughts?

EGW's writings demonstrate clear organization, insight, wisdom and truth consistent with scripture. Therefore, her writings are not products of a seizure disorder.

What about reported physical phenomenon that accompanied the visions of Ellen White?

- Did not breathe for over an hour, examined by physicians, no cyanosis
- Supernatural strength
- Unaware of her surroundings

Are these good reasons to believe anything she wrote? Why or why not?

Are these proof she had the genuine prophetic gift? Why or why not?

Supernatural signs and wonders can be counterfeited and thus are not good evidence to determine whether someone is from God or not.

Moses threw his staff down and it became a serpent and so did Janis and Jambres the sorcerers of pharaoh.

Satanic agencies have the ability to perform supernatural feats, strength etc yet this doesn't prove a message from such a person is true.

MONDAY

Agreement with the Bible

A test of a true prophet is that their writings always agree with the Bible – notice this written by EGW:

> The Lord designs to warn you, to reprove, to counsel, through the testimonies given, and to impress your minds with the importance of the truth of His Word. The written testimonies are not to give new light, but to impress vividly upon the heart the truths of inspiration already revealed. Man's duty to God and to his fellow man has been distinctly specified in God's Word; yet but few of you are obedient to the light given. Additional truth is not brought out; but God has through the Testimonies simplified the great truths already given and in His own chosen way brought them before the people to awaken and impress the mind with them, that all may be left without excuse. {FLB 295.5}

What does it sound like she says her writings were to do? A children's Bible commentary, making the Bible easier to understand but not presenting new truths.

> You must bring your creed to the Bible and let the light of the Bible define your creed and show where it comes short and where the difficulty is. The Bible is to be your standard, the living oracles of Jehovah are to be your guide. FW 77

> Let the Testimonies be judged by their fruits. What is the spirit of their teaching? What has been the result of their influence? "All who desire to do so can acquaint

> themselves with the fruits of these visions. . . ." This work is of God, or it is not. God does nothing in partnership with Satan. My work . . . bears the stamp of God or the stamp of the enemy. There is no halfway work in the matter. The Testimonies are of the Spirit of God, or of the devil." {FLB 296}

Thoughts? What do you notice about her attitude? Think for yourself, examine the evidence, come to your own conclusion, don't believe because someone says to, don't believe because of supernatural signs. Do you like this approach?

What evidence can we look to? How about testable things she wrote?

> What the parents are, that to a great extent the children will be. The physical conditions of the parents, their dispositions and appetites, their mental and moral tendencies, are to a greater or less degree reproduced in their children.
>
> The nobler the aims, the higher the mental and spiritual endowments, and the better developed the physical powers of the parents, the better will be the life equipment they give their children. In cultivating that which is best in themselves, parents are exerting an influence to mold society and to uplift future generations....
>
> Through the indulgence of appetite and passion their energies are wasted, and millions are ruined for this world and for the world to come. Parents should remember that their children must encounter these temptations. Even before the birth of the child, the preparation should begin that will enable it to fight successfully the battle against evil.
>
> Especially does responsibility rest upon the mother. She, by whose lifeblood the child is nourished and its physical frame built up, imparts to it also mental and spiritual influences that tend to the shaping of mind and character.--MH 371, 372 (1905).

Thoughts?

Science has now documented that the choices we make, the foods we eat, the activities we engage in result in changes in our DNA expression. This is called epigenetic changes. Chemical groups called methyl groups attached to DNA regions modifying how genes are expressed and these modifications which occur during our lifetime are passed along to our children. Thus, EGW was correct. How could she know this 100 years before science revealed it to be true? Good guess? (See articles at end of notes)

Other examples of scientific truth revealed before its time?

- Tobacco was prescribed by doctors in her day for lung disease, she warned of its damaging effects
- She warned that meat eating increases cancer when everyone thought meat and potatoes was the best diet to eat
- She warned of "cancerous germs" now science has documented various viruses cause cancer HPV, it wasn't until the 1980's that HPV was discovered to cause cervical cancer

How could a woman with a third grade education write counsels on health so accurately that went against the scientific knowledge of her time?

Read first paragraph Monday – thoughts?

What does the test of a prophet apply to? Does it apply to everything the prophet says, does or writes?

What if a prophet gets a message from God that contradicts a message previously sent by God? What then?

- Did Abraham get a message from God to sacrifice Isaac? Did he later get a message contradicting that?

- Did Balaam get a message from God not to go with the pagan emissaries? Did he later get a message to go?

- Did Jonah get a message that God was going to destroy Nineveh? Did God do something different?

- Did God tell the Israelites through Samuel, no kings? Did God through Samuel pick their first two kings?

What is the point? Does God ever say, “Stop thinking, become mindless robots and do what you are told?” Or does God want each of us to think for ourselves, even when a message comes from a prophet, and come to our own conclusion?

What is more important than being able to tell who is a prophet from God and who is not a prophet of God? Becoming a friend of God so that you can learn to think for yourself and discern the right from the wrong. So that even if an angel from heaven comes with another message you won’t be deceived.

In the end of time when Satanic delusion reaches a crescendo only those who have developed the ability to think for themselves and weigh the evidence will be safe from being drawn into the power of the lie.

Read bottom green question – thoughts?

What is it that makes someone or something ultimately authoritative? The truth itself!

TUESDAY

Read second paragraph, “The fulfillment…” thoughts?

I am not a Hebrew scholar but it struck me that words can have multiple meanings. Overthrow could merely refer to physical destruction and overthrow, but could also refer to a

overthrow of nature, heart, motive etc. i.e conversion or repentance.

I wondered if the Hebrew would support this possibility.

From The Dictionary of Biblical Languages:

> **200** הָפַךְ (*hā·pǎḵ*): v.; ≡ Str 2015; TWOT 512—**1.** LN 20.31-20.60 (qal) **overthrow**, i.e., to cause ruin as an extension of flipping over an object (Ge 19:21); (qal pass.) **be destroyed**, formally, overturned (La 4:6+); **2.** LN 13.48-13.68 (qal) **change**, turn into, i.e., change the essential form or nature of something (Lev 13:3); (nif) **change**, transformed, be turned into (Ex 7:15); **3.** LN 25.223-25.250 (nif) **be disturbed**, i.e., have great feelings of distress which are difficult to control as an extension of the chaotic flipping over of an object[1]

From Enhances Strong's Lexicon:

> **2015** הָפַךְ [*haphak* /haw·**fak**/] v. A primitive root; TWOT 512; GK 2200; 94 occurrences; AV translates as "turn" 57 times, "overthrow" 13 times, "overturn" five times, "change" three times, "turn …" six times, "become" once, "came" once, "converted" once, "gave" once, "make" once, "perverse" once, "perverted" once, "retired" once, and "tumbled" once. **1** to turn, overthrow, overturn. 1A (Qal). *1A1* to overturn, overthrow. *1A2* to turn, turn about, turn over, turn around. *1A3* to change, transform. 1B (Niphal). *1B1* to turn oneself, turn

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v. verb
Str *Strong's Lexicon*
TWOT *Theological Wordbook of the Old Testament*
LN *Louw-Nida Greek-English Lexicon*
qal *Qal*
pass. passive
+ I have cited every reference in regard to this lexeme discussed under this definition.
nif *Niphal*

[1]Swanson, James: *Dictionary of Biblical Languages With Semantic Domains : Hebrew (Old Testament)*. electronic ed. Oak Harbor : Logos Research Systems, Inc., 1997, S. DBLH 2200, #3
v **v**: verb
TWOT Theological Wordbook of the Old Testament
GK Goodrick-Kohlenberger
AV Authorized Version

> back. *1B2* to change oneself. *1B3* to be perverse. *1B4* to be turned, be turned over, be changed, be turned against. *1B5* to be reversed. *1B6* to be overturned, be overthrown. *1B7* to be upturned. 1C (Hithpael). *1C1* to transform oneself. *1C2* to turn this way and that, turn every way. 1D (Hophal) to turn on someone.

Could it be possible that the prophecy of Jonah meant more than just physical destruction? Was God moving to reach the people of Nineveh for salvation? Is it possible that Nineveh was not overturned physically because they were overturned spiritually?

WEDNESDAY

Read second paragraph – thoughts? What purpose did Jesus take humanity upon Himself?

> "In assuming human nature, that he might reach to the very depths of human woe and misery and lift man up, Christ has shown what estimate he places upon the human race. In this work everything was at stake. Satan claimed to be the lawful owner of the fallen race; and with what persistent effort did he seek to overthrow Christ through his subtilty! It was only by the most desperate conflict with the powers of Satan that Christ could accomplish his **purpose of restoring the almost obliterated image of God in man, and place his own signature upon his forehead.** It was a desperate battle; for Satan had so long worked in league with human intelligencies as to almost completely intercept every ray of light shining from the throne of God upon the human mind. The cross of Calvary alone could destroy the works of the devil. In that wondrous sacrifice all eyes were called to 'behold the Lamb of God, which taketh away the sin of the world.' The love of Christ kindles in the heart of all who continue to behold him. {General Conference Daily Bulletin, March 2, 1897 par. 17}

Do you hear the uplifting of Jesus Christ as our Savior?

THURSDAY

Read first paragraph – thoughts?

Might the picture of God one presents make a difference? Would the fruits of the life and the outcome of health depend on the type of God one believes in?

- Extrinsic religiosity was a significant predictor of child abuse potential
- Intrinsic religiosity was not (Dyslin & Thomsen, 2005)
- Physical abuse has a negative relationship with spiritual development, but not with religiosity (Webber & Cummings, 2003)
- Religion without knowing God results in greater abuse of children
- A 1996 study of 596 hospitalized elderly patients found those who believed in a punishing God were more likely to have died two years later than those who believed in a more loving God.

Thoughts?

FRIDAY questions 1 and 3 read and discuss

Rewriting Darwin: The new non-genetic inheritance

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Emma Young

HALF a century before Charles Darwin published *On the Origin of Species*, the French naturalist Jean-Baptiste Lamarck outlined his own theory of evolution. A cornerstone of this was the idea that characteristics acquired during an individual's lifetime can be passed on to their offspring. In its day, Lamarck's theory was generally ignored or lampooned. Then came Darwin, and Gregor Mendel's discovery of genetics. In recent years, ideas along the lines of Richard Dawkins's concept of the "selfish gene" have come to dominate discussions about heritability, and with the exception of a brief surge of interest in the late 19th and early 20th centuries, "Lamarckism" has long been consigned to the theory junkyard.

Now all that is changing. No one is arguing that Lamarck got everything right, but over the past decade it has become increasingly clear that environmental factors, such as diet or stress, can have biological consequences that are transmitted to offspring without a single change to gene sequences taking place. In fact, some biologists are already starting to consider this process as routine. However, fully accepting the idea, provocatively dubbed the "new Lamarckism", would mean a radical rewrite of modern evolutionary theory. Not surprisingly, there are some who see that as heresy. "It means the demise of the selfish-gene theory," says Eva Jablonka at Tel Aviv University, Israel. "The whole discourse about heredity and evolution will change" (see "Rewriting Darwin and Dawkins?").

That's not all. The implications for public health could also be immense. Some researchers are talking about a paradigm shift in understanding the causes of disease. For example, non-genetic inheritance might help explain the current obesity epidemic, or why there are family patterns for certain cancers and other disorders, but no discernible genetic cause. "It's a whole new way of looking at the inheritance and causes of various diseases, including schizophrenia, bipolar disorder and diabetes, as well as cancer," says Robyn Ward of the cancer research centre at the University of New South Wales in Sydney, Australia.

Lamarck's ideas about exactly how non-genetic inheritance might work were woolly at best. He wrote, for example, of the giraffe's neck becoming elongated over generations because of the animal's habit of stretching up to feed on leaves in high treetops. The recent research, by contrast, has a firm basis in biological mechanisms - in so-called "epigenetic" change.

Epigenetics deals with how gene activity is regulated within a cell - which genes are switched on or off, which are dimmed and how, and when all this happens. For instance, while the cells in the liver and skin of an individual contain exactly the same DNA, their specific epigenetic settings mean the tissues look very different and do a totally different job. Likewise, different genes may be expressed in the same tissue at different stages of development and throughout life. Researchers are a long way from knowing exactly what mechanisms control all this, but they have made some headway.

Inside the nucleus, DNA is packaged around bundles of proteins called histones, which have tails that stick out from the core. One factor that affects gene expression is the pattern of chemical modifications to these tails, such as the presence or absence of acetyl and methyl groups. Genes can also be silenced directly via enzymes that bind methyl groups onto the DNA. The so-called RNA interference (RNAi) system can direct this activity, via small RNA strands. As well as controlling DNA methylation and modifying histones, these RNAi molecules target messenger RNA - much longer strands that act as intermediaries between DNA sequences and the proteins they code for. By breaking mRNA down into small segments, the RNAi molecules ensure that a certain gene cannot be translated into its protein. In short, RNAi creates the epigenetic "marks" that control the activity of genes.

We know that genes - and possibly also non-coding DNA - control RNAi and so are involved in determining an individual's epigenetic settings. It is becoming increasingly apparent, though, that environmental factors can have a direct impact too, with potentially life-changing implications. The clearest example of this comes from honeybees. All female honeybees develop from genetically identical larvae, but those fed on royal jelly become fertile queens while the rest are doomed to life as sterile workers. In March this year, an Australian team led by Ryszard Maleszka at the Australian National University in Canberra showed that epigenetic mechanisms account for this. They used RNAi to silence a gene for DNA methyltransferase - an enzyme necessary for adding methyl groups to DNA - in honeybee larvae. Most of these larvae emerged as queens, without ever having tasted royal jelly (*Science*, DOI: 10.1126/science.1153069).

"All female honeybees, including queens, develop from genetically identical larvae"

For honeybees then, what they eat during early development creates an epigenetic setting that has fundamental lifelong implications. This is an extreme example, but researchers are starting to realise that similar mechanisms are at play in other animals, and even in humans. And, as for honeybees, it seems there is a critical early period during which an individual's pattern of gene expression is "programmed" to a large extent. Environmental factors can feed into this programming, possibly with long-term health impacts.

In 2000, Randy Jirtle at Duke University in Durham, North Carolina, led a ground-breaking experiment on a strain of genetically identical mice. These mice carried the *agouti* gene, which makes them fat and prone to diabetes and cancer. Jirtle and his student Robert Waterland gave one group of females a diet rich in methyl groups before conception and during pregnancy. They found that the offspring were very different to their parents - they were slim and lived to a ripe old age. Though the pups had inherited the damaging *agouti* gene, the methyl groups had attached to the gene and dimmed its expression.

Jirtle then tried supplementing the diets of pregnant *agouti* mice with genistein, an oestrogen-like chemical found in soya. The dose was designed to be comparable to the amount consumed by a person on a high-soya diet, which is associated with a reduced risk of cancer and less body fat. These mice were also more likely to give birth to slim, healthy offspring which had less chance of becoming obese in adulthood. This change was associated with increased methylation of six DNA base-pair sites involved in regulating activity of the *agouti* gene.

These and other animal studies strongly suggest that a pregnant woman's diet can affect her child's epigenetic marks. So perhaps it is not surprising that the effect of certain nutrients is being called into question. Folate, for example, is a potent methyl donor. It is routinely recommended during pregnancy and added to cereal products in certain countries, including the US, because it reduces the risk of spinal tube defects if eaten around the time of conception. But Jirtle wonders whether it could also be inducing as-yet-unknown, damaging epigenetic effects.

The legacy of stress

Diet is not the only environmental factor that can influence the epigenetic setting of some genes. Michael Meaney at McGill University in Montreal, Canada, and colleagues have found that newborn mice neglected by their mothers are more fearful in adulthood - and that these mice show much higher than normal levels of methylation of certain genes involved in the stress response. On a brighter note, these mice also point the way to a possible way to reverse epigenetic changes (see "In sickness and in health").

In humans, too, there are troubling hints that damaging experiences early in life, while the brain is still developing, can affect epigenetic settings, perhaps with catastrophic consequences. In May, Meaney and his colleagues reported a study of 13 men who had committed suicide, all of whom had been victims of child abuse. They showed clear epigenetic differences in their brains, compared with the brains of men who had died of other causes. It is possible that the changes in epigenetic marks were

caused by the exposure to childhood abuse, says the team. Could the changes have contributed to their suicides too?

There is recent evidence that abnormal epigenetic patterns play a role in mental health disorders. In March, Arturas Petronis at the Centre for Addiction and Mental Health in Toronto, Canada, and colleagues reported the first epigenome-wide scan of post-mortem brain tissue from 35 people who had suffered from schizophrenia. They found a distinctive epigenetic pattern, controlling the expression of roughly 40 genes (*The American Journal of Human Genetics*, vol 82, p 696). Several of the genes were related to neurotransmitters, to brain development and to other processes linked to schizophrenia. These findings lay the groundwork for a new way of understanding mental illness, says Petronis, as a disease with a significant epigenetic component.

“These findings lay the groundwork for a new way of understanding mental illness”

As with the people who had committed suicide in Meaney's study, these epigenetic marks may have arisen during development. Yet there are also hints that the people with schizophrenia might instead have inherited them from their parents - and that they in turn might pass the marks on to their own children. In theory, epigenetic marks are wiped clear between generations in mammals. Intriguingly, though, the abnormalities in DNA methylation in Petronis's subjects were not restricted to their frontal cortex: they were also present in their sperm. "[This] suggests that it is possible that inherited epigenetic abnormalities may be contributing to the familial nature of schizophrenia and bipolar disorder," says team member Jonathan Mill at the Institute of Psychiatry at King's College London.

This work is only suggestive, but when it comes to cancer, the evidence is stronger. Some colorectal cancers are known to develop when a key DNA-repair gene called *MHL1* becomes coated in methyl groups, preventing it from working. In 2007, Ward and her colleagues published a study of a woman with this type of cancer and her three children. The *MHL1* gene was active in two of the children, but one son had a heavily methylated, silenced gene like his mother (*The New England Journal of Medicine*, vol 356, p 697).

The paper caused a sensation among cancer researchers because it suggested an entirely new way in which disease risk might be inherited. Of course the finding could have been a coincidence, or the son might have inherited a genetic propensity to methylation of this gene, rather than the epigenetic mark itself. Since the paper came out, though, direct inheritance is starting to look more likely. Other teams have identified similar families, and in all cases the effect seems to be transmitted down the maternal line via the egg. The *MHL1* gene in the sperm of affected men appears normal.

Some epigenetic marks may also be inherited from fathers, however. In a now classic study published in 2005, Matthew Anway at the University of Idaho in Moscow and colleagues showed that male rats exposed to the common crop fungicide vinclozolin in the womb were less fertile and had a higher than normal risk of developing cancer and kidney defects. Not only were these effects transmitted to their offspring, they were passed from father to son through the three following generations as well (*Science*, vol 308, p 1466). The team found no DNA changes, only altered DNA methylation patterns in the sperm of these rats, suggesting that epigenetic factors were to blame.

The following year, a team at the University of Maryland in Baltimore found that male mice that had inhaled cocaine passed memory problems onto their pups. Again, their sperm showed no apparent DNA damage, but in the seminiferous tubules, where sperm are produced, the researchers found changes in the levels of two enzymes involved in methylating DNA.

In people, too, there is evidence that environmental impacts on fathers and mothers can produce changes in their children. This has led some researchers to consider a startling possibility. Could the current epidemic of type II diabetes and obesity in developed countries be related to what our parents and our grandparents ate?

“Could the current epidemic of obesity be related to what our parents and grandparents ate?”

Nutrition does seem to have some lasting effect, according to a study by Marcus Pembrey of the Institute of Child Health at University College London and his colleagues. They analysed records from the isolated community of Överkalix in northern Sweden and found that men whose paternal grandfathers had suffered a shortage of food between the ages of 9 and 12 lived longer than their peers (*European Journal of Human Genetics*, vol 14, p 159). A similar maternal-line effect existed for women, but in this case by far the biggest effect on longevity of the granddaughters occurred when food was limited while grandmothers were in the womb or were infants. It would appear that humans thrive on relatively meagre rations, and the team concluded that under these conditions some sort of key information - perhaps epigenetic in nature - was being captured at the crucial stages of sperm and egg formation, then passed down generations.

Pembrey's team also looked at more recent records from the UK, collected for the Avon Longitudinal Study of Parents and Children. They identified 166 fathers who reported starting smoking before the age of 11 and found that their sons - but not their daughters - had a significantly higher than average body mass index at the age of 9.

Also in 2006, Tony Hsiu-Hsi Chen at the National Taiwan University in Taipei and colleagues reported that the offspring of men who regularly chewed betel nuts had twice the normal risk of developing metabolic syndrome during childhood. Betel nuts are also associated with several symptoms of metabolic syndrome in chewers including increased heart rate, blood pressure, waist size and body weight.

The mother's nutrition might affect a child's risk of obesity, too. Women in the Netherlands who were in the first two trimesters of pregnancy during a famine in 1944 and 1945 gave birth to boys who, at 19, were much more likely to be obese.

All these results raise an important question. Why should factors like food intake or smoking around the time sperm or eggs are created, or at the embryo stage, have such an influence on a child's metabolism and weight?

Extended periods of too much or too little food might trigger a switch to a pattern of gene expression that results in earlier puberty and so earlier mortality, says Pembrey - and this might be heritable. "The reason why some people gain weight more easily is because their metabolic genes are used differently," says Reinhard Stöeger at the University of Washington in Seattle. He suggests that long before the emergence of modern humans, a network of metabolic genes evolved that was honed for a relative scarcity of food, but not feast or famine. "These genes have become epigenetically programmed during the early stages of life in response to adverse environmental conditions - such as feast. This might explain the current epidemic of type II diabetes and obesity in the west, where food is plentiful." Prolonged epigenetic silencing in response to the environment might also lead to a DNA change that "locks in" epigenetic marks, Stöeger suggests.

Out of the melting pot of recent findings, a host of fundamental questions are now being thrown up. If what we eat could affect our grandchildren, should we be more careful? If so, in what ways? Should we be more concerned about the long-term impact of war or child abuse? Could we choose a diet to reduce our own cancer risk, and that of our children? We are only starting to get an inkling about how to answer these, but one thing is clear: genes are only part of the story.

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From issue 2664 of New Scientist magazine, 09 July 2008, page 28-33

Rewriting Darwin and Dawkins?

The realisation that individuals can acquire characteristics through interaction with their environment and then pass these on to their offspring may force us to rethink evolutionary theory. While examples of this "transgenerational epigenetic inheritance" are only just emerging in mammals, there is long-standing and widespread evidence for it in plants and fungi. That may explain why botanists are much more ready to acknowledge and promote the idea that epigenetic inheritance has a significant role in evolution, whereas zoologists are generally reluctant to do so, says Eva Jablonka from Tel Aviv University, Israel.

That looks set to change. "There was a trickle of findings of epigenetic inheritance in animals through the 20th century, and it is turning into a flood about now," says Russell Bonduriansky, at the University of New South Wales in Sydney, Australia. One of his favourite recent examples involves the water flea, daphnia. When predators are around, the fleas develop large, defensive spines. If they then reproduce, their offspring also develop these spines - even when not exposed to predators.

For Bonduriansky, this suggests a possible adaptive function of epigenetic inheritance - the fine-tuning of an individual to short-term variations in its environment. "There's no lag time for the offspring to respond to the environment on their own," he says.

The idea that epigenetic variation could be adaptive - rather than a form of random, non-directed variation - is very controversial, harking back as it does to the discredited theory of Lamarckian evolution. Nevertheless, this has not deterred some researchers from exploring the full implications of epigenetic inheritance.

For example, there is evidence that epigenetic changes can affect mate preference. Last year, David Crews and Andrea Gore at the University of Texas at Austin published a study of male rats whose great-grandfathers had been exposed to the fungicide vinclozalin. Previous research has revealed that such exposure leads to increased infertility and higher risks of cancer even four generations later. Crews and Gore found that female rats tended to avoid these males. They could sense something was wrong, says Gore. The females seemed to select mates on the basis of an epigenetic pattern, as opposed to a genetic difference, she adds.

Back to the future

For Bonduriansky the accumulating evidence calls for a radical rethink of how evolution works. Jablonka, too, believes that "Lamarckian" mechanisms should now be integrated into evolutionary theory, which should focus on mechanisms, rather than units, of inheritance. "This would be very significant," she says. "It would reintroduce development, in a very direct and strong sense, into heredity and hence evolution. It would mean the pre-synthesis view of evolution, which was very diverse and very rich, can return, but with molecular mechanisms attached."

That needn't necessarily mean an end to the idea of the gene as the basic unit of inheritance, or Richard Dawkins's selfish gene, according to some. "I don't think it violates the basic concept that Dawkins articulated," says Eric Richards, at Washington University in St Louis, Missouri. "Epigenetic marks can also be viewed as part of that basic unit in a more inclusive definition of a gene," he says.

What does Dawkins himself think? "The 'transgenerational' effects now being described are mildly interesting, but they cast no doubt whatsoever on the theory of the selfish gene," he says. He suggests, though, that the word "gene" should be replaced with "replicator". This selfish replicator, acting as the unit of selection, does not have to be a gene, but it does have to be replicated accurately, the occasional mutation aside. "Whether [epigenetic marks] will eventually be deemed to qualify as 'selfish replicators' will depend upon whether they are genuinely high-fidelity replicators with the capacity to go on for ever. This is important because otherwise there will be no interesting differences between those that are successful in natural selection and those that are not." If all the effects fade out within the first few generations, they cannot be said to be positively selected, Dawkins points out.

In sickness and in health

Epigenetic abnormalities have been found in nearly every type of cancer and in other diseases, such as cardiovascular disease. But the discovery that diseases can be caused by environmental factors influencing the expression of genes has an upside. "The beauty of any epigenetic modification is that it is reversible by drugs," says Robyn Ward from the University of New South Wales in Sydney, Australia.

Take the epigenetic marks acquired by mice as a result of maternal neglect during infancy. Here, methyl groups become attached to genes involved in the stress response, resulting in heightened anxiety. But, using drugs, Michael Meaney at McGill University in Montreal, Canada, and his team have reversed the methylation of these genes and their associated behavioural responses in adulthood (*Journal of Neuroscience*, vol 25, p 11045). They injected the drugs directly into the brain although it is possible that a special diet could do the same trick, Meaney says.

NEW ROLE FOR OLD DRUGS

Other drugs that influence methylation are now in early-stage anti-cancer trials. Some of them are not new, but are being reassessed in the light of new knowledge about how they work. Azacytidine, for example, which was used years ago with limited success to treat a range of bone-marrow stem-cell disorders, is undergoing trials again on these very same disorders. Now that it has become clear the drug induces epigenetic changes, researchers are altering doses and redesigning trials with the aim of activating tumour-suppressor genes that have been silenced by methylation.

This approach does have a major drawback - epigenetic drugs are not specific. Side effects, such as nausea and diarrhoea, are probably down to their broad range of action, says Ward. It might be possible to target drugs more specifically, but that is a very long way off. Still, the fact that it offers a whole new way of treating disease leads many to consider the epigenetics approach to be very promising.

You are what your mother ate

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WHETHER or not some of your genes are active may depend on what food supplements your mother took.

That is the implication of an intriguing study in mice. The coat colour of offspring was changed by simply giving females extra doses of four common nutrients, including folic acid and vitamin B12. The offspring were also less prone to obesity and diabetes than genetically identical mice whose mothers had not been given supplements. The differences were due to heritable changes in the activity of at least one gene in the offspring.

It is not yet clear if the same phenomenon occurs in people. If it does, what women eat during the formation of the egg and early embryo, including supplements, could have an even more profound effect than anyone thought. Changes in gene activity could make their descendants more or less likely to suffer from a range of disorders, including obesity, cancer, diabetes and possibly even autism.

Many people think that there is no downside to food supplements, says the senior researcher, Randy Jirtle of Duke University Medical Center in Durham, North Carolina. "But there could be a lifelong downside and we have no clue yet what those effects are."

His team's work establishes the tightest link yet between diet and a strange form of inheritance known as epigenetics: characteristics passed on to offspring that cannot be explained by changes in the DNA

sequence. Scientists have long been intrigued by possible epigenetic effects. For example, Dutch women who went hungry during the second world war unsurprisingly gave birth to small babies. These children had normal diets most of their lives, yet when they had children of their own, they too were undersized.

While such cases remain controversial, several mechanisms have since been discovered that can explain epigenetic inheritance. For instance, adding tags known as methyl groups to DNA - a chemical change that does not alter the underlying sequence - can switch off a gene. These methylation marks can be passed to future generations, and experiments in mice have shown that various factors can alter them, including certain drugs, viral infections and the way an embryo is handled during IVF.

Jirtle and his colleague Robert Waterland wondered whether even subtle differences in diet could affect methylation. To find out, they used a mouse strain in which the activity of a gene called agouti, which establishes coat colour, is controlled by the degree of methylation. The more the gene is methylated, the less agouti activity there is and the browner the coat becomes.

The team fed female mice either a normal diet or a diet supplemented with choline and betaine as well as folic acid and vitamin B12. Sure enough, the vitamin-enriched mums were more likely to give birth to pups with browner coats, and chemical analysis showed the agouti gene was more highly methylated (Molecular and Cellular Biology, vol 23, p 5293). Because agouti also affects other aspects of metabolism, the brown mice are less prone to obesity and diabetes.

"It's a very important result," says Emma Whitelaw of the University of Sydney in Australia, whose team helped prove that epigenetic effects really can determine an offspring's traits (New Scientist, 13 November 1999, p 16). "It establishes a close link between diet, methylation and gene activity, which is going to lead to some interesting experiments." But she is not convinced the results have any immediate relevance to humans.

While Jirtle's group plans to look for similar dietary effects in people, Whitelaw points out that the agouti gene is very unusual. It is not clear if there are equivalents in humans, she says.

But Jirtle's team already has unpublished mouse data suggesting that early nutrition can also alter the methylation of "imprinted genes". These are genes where one of the two parental copies must be turned off for normal development. Incorrect methylation of imprinted human genes is known to cause certain diseases and can contribute to the development of cancer. If nutrition affects imprinted genes in people, it might even explain the rise in some disorders. "People ask themselves why autism is going up, why asthma is going up," says Jirtle. "Is something as subtle as this going to be the cause?"

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