VITABIOTICS
SCIENCE OF HEALTHY LIVING

Fertility & Prenatal Nutrition

- Mr Michael Dooley MMs FFSRH FRCOG
- Consultant Gynaecologist
- Poundbury Clinic – September 2021

Pregnacare

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Fertility Facts

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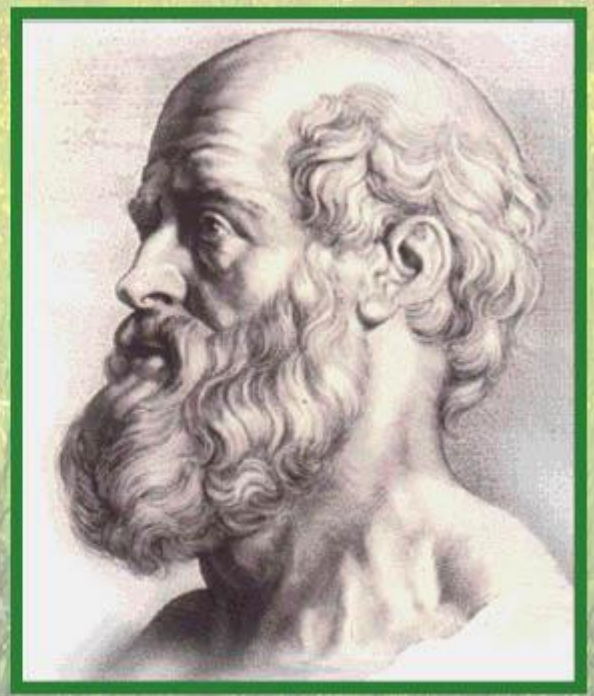
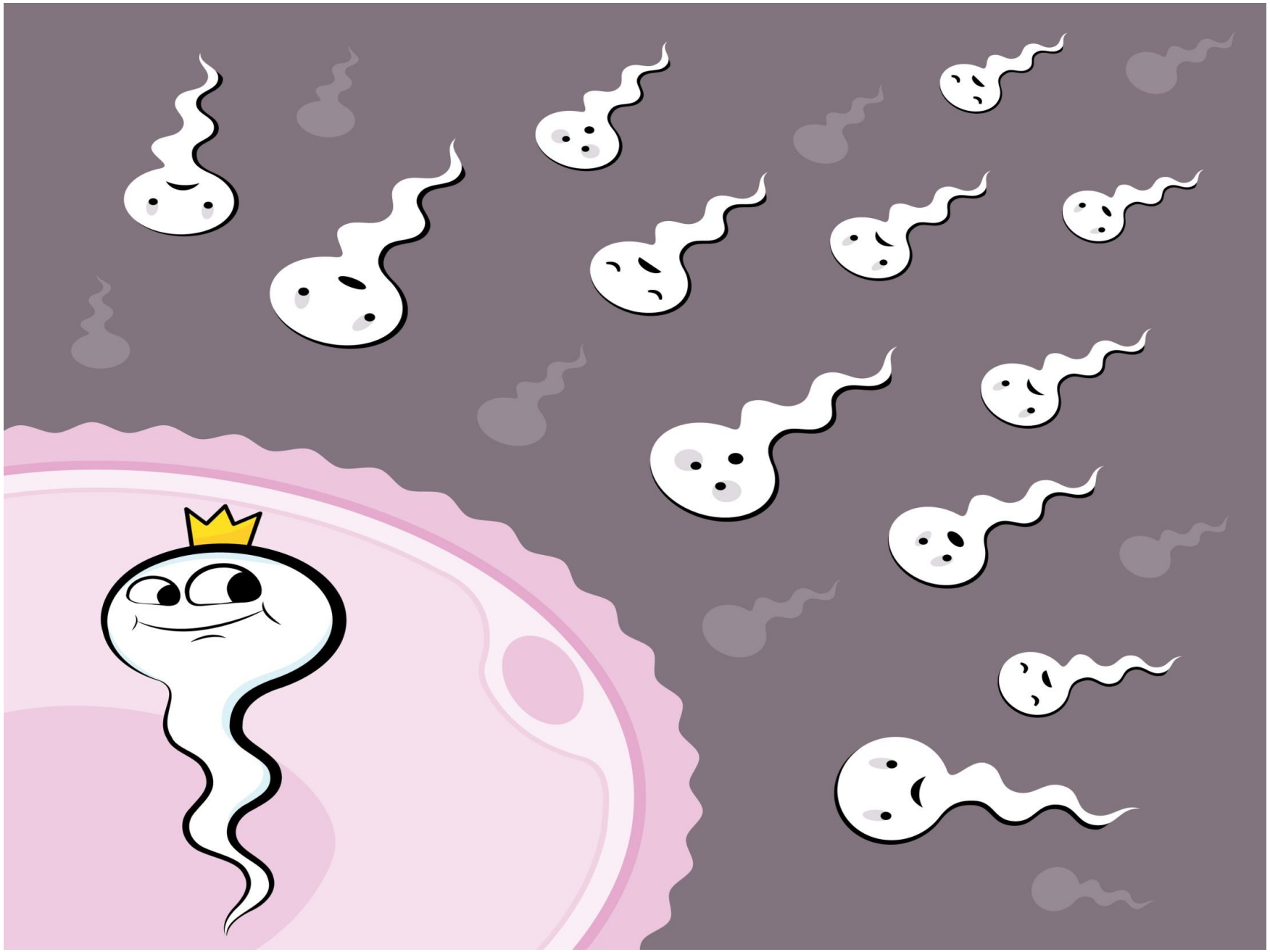
Nature is the Healer of Disease

Hippocrates (460 - 370 BC)



Conception is a story of transport



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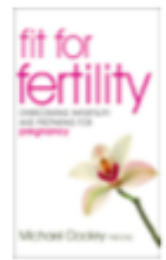


Fit For Fertility

Fit for fertility Checklist

By looking at the* Fit For Fertility Checklist *together, you and your partner may quickly be able to pinpoint areas in your heath and lifestyle that could be affecting your chances of becoming pregnant. If you have answered 'yes' to one or more of the questions, then it is possible that this factor/s affecting your chances of conceiving. Make an appointment to see your GP so that you can discuss things further.

The Egg:

1) Are you having irregular, short (less than 21 days) or long (greater than 34 days) periods? *Yes/No*

2) Do you bleed between periods? *Yes/No*

3) Are you overweight (with a body mass index greater than 25) or are you underweight (with a body mass index under 18.5)? *Yes/No*

4) Are you over 35 years old? *Yes/No*

5) Do you exercise excessively? *Yes /No*

6) Have you had treatment for cancer? *Yes/No*

7) Are you being treated for depression? *Yes/No*

8) Do you have diabetes? *Yes/No*

9) Have you ever had thyroid problems? *Yes/No*

10) Have you ever stopped having periods? *Yes/No*

The Sperm:

1) Have you ever had an operation on your testicles? *Yes/No*

2) Have you had a hernia repair? *Yes/No*

3) Is there blood in your ejaculate? *Yes/No*

4) Have you had mumps? *Yes/No*

5) Have you had an injury to your testicles? *Yes/No*

6) Have you got or have you had any relations with cystic fibrosis? *Yes/No*

7) Have you had a vasectomy? *Yes/No*

8) Are you overweight (with a body mass index over 25)? *Yes/No*

9) Are you taking medication for a peptic ulcer? *Yes/No*

10) Do you have diabetes? *Yes/No*

Can the two get together? (Female)

1) Do you have intercourse less than twice a week? *Yes/No*

2) Do you have a problem with intercourse? *Yes/No*

3) Do you bleed after intercourse? *Yes/No*

4) Do you have pain with intercourse? *Yes/No*

5) Does your partner have problems with erection? *Yes/No*

6) Does your partner have premature ejaculation? *Yes/No*

7) Have you had pelvic inflammatory disease? *Yes/No*

8) Have you had an operation on your abdomen (e.g. a burst appendix or a laparoscopy)? *Yes/No*

9) Do you have a discharge? *Yes/No*

10) Have you had an ectopic pregnancy? *Yes/No*

General Health (Male and Female)

1) Do you have a healthy diet? *Yes/No*

2) Do either of you smoke or drink excessive amounts of alcohol (for men, this is more than 21 units per week, and for women, it is more than 14 units per week)? *Yes/No*

3) Have either of you been exposed to environmental hazards? *Yes/No*

4) Have either of you tried to conceive before without success? *Yes/No*

5) Are either of you under significant stress? *Yes/No*

6) Do you spend a lot of time apart? *Yes/No*

7) Do you drink excessive amounts of caffeine? *Yes/No*

8) Do either of you take regular medications? *Yes/No*

9) Do either of you use recreational drugs? *Yes/No*

10) Is there a family history of genetic problems ? *Yes/No*

Focus On **Fertility Facts - Couples**

It’s estimated that one in seven UK couples - approximately 3.5 million people - have difficulty in conceiving (HFEA 2006-07)

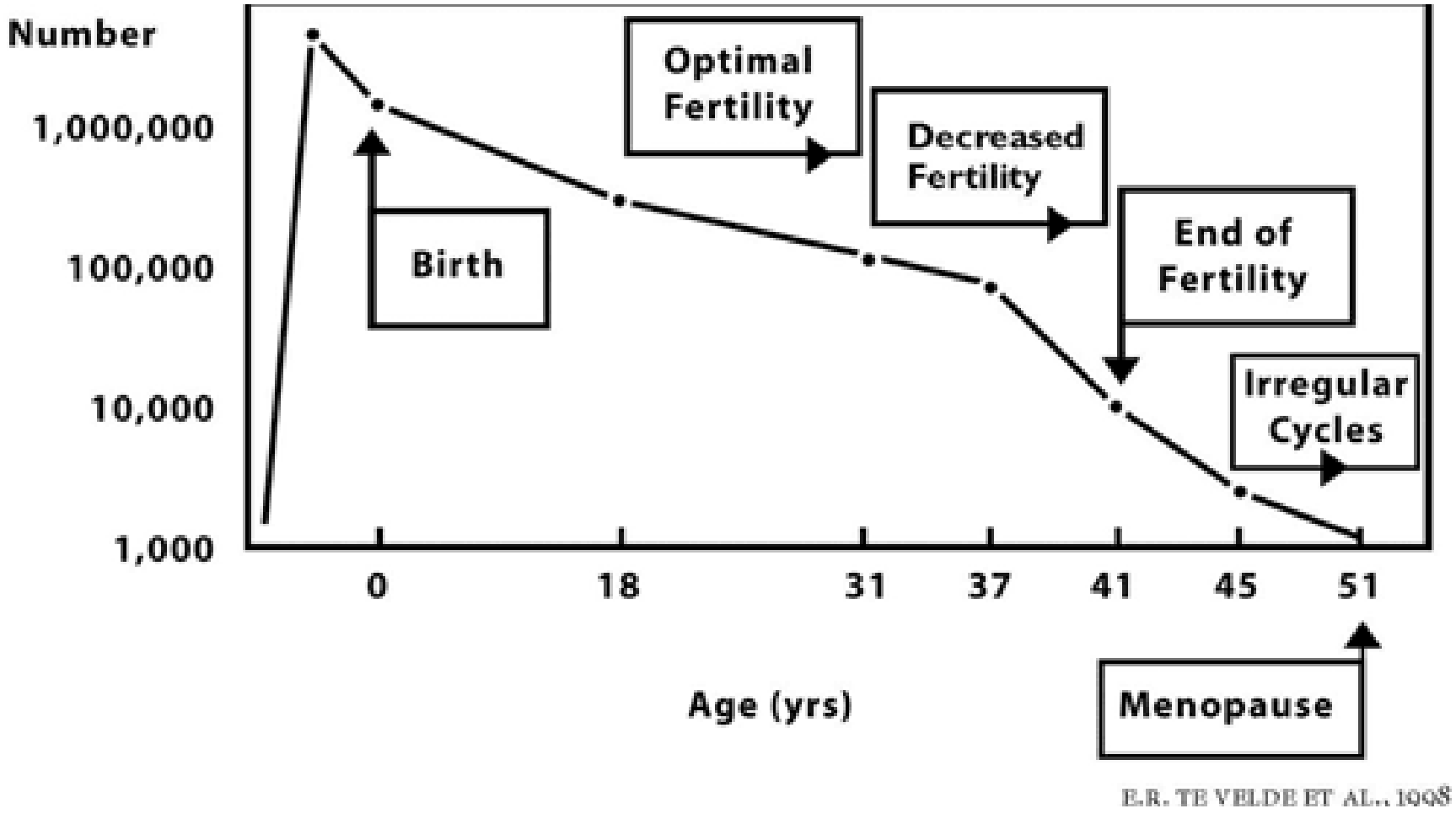
Infertility is the most common reason for women aged 20-45 to see their GP, after pregnancy itself (HFEA)

Potential causes:

- Age*
- Stress *
- Tobacco use **
- Alcohol **
- Sexually transmitted diseases (STDs) **
- Environmental pollutants **
- Obesity and malnutrition *
- Nutritional deficiencies

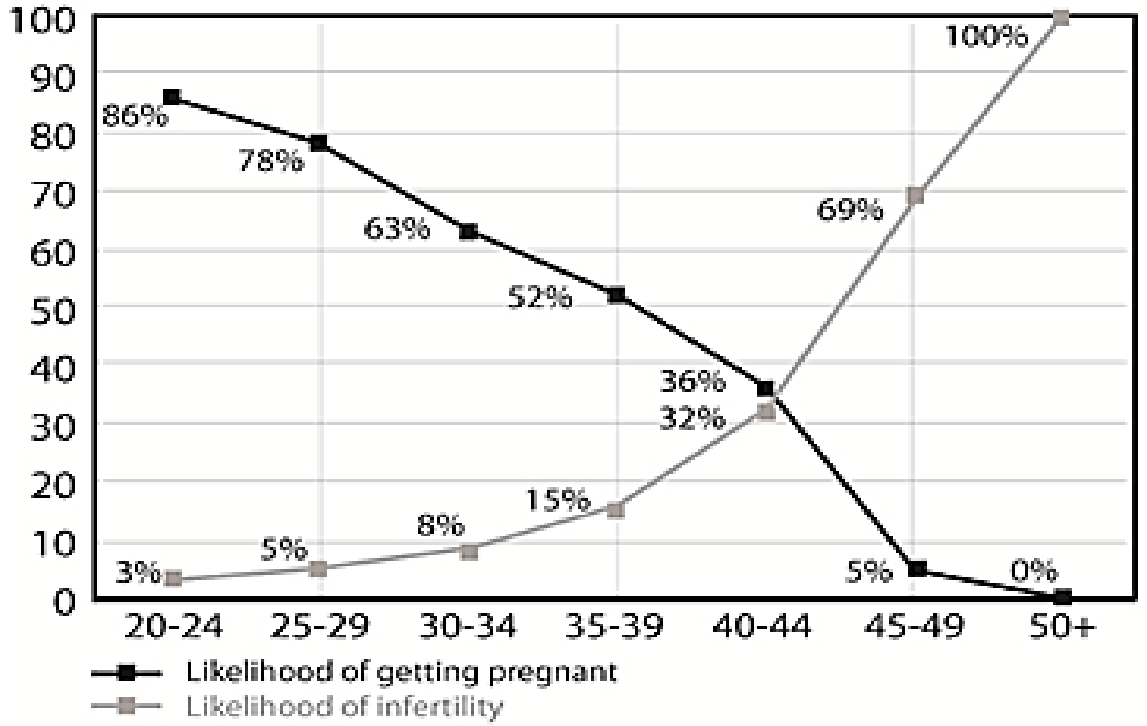
* Sharma, R. K, Agarwal, A. Role of Reactive Oxygen Species in Male Infertility. Elsevier: 835, 1996.
**Agarwal et al. Prevention of Oxidative Stress Injury to Sperm. Journal of Andrology 26: 654-655. 2005B

Follicle Number And Age



Fertility Facts – Women

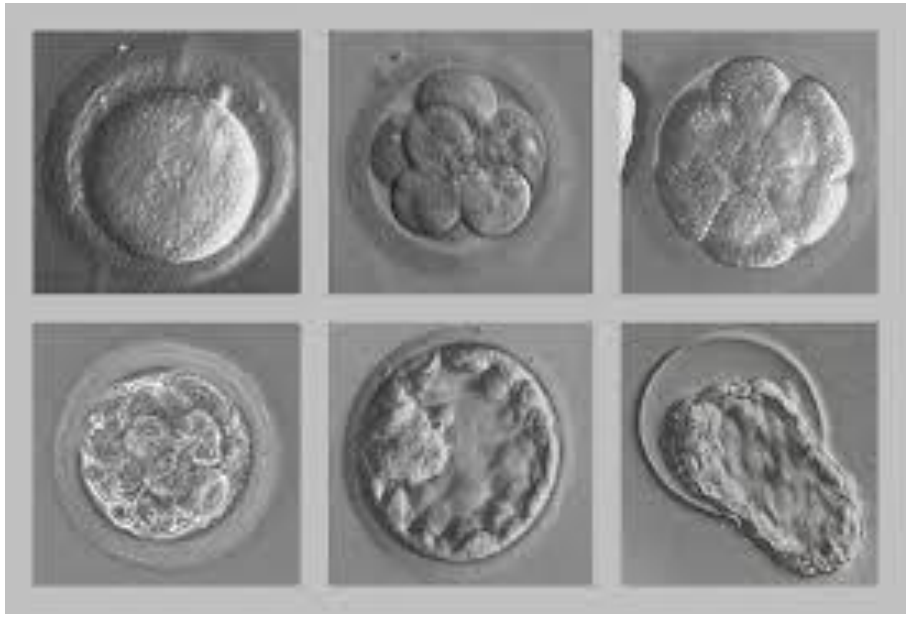
Fertility declines more sharply for women as they age.



Fertility Facts – Women

Nutritional deficiencies in women may cause:

- Mid-luteal phase effects of corpus luteum[1]
- Normal endometrial physiologic changes[1]
- Defective embryo development[2]
- Retardation of embryo growth[2]



[1] *Agrawal A, and S.S.R Allamaneni. 2004, Oxidants and antioxidants in human fertility. Middle East Fertility Society Journal: 188*

[2] *Gupta, et al., 2006, The Impact of Reactive Oxygen Species on Early Human Embryos: A Systematic Review of the Literature. Embryo Talk 1.2: 87*

Nutrients Important To Fertility & Pre-conception

Micronutrients & Fertility

Table 1. Characteristics and Results of Studies on the Association Between Micronutrients and Female Infertility [a]

	Study		
	Design	**Comment**	**Results**
Paszkowski et al. (10)	Case-Control	112 women with idiopathic infertility, tubal infertility vs healthy women	Lower levels of selenium and glutathione peroxidase in patients with idiopathic infertility
Polak et al. (11)	Case-Control	53 women with fertility disorders vs 13 healthy women	Lower total antioxidant status in idiopathic infertile patients
Madhur Mahesh Gupta (12)	Case-Control	50 women with idiopathic infertility vs 50 healthy women	Higher levels of serum MDA and Hcys in infertile patients
Howard et al. (6)	Clinical trial	Supplementation with magnesium and selenium in infertile women	100% of infertile patients become pregnant within the 8 months
Badawy et al. (8)	Clinical trial	NAC supplements in combination with clomiphene citrate in infertile women	No significant differences were observed with NAC supplements
Mier-Cabrera et al. (7)	Clinical trial	Supplementation with vitamins C and E in infertile women	No significant differences were observed in pregnancy rates
Cicek et al. (9)	Clinical trial	Vitamin E supplements in combination with clomiphene citrate in infertile women	Increased endometrial thickness in vitamin group
Altmae et al. (13)	Case-Control	Folate-metabolizing gene variations and unexplained infertility	Significant differences in the frequencies of heterozygous genotype between controls and infertile patients
Thaler et al. (14)	Clinical trial	The effects of 677 C>T mutations of *MTHFR* gene on ovarian responsive to r-FSH	Less r-FSH was required in patients with 677 c homozygote
Szymanski et al. (15)	Clinical trial	Folic acid supplement in IVF	Higher degree of maturity of oocytes in vitamin group
Chavarro et al. (3)	Cohort	Supplementation with multivitamin and ovulatory infertility risk	RR=0.59 for women using 6 or more tablets weekly
Chavarro et al. (16)	Cohort	the association of iron intake with ovulatory infertility	RR=0.53 for women in highest quintile of total iron intake
Li et al. (32)	Cross-Sectional	The prevalence of vitamin D deficiency in 1192 infertile patients	68.6% and 22.2% of patients had been considered insufficient and deficient, respectively
Ozkan et al. (18)	Cohort	Association between serum levels of vitamin D and IVF outcomes	Each ng/ml increase in 25(OH)-D levels in follicular fluid had correlated with 6% increase in clinical pregnancy rates

Thrita. 2015 March; 4(1): e25586

Many studies prove that there is a strong positive relationship between micronutrients and fertility

Vitamin B12

New vitamin B12 advice could help to prevent more Neural Tube Defects

October, 2012

"All women who may become pregnant should take a **daily supplement containing 400mcg of folic acid and at least 2.5mcg of B12** once a day with a meal.
These vitamins should ideally be taken from at least 3 months prior to conception and for the first 3 months of pregnancy to help prevent NTDs."

Shine

Spina bifida • Hydrocephalus
Information • Networking • Equality

New Vitamin B12 advice could help to prevent more Neural Tube Defects says report

October 31st 2012 - London - A new report by a world authority on vitamin B12 calls for all women who may become pregnant to follow updated pre-conceptual supplement recommendations, which could further reduce the number of pregnancies affected by Neural Tube Defects (NTDs), such as spina bifida and anencephaly.

It is now believed that taking vitamin B12 alongside folic acid may be more effective in NTD prevention than taking folic acid alone. On the basis of the new report and mounting global scientific evidence, SHINE, Europe's largest organisation dedicated to individuals and families affected by spina bifida and hydrocephalus, has announced an update to its folic acid recommendations:

"All women who may become pregnant should take a daily supplement containing 400mcg of folic acid and at least 2.5mcg of B12 once a day with a meal. These vitamins should ideally be taken from at least 3 months prior to conception and for the first 3 months of pregnancy to help prevent NTDs."

SHINE is also launching an initiative to urge all UK health authorities and organisations to recognise the potential benefits of B12 and help support the work necessary to optimise the prevention of NTDs.

The author of the report, Professor John Scott, founder of the Vitamin Research Unit at the Institute of Molecular Medicine, Trinity College, Dublin, concludes: *'It is clear that, as well as the addition of a folic acid supplement (400 mcg per day), the addition of a vitamin B12 component of at least 2.5 mcg per day would bring about a further significant and worthwhile risk reduction for NTDs.'*

SHINE CEO, Jackie Bland commented, *"NTDs are a serious health threat which can lead to enormous challenges and painful decisions. The most serious form, anencephaly, means that the baby will not live long beyond birth, and many babies born with spina bifida face a life with serious, multiple disabilities. SHINE is committed to the primary prevention of NTDs and as such it is our duty to make women aware of the potential benefits of B12."*

NTDs still affect 1 in 1000 pregnancies in the UK. When taken correctly before and during pregnancy, folic acid could prevent up to 72% of these cases, but it's not the only answer.

Scientists worldwide have searched for ways to reduce the risk further, including studying the potential benefits of vitamin B12 which is essential for the body to metabolise folic acid. This has highlighted a link between low folate and low B12 levels, with some studies suggesting a possible 2-3 fold risk increase for NTDs in women with low B12 status.

Ascorbic Acid – Vitamin C

'Effects of ascorbic acid supplementation on patients with luteal phase defects'

- The clinical pregnancy rate was significantly higher in the ascorbic acid supplementation group than the control group.
- Thus, ascorbic acid supplementation is an effective treatment for some patients with luteal phase defect.

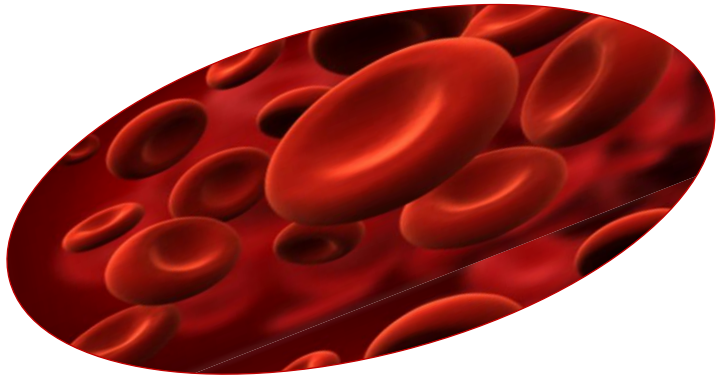
Characteristic	Control group (n = 46)		Ascorbic acid group (n = 76)		*P* value[a]
	Pretreatment	Post-treatment	Pretreatment	Post-treatment	
Age (y)	34.1 ± 0.6		35.3 ± 0.4		.098
Serum P level (ng/ml)	7.95 ± 0.25[b]	8.73 ± 0.50[b]	7.51 ± 0.22[c]	13.27 ± 0.63[c]	
Improvement rate		10/46 (21.7)[a]		40/76 (52.6)[a]	<.01
Serum E_2 level (pg/mL)	102.1 ± 0.78[b]	104.3 ± 6.41[b]	105.7 ± 6.7[c]	138.7 ± 7.8[c]	
Pregnancy rate		5/46 (10.9)[a]		19/76 (25.0)[a]	.0447
Miscarriage rate		1/5 (20.0)[d]		3/19 (15.8)[d]	.635

H Henmi et al., 2003, Fertility & Sterility, Vol 80, no 2

Iron

‘Iron Intake and Risk of Ovulatory Infertility’

- As part of a large scale, prospective cohort study, 438 women reported infertility due to ovulatory disorder.
- Women who consumed iron supplements had a significantly lower risk of ovulatory infertility than women who did not use iron supplements.
- Total iron intake, primarily consumed as multivitamins and iron supplements, was inversely associated with the risk of infertility.



JE Chavarro et al., 2006, Obstetrics & Gynaecology, Vol. 108, Iss. 5

Zinc

- Zinc plays an important role in **hormone production and balance**. It helps the pituitary gland to release follicle-stimulating hormone which encourages ovulation. Regular ovulation is key to fertility and unassisted reproduction.

- The rising vegetarian and vegan trend may contribute to zinc deficiencies due to a lack of protein in the diet, which is needed for zinc to bind with.

- A decrease in zinc can cause an excess of copper in the body, which has a negative impact on fertility by lowering progesterone levels.

Zinc	  

Selenium

- The essential trace mineral selenium is of fundamental importance to human health. It is a catalyst for the production of active thyroid hormone.
- **Numerous reports implicate selenium deficiency in several reproductive and obstetric complications including male and female infertility*.**
- A low concentration of selenium in blood serum in the early stage of pregnancy has been proved to be a predictor of low birth weight of a newborn**.

Selenium	  

**HD Mistry, 2012, Selenium in reproductive health, American Journal of Obstetrics & Gynaecology*
***J Pieczynska, H Grajeta, 2015, The role of selenium in human conception and pregnancy, Journal of Trace Elements & Biology, no.29*

Why Pregnacare Is The Ideal Pre-conception Supplement

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A range of 21 nutrients to support reproductive health:

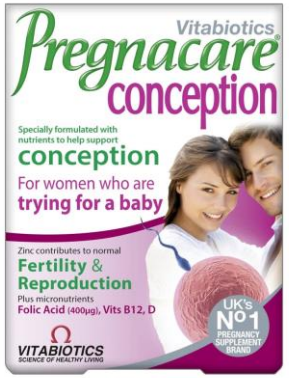
- **400mcg folic acid**; the exact level **recommended by the UK Department of Health** for all women trying to conceive

- Iodine, crucial in the early stages of pregnancy. Iodine is a key micronutrient for the synthesis of thyroid hormones

- Zinc which contributes to normal **fertility** and **reproduction,** and **DNA synthesis**

- Vitamin B12 and D, zinc and magnesium which contribute to normal **cell division**

- Includes L-arginine, N-acetyl Cysteine and inositol
  - **L-arginine** – influences follicular release as well as healthy follicular blood flow and implantation
  - **N-acetyl Cysteine** – antioxidant
  - **Inositol –** required for the proper formation of cell membranes and for several aspects of reproduction



Pregnacare

Clinical Trial

A clinical trial published by Reproductive BioMedicine Online in 2012 showed that women taking multiple micronutrient supplements compared with folic acid alone had a higher chance of pregnancy.

The collaborative study of 56 subfertile women was carried out by University College London, The Royal Free Hospital Medical School, University Hospital of Warwickshire and Warwick University.

Reproductive BioMedicine Online (2012) 24, 54–60

www.sciencedirect.com
www.rbmonline.com

ELSEVIER

ARTICLE

Prospective randomized trial of multiple micronutrients in subfertile women undergoing ovulation induction: a pilot study

Rina Agrawal [a,b,*], Elizabeth Burt [a], Anne Marie Gallagher [a], Lisa Butler [a], Radha Venkatakrishnan [b], Panagiotis Peitsidis [a]

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Dr Rina Agrawal is a consultant and associate professor in reproductive medicine and obstetrics/gynaecology at the University Hospital at Warwick University. She works both in London and in Warwickshire in the UK. She received her degree in 1985, MD in 1989 and formal training in reproductive medicine at the University College London with Prof Howard Jacobs, where she completed her PhD on angiogenic factors in 2000. Other areas of expertise are polycystic ovary syndrome, ovarian hyperstimulation syndrome, ovarian stimulation protocols, lifestyle and fertility and gynaecological ultrasonography including Doppler and 3D ultrasonography. Rina has published extensively over the years and referees for several international journals.

Abstract This study investigated whether subfertile women undergoing ovulation induction using standard treatment regimens with clomiphene citrate/gonadotrophins have higher pregnancy rates when on an adjuvant multiple micronutrient (MMN) nutritional supplement compared with folic acid alone. A prospective randomized controlled trial was conducted in a teaching-hospital fertility clinic on 58 subfertile women, of which 56 women completed the study. Women undergoing ovulation induction were allocated to either receive adjuvant MMN supplementation or folic acid. Clinical pregnancy rates and blood nutrient concentrations were assessed after the third treatment attempt or as soon as the women achieved pregnancy. Using intention-to-treat analysis, it was observed that women on adjuvant MMN supplementation had a significantly higher cumulative clinical pregnancy rate (66.7%) compared with those on folic acid (39.3%; $P = 0.013$). The ongoing pregnancy rate in women on MMN supplementation was 60.0% versus 25.0% ($P < 0.02$) in the folic-acid group. Further, women who were on MMN supplementation had significantly fewer attempts to achieve pregnancy compared with women on folic acid ($P < 0.001$). The results of this pilot study suggest that women who take adjuvant MMN supplementation during ovulation induction have a higher chance of pregnancy compared with women on folic acid.

KEYWORDS: multiple micronutrient (MMN) supplementation, pregnancy rates, subfertility, vitamins

*Pregnacare Conception (Vitabiotics, London)

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doi:10.1016/j.rbmo.2011.10.004

Prospective randomized trial of multiple micronutrients in subfertile women undergoing ovulation induction:
a pilot study

Rina Agrawal, Elizabeth Burt, Anne Marie Gallagher, Lisa Butler, Radha Venkatakrishnan, Panagiotis Peitsidis

Clinical Trial

Women taking **Pregnacare Conception** benefited from higher pregnancy rates.

66.6% of women became pregnant in the micronutrient group compared with 39.3% of women in the folic acid group[1].

The ongoing pregnancy rate in women on the prenatal micronutrient supplement was 60 percent vs 25 percent[2] in the folic acid group.

	Folic acid alone	Prenatal supplement
Clinical Pregnancy Rate	39.3%	66.6%
On-going pregnancy (12 weeks)	25.0%	60.0%

1 p=0.013
2 p<0.02

Clinical Trial Media Coverage

30p pill that can double chances of having a baby

Essential: Nutrients affect fertility

A MULTIVITAMIN pill costing just 30p could more than double a woman's chance of having a baby, according to a study.

It found 60 per cent of those taking the supplement while having IVF treatment became pregnant compared with a quarter who did not take it.

Researchers say the pill contains nutrients that may boost fertility but are often absent from our diets, including vitamins A, C and E, zinc and selenium.

The study at University College London involved 56 women aged 18 to 40 who had all tried IVF for at least a year unsuccessfully.

Half were given the pill containing vitamins and minerals to take every day and the other half folic acid tablets.

The multivitamin pill also contained folic acid, which prevents birth defects and has been shown to help boost fertility.

The researchers found 60 per cent of women taking the multivitamin pill became pregnant, and did not miscarry in the first three months, the period when this is most likely to happen. This compared with 25 per cent of the women taking folic acid.

By **Sophie Borland**
Health Reporter

The study, published in the journal Reproductive Biomedicine, also found women taking the vitamin pill needed far fewer attempts to become pregnant.

Of those who became pregnant, 75 per cent conceived in the first course of IVF treatment. By comparison. This compares with just 18 per cent of those on folic acid.

The pill, Vitabiotics Pregnacare-Conception contains folic acid, vitamins A, B, C and E, zinc, selenium and some antioxidants. It costs just over £10 over the counter for a month's supply.

Lead researcher Dr Rina Agrawal said: 'The implications of this study are far-reaching as they suggest that prenatal micronutrient supplementation in women undergoing ovulation induction improves pregnancy rates.

'There is a large body of evidence establishing the relationship between placental development, foetal growth, pregnancy outcomes and adequate nutrition, particularly vitamin intake.'

But other scientists pointed out that the study was small and said the results should not be taken too seriously.

Dr Allan Pacey, who specialises in fertility at the University of Sheffield, said: 'The influence of nutrition on our fertility is of general interest to the public and professionals, but there are relatively few studies which have examined this systematically and few which have shown direct benefits of taking supplements to enhance things.

'On the face of it, this study is interesting, but we should acknowledge that this is a relatively small number of patients and the study would need to be repeated in a larger trial before we could be certain of the results.'

A woman's fertility is known to be affected by factors including her age, weight, alcohol consumption and whether she smokes. High levels of stress and even drinking too much coffee have also been shown to reduce the chances of getting pregnant.

Daily Mail

FERTILITY

Vitamins 'aid baby chance'

VITAMIN pills can help women conceive, according to a fertility study.

Almost twice as many patients who took the tablets during fertility treatment had babies compared to those not on supplements.

It worked out at a 60% success rate, instead of 25%, said the study in the journal Reproductive Biomedicine.

But Dr Allan Pacey, of the University of Sheffield, dismissed the results, saying: "I can't help but thinking that for most people, fresh fruit and vegetables would have much the same effect."

Daily Mirror

PREGNANCY PILL

Vitamin lift for wannabe mums

A DAILY multivitamin pill could help wannabe mums have a baby, a study revealed.

Researchers found it can improve blood flow to the womb and ovaries – boosting fertility.

And it could help thousands of women avoid IVF treatment. In a trial,

By **EMMA LITTLE,** Health and Science Editor

SEVENTY PER CENT fell pregnant after taking a pill packed with vitamins and minerals for a month. That compared to just 40 per cent in a similar group who took only a folic acid supplement.

The trial involved 58 women – average age 32 – who had unsuccessfully tried for a baby for a year. A supplement called Pregnacare-Conception by British firm Vitabiotics was used in the trial by University College London researchers. A larger trial will now take place.

Study leader Dr Rina Agrawal said: "There is a large body of evidence establishing the relationship between pregnancy and adequate nutrition."

e.little@the-sun.co.uk

The Sun

Male Fertility

Fertility Facts – Men

- Men can remain fertile for much longer than women, but male fertility still declines with age, although less dramatically

- Nutritional deficiencies in men may cause:
  - Oligospermia (Reduced sperm numbers)*
  - Asthenospermia (Decreased motility)**
  - Impairment of sperm-oocyte fusion***
  - Abnormal sperm morphology (Teratospermia)*

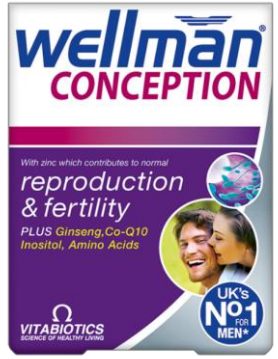
- Folic acid in particular is associated with increased numbers of sperm, sperm motility and decreases in the number of abnormal forms

**Agrawal, et al. 2003, Role of reactive oxygen species in the pathophysiology of human reproduction. Fertility & Sterility, 79:829*
***Agrawal, et al. 2005, Oxidative stress and antioxidants in male infertility: a difficult balance. Iranian Journal of Reproductive Medicine, 3:2*
****Agrawal, et al. 2006, What an Andrologist/Urologist should know about free radicals and why. Journal of Urology, 67:3*

Why Wellman Conception Is Ideal For Men Starting A Family

Over 30 nutrients, including:

- Selenium contributes to normal **spermatogenesis**
- Zinc contributes to normal **fertility** and **reproduction**
- Folic acid, iron, magnesium and vitamin B12 contribute to **normal cell division**
- Zinc and vitamin C contribute to the **protection of cells from oxidative stress**
- Vitamin B6 contributes to the **regulation of hormonal activity**
- Zinc contributes to the maintenance of normal **testosterone levels in the blood**
- Includes **L-arginine** and **inositol** which both play important roles in male reproduction and the health of sperm



wellman

Nutrients Important In Pregnancy

Prenatal Nutrition- Beyond Folic Acid

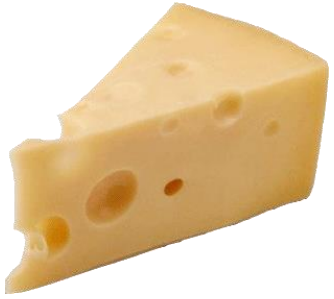
In the ‘Annual Report of the Chief Medical Officer, 2012’, senior clinical researcher Professor Ron Gray stated that under-nutrition in pregnancy is associated with the development of heart disease in the adult offspring. There may even be effects transmitted to future generations.

Annual Report of the Chief Medical Officer 2012, Our Children Deserve Better: Prevention Pays, Ron Gray, Senior Clinical Research Fellow, Policy Research Unit in Maternal Health and Care, National Perinatal Epidemiology Unit, University of Oxford, and, Honorary Consultant in Public Health, Public Health England

Vitamin D

- Since it is difficult for people to get enough vitamin D from food or sunlight alone, the UK Department of Health recommends pregnant and breastfeeding women to take daily 10mcg vitamin D supplement.

- The National Diet & Nutrition Survey found that 15% of women of reproductive age (19-64 years) were vitamin D deficient*.

Vitamin D	  

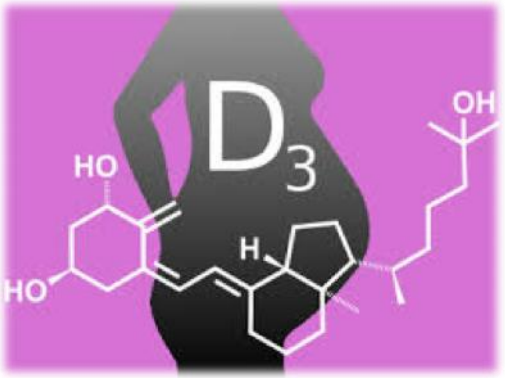
**National Diet & Nutrition Survery, 2016, Vitamin D levels, Table 8.6*

Vitamin D and Pregnancy
New Clinical Research

- Initial research shows how common vitamin D deficiency is in pregnant women*. Further research ongoing at the Institute of Metabolism and Systems Research, University of Birmingham.

- Focus on
  - how vitamin D affects immune responses in pregnancy
  - why low vitamin D levels increase a women's risk of complications such as pre-eclampsia, pre-term birth and miscarriage

- **Pregnacare is providing a long term grant to Wellbeing of Women, supporting Dr Tamblyn's research into the role and importance of vitamin D supplementation in pregnancy.**



*Tamblyn et. al., Dec 2016

WELLBEING OF WOMEN

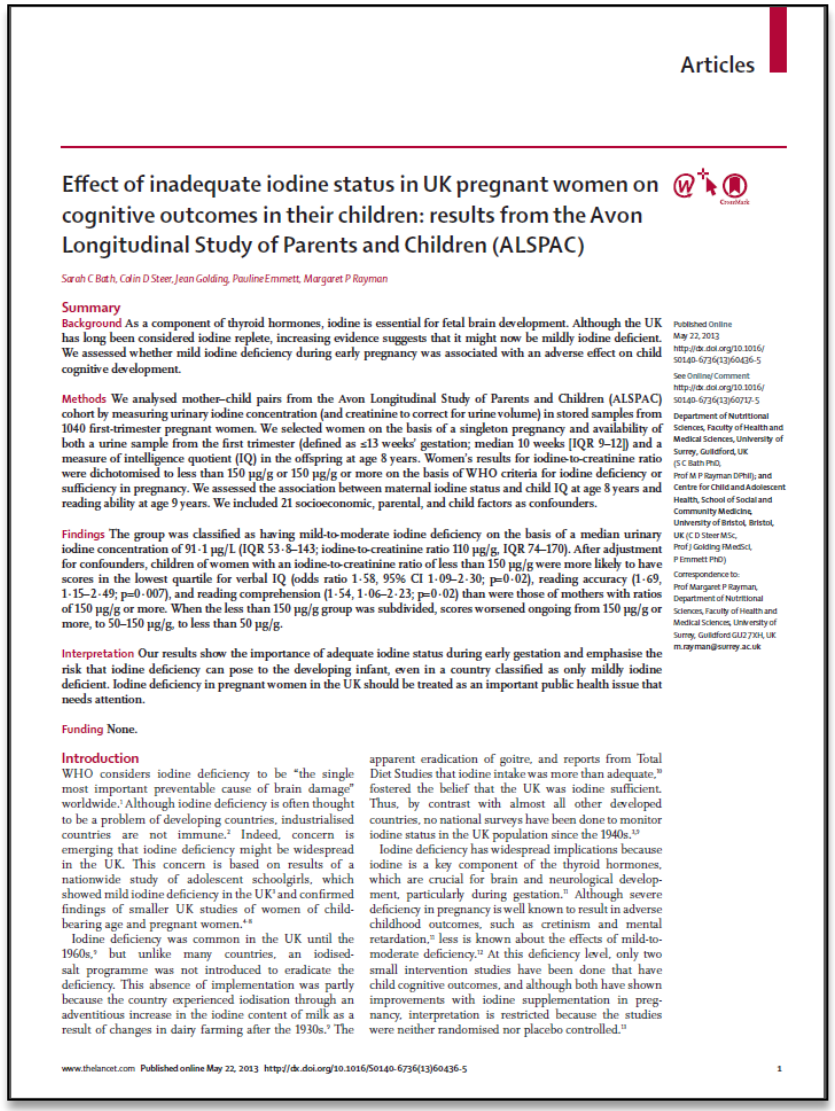
Iodine

- Iodine is very important before conception and around pregnancy. There is a link between inadequate iodine status in pregnant women and cognitive outcomes in their children*.
- The World Health Organization (WHO) considers iodine deficiency to be the single most important preventable cause of brain damage in the developing foetus worldwide**.
- New, official studies of UK iodine status have shown deficiencies in women of childbearing age and pregnant women***.

Iodine	  

**SC Bath et al., 2013 Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from ALSPAC, The Lancet*
**WHO, Micronutrient Deficiencies*
****National Diet and Nutrition Survey Results from Years 7 and 8 (combined) of the Rolling Programme, Public Health England, 2018*

Iodine



Articles

Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

Sarah C Bath, Colin D Steer, Jean Golding, Pauline Emmett, Margaret P Rayman

Summary

Background As a component of thyroid hormones, iodine is essential for fetal brain development. Although the UK has long been considered iodine replete, increasing evidence suggests that it might now be mildly iodine deficient. We assessed whether mild iodine deficiency during early pregnancy was associated with an adverse effect on child cognitive development.

Methods We analysed mother–child pairs from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort by measuring urinary iodine concentration (and creatinine to correct for urine volume) in stored samples from 1040 first-trimester pregnant women. We selected women on the basis of a singleton pregnancy and availability of both a urine sample from the first trimester (defined as ≤13 weeks' gestation; median 10 weeks [IQR 9–12]) and a measure of intelligence quotient (IQ) in the offspring at age 8 years. Women's results for iodine-to-creatinine ratio were dichotomised to less than 150 μg/g or 150 μg/g or more on the basis of WHO criteria for iodine deficiency or sufficiency in pregnancy. We assessed the association between maternal iodine status and child IQ at age 8 years and reading ability at age 9 years. We included 21 socioeconomic, parental, and child factors as confounders.

Findings The group was classified as having mild-to-moderate iodine deficiency on the basis of a median urinary iodine concentration of 91·1 μg/L (IQR 53·8–143; iodine-to-creatinine ratio 110 μg/g, IQR 74–170). After adjustment for confounders, children of women with an iodine-to-creatinine ratio of less than 150 μg/g were more likely to have scores in the lowest quartile for verbal IQ (odds ratio 1·58, 95% CI 1·09–2·30; p=0·02), reading accuracy (1·69, 1·15–2·49; p=0·007), and reading comprehension (1·54, 1·06–2·23; p=0·02) than were those of mothers with ratios of 150 μg/g or more. When the less than 150 μg/g group was subdivided, scores worsened ongoing from 150 μg/g or more, to 50–150 μg/g, to less than 50 μg/g.

Interpretation Our results show the importance of adequate iodine status during early gestation and emphasise the risk that iodine deficiency can pose to the developing infant, even in a country classified as only mildly iodine deficient. Iodine deficiency in pregnant women in the UK should be treated as an important public health issue that needs attention.

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Introduction

WHO considers iodine deficiency to be "the single most important preventable cause of brain damage" worldwide.[1] Although iodine deficiency is often thought to be a problem of developing countries, industrialised countries are not immune.[2] Indeed, concern is emerging that iodine deficiency might be widespread in the UK. This concern is based on results of a nationwide study of adolescent schoolgirls, which showed mild iodine deficiency in the UK[3] and confirmed findings of smaller UK studies of women of childbearing age and pregnant women.[4–8]

Iodine deficiency was common in the UK until the 1960s,[9] but unlike many countries, an iodised-salt programme was not introduced to eradicate the deficiency. This absence of implementation was partly because the country experienced iodisation through an adventitious increase in the iodine content of milk as a result of changes in dairy farming after the 1930s.[9] The apparent eradication of goitre, and reports from Total Diet Studies that iodine intake was more than adequate,[10] fostered the belief that the UK was iodine sufficient. Thus, by contrast with almost all other developed countries, no national surveys have been done to monitor iodine status in the UK population since the 1940s.[3,9]

Iodine deficiency has widespread implications because iodine is a key component of the thyroid hormones, which are crucial for brain and neurological development, particularly during gestation.[11] Although severe deficiency in pregnancy is well known to result in adverse childhood outcomes, such as cretinism and mental retardation,[11] less is known about the effects of mild-to-moderate deficiency.[12] At this deficiency level, only two small intervention studies have been done that have child cognitive outcomes, and although both have shown improvements with iodine supplementation in pregnancy, interpretation is restricted because the studies were neither randomised nor placebo controlled.[13]

Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

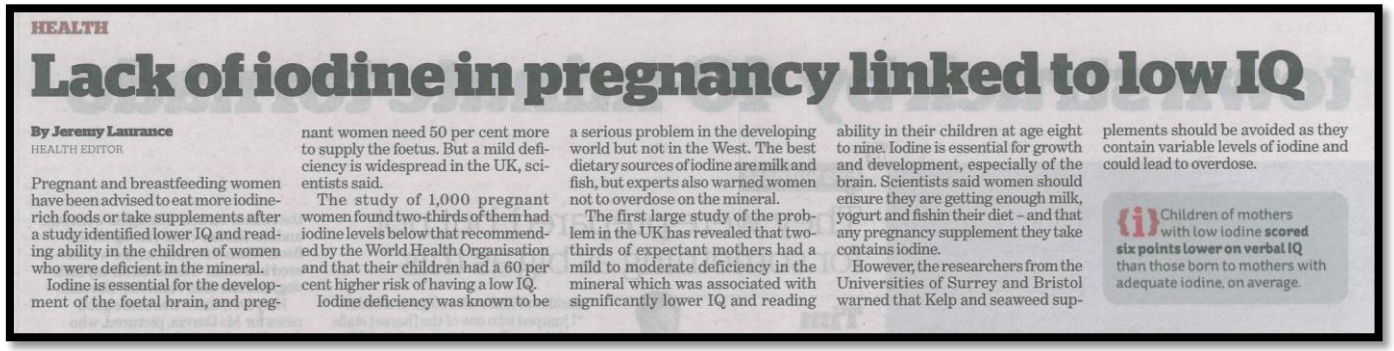
Sarah C Bath, Colin D Steer, Jean Golding, Pauline Emmett, Margaret P Rayman

Published May 2013

Findings – pregnant women with an iodine deficiency had children with significantly lower IQ and reading ability

Iodine In The News

Thyroid hormone deficiency can lead to a lower IQ, hearing and learning difficulties, as well as other forms of neurological impairment in later life.



HEALTH

Lack of iodine in pregnancy linked to low IQ

By Jeremy Laurance
HEALTH EDITOR

Pregnant and breastfeeding women have been advised to eat more iodine-rich foods or take supplements after a study identified lower IQ and reading ability in the children of women who were deficient in the mineral.

Iodine is essential for the development of the foetal brain, and pregnant women need 50 per cent more to supply the foetus. But a mild deficiency is widespread in the UK, scientists said.

The study of 1,000 pregnant women found two-thirds of them had iodine levels below that recommended by the World Health Organisation and that their children had a 60 per cent higher risk of having a low IQ.

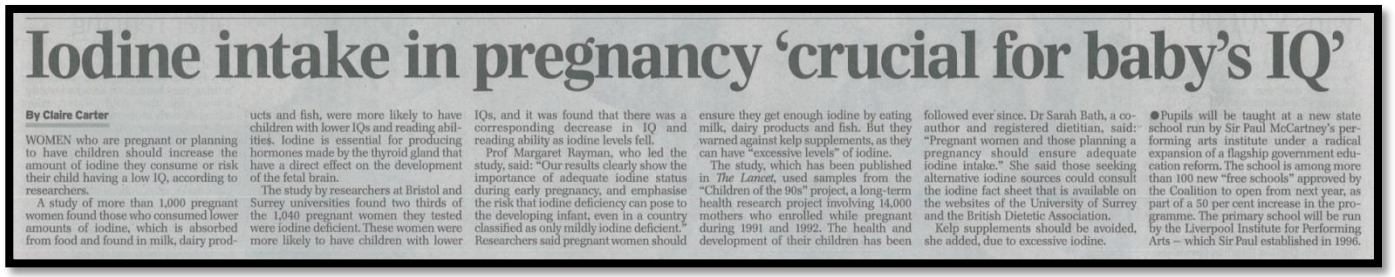
Iodine deficiency was known to be a serious problem in the developing world but not in the West. The best dietary sources of iodine are milk and fish, but experts also warned women not to overdose on the mineral.

The first large study of the problem in the UK has revealed that two-thirds of expectant mothers had a mild to moderate deficiency in the mineral which was associated with significantly lower IQ and reading ability in their children at age eight to nine. Iodine is essential for growth and development, especially of the brain. Scientists said women should ensure they are getting enough milk, yogurt and fish in their diet – and that any pregnancy supplement they take contains iodine.

However, the researchers from the Universities of Surrey and Bristol warned that Kelp and seaweed supplements should be avoided as they contain variable levels of iodine and could lead to overdose.

{i} Children of mothers with low iodine **scored six points lower on verbal IQ** than those born to mothers with adequate iodine, on average.

The Independent, May 2013



Iodine intake in pregnancy 'crucial for baby's IQ'

By Claire Carter

WOMEN who are pregnant or planning to have children should increase the amount of iodine they consume or risk their child having a low IQ, according to researchers.

A study of more than 1,000 pregnant women found those who consumed lower amounts of iodine, which is absorbed from food and found in milk, dairy products and fish, were more likely to have children with lower IQs and reading abilities. Iodine is essential for producing hormones made by the thyroid gland that have a direct effect on the development of the fetal brain.

The study by researchers at Bristol and Surrey universities found two thirds of the 1,040 pregnant women they tested were iodine deficient. These women were more likely to have children with lower IQs, and it was found that there was a corresponding decrease in IQ and reading ability as iodine levels fell.

Prof Margaret Rayman, who led the study, said: "Our results clearly show the importance of adequate iodine status during early pregnancy, and emphasise the risk that iodine deficiency can pose to the developing infant, even in a country classified as only mildly iodine deficient." Researchers said pregnant women should ensure they get enough iodine by eating milk, dairy products and fish. But they warned against kelp supplements, as they can have "excessive levels" of iodine.

The study, which has been published in *The Lancet*, used samples from the "Children of the 90s" project, a long-term health research project involving 14,000 mothers who enrolled while pregnant during 1991 and 1992. The health and development of their children has been followed ever since. Dr Sarah Bath, a co-author and registered dietitian, said: "Pregnant women and those planning a pregnancy should ensure adequate iodine intake." She said those seeking alternative iodine sources could consult the iodine fact sheet that is available on the websites of the University of Surrey and the British Dietetic Association.

Kelp supplements should be avoided, she added, due to excessive iodine.

● Pupils will be taught at a new state school run by Sir Paul McCartney's performing arts institute under a radical expansion of a flagship government education reform. The school is among more than 100 new "free schools" approved by the Coalition to open from next year, as part of a 50 per cent increase in the programme. The primary school will be run by the Liverpool Institute for Performing Arts – which Sir Paul established in 1996.

The Daily Telegraph, May 2013

Iron

- Women of childbearing age, 25 to 49 years, are at most risk of iron deficiency. National Diet & Nutrition Survey (2017) showed that 29% of these women had iron intakes below the LRNI.

- Many pregnant women are low in iron since it is difficult to consume enough solely through the diet.

- **In a large international study conducted across 29 countries, the researchers of the Queen Mary University of London found that pregnant women with anaemia are twice as likely to die during, or shortly after pregnancy compared to those without the condition*.**

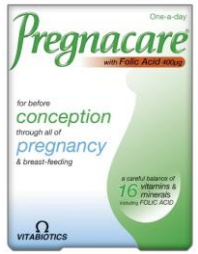
Iron	

**J Dahru et al., 2018, Risk of maternal mortality in women with severe anaemia during pregnancy and post partum: a multilevel analysis, The Lancet Global Health, volume 6*

Why Pregnacare Is The Ideal Pregnancy Supplement

VITABIOTICS
SCIENCE OF HEALTHY LIVING

- A range with over 20 nutrients to support pregnancy health including folic acid, vitamin D, vitamin C, vitamin B12, iron, iodine, zinc and selenium
- Because you need more than just folic acid
- Most trusted by mums
- Most recommended by midwives
- Helping healthy pregnancies for 30 years
- Supported by award winning UK research



Pregnacare

Clinical Trial

A ground breaking clinical trial published in the British Journal of Nutrition in 2010 showed that **Pregnacare** reduced the risk of small-for-gestational-age babies.

The collaborative study of over 400 newly pregnant women in London was carried out by the Institute of Brain Chemistry and Human Nutrition, London Metropolitan University and Homerton University Hospital.

British Journal of Nutrition (2010), 104, 437–445
doi:10.1017/S0007114510000747

Effect of multiple-micronutrient supplementation on maternal nutrient status, infant birth weight and gestational age at birth in a low-income, multi-ethnic population

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Poor nutrient intake during pregnancy can adversely affect both infant and maternal health. The aim was to investigate the efficacy of multiple-micronutrient supplementation during pregnancy in a socially deprived population in the developed world. We conducted a randomised, double-blind, placebo-controlled trial of multiple-micronutrient supplementation including 20 mg Fe and 400 μg folic acid, from the first trimester of pregnancy in 402 mothers, in East London, UK. Nutrient status was measured at recruitment, and at 26 and 34 weeks of gestation. Infants were weighed at birth. At recruitment the prevalence of anaemia was 13 %, vitamin D insufficiency 72 %, thiamin deficiency 12 % and folate deficiency 5 %, with no differences between groups. Only 39 % of women completed the study; rates of non-compliance were similar in both groups. Intention-to-treat analysis showed that participants receiving treatment had higher mean Hb at 26 weeks of gestation (110 (SD 10) *v.* 108 (SD 10) g/l; $P=0·041$) and 34 weeks of gestation (113 (SD 12) *v.* 109 (SD 10) g/l; $P=0·003$) and packed cell volume concentrations at 26 weeks of gestation (0·330 (SD 0·025) *v.* 0·323 (SD 0·026) l/l; $P=0·011$) and 34 weeks of gestation (0·338 (SD 0·029) *v.* 0·330 (SD 0·028) l/l; $P=0·014$) compared with controls. Analysis of compliant women showed supplemented women had higher median concentrations of serum ferritin, erythrocyte folate and 25-hydroxyvitamin D later in gestation than controls. In the compliant subset (n 149), placebo mothers had more small-for-gestational age (SGA) infants (eight SGA *v.* thirteen; $P=0·042$) than treatment mothers. Baseline micronutrient deficiencies were common; the multiple-micronutrient supplement was well-tolerated and improved nutrient status. Multiple-micronutrient supplements from early pregnancy may be beneficial and larger studies are required to assess impact on birth outcomes and infant development.

Multiple-micronutrient supplementation: Low-income populations: Multi-ethnic populations: Micronutrient status

It is well established that nutrient intake during pregnancy plays a significant role in maternal and child health[1]. Hackney in the East End of London has a substantial immigrant population with high levels of social and economic deprivation, mirroring many large cities throughout the developed world. Deprivation is associated with poor birth outcomes such as low birth weight (LBW), preterm birth and intra-uterine growth restriction[2]. Previous research here has demonstrated poor micronutrient intakes and status, including Fe, folate and thiamin, which have been associated with such adverse pregnancy outcomes[3–5].

The most recent Cochrane review[6] states that there is insufficient evidence to suggest that multiple-micronutrient supplementation is any more effective at improving birth outcome than Fe and folic acid supplements alone. However, the authors concede that further research is required due to a lack of well-controlled studies in this area. Furthermore, many studies are now over 20 years old and more recent studies have been in developing countries, making it difficult to extrapolate the results to industrialised populations.

An observational study of multiple-micronutrient supplement use in early pregnancy amongst low-income women (n 1430) in the USA found supplement users had a twofold reduced risk of preterm birth and LBW; beginning supplement use in the first trimester led to a greater reduction in risk compared with the second trimester[7]. However, this was not a randomised, controlled trial, and women choosing to use supplements may have had an intrinsically lower risk of poor birth outcome compared with non-users. A small randomised controlled trial in France (n 65) showed that women receiving multiple-micronutrient supplements from about 14 weeks of gestation had improved micronutrient

Abbreviations: LBW, low birth weight; PCV, packed cell volume; RNI, reference nutrient intake; SGA, small for gestational age; TDP, thiamin diphosphate.
* Corresponding author: Dr Louise Brough, fax +64 6350 5657, email L.Brough@massey.ac.nz

Effect of multiple-micronutrient supplementation on maternal nutrient status, infant birth weight and age at birth in a low-income, multi-ethnic population.

Louise Brough, Gail A. Rees, Michael A. Crawford,
R. Hugh Morton and Edgar K. Dorman

Clinical Trial

Results

Women taking Pregnacare benefited from:

Improved Nutrient Status when taking Pregnacare

- **Improvement in nutrient status** relative to the placebo.
  - Markers of iron, folate, thiamine and vitamin D status were all higher during the third trimester in the vitamin group.

Improved Gestational Weight when taking Pregnacare

- **A reduction in numbers of small-for-gestational-age (SGA) infants** (low birth weight for time of birth) relative to the placebo.
  - To the best of our knowledge, this is the first reporting of clinical findings in a study performed in either the UK or developed world showing that supplementing with a specific multivitamin supplement may help reduce the number of SGA infants born.

Clinical Trial Media Coverage

Vitamin boost for baby

Daily pill during pregnancy beats low birth weight

By **Jenny Hope**
Medical Correspondent

PREGNANT women taking a daily multivitamin pill have bigger babies, a study shows.

Taking the supplement cuts the risk of having low birthweight babies, which can have health problems.

This is the first study to show multivitamins specially tailored for pregnancy make a difference for women living in developed countries.

It was already known that the pills work in developing countries, where food may be scarce and diets lacking in nutrients. The study looked at the effect of multivitamins on 400 pregnant women with vitamin and mineral deficiencies living in East London.

During the first 12 weeks of pregnancy, half started taking Pregnacare pills. These contain 19 vitamins and minerals, including iron, folic acid and vitamin D. The rest had dummy starch tablets. After the babies were born, doctors found those taking the supplements had higher levels of iron, folate, thiamin and vitamin D.

Although iron levels fell in both groups, in late pregnancy 55 per cent of women taking dummy pills were deficient compared with 36 per cent of those on supplements.

The most significant finding was that mothers taking multivitamins had fewer small babies.

Eight out of the 88 babies born to women on supplements were considered small, compared with 13 out of 61 on dummy pills. Women on supplements had babies four ounces heavier on average.

Consultant obstetrician Pat O'Brien, of University College London, said: 'What happens in the womb can almost programme the baby for life.'

Small babies are more likely to have breathing problems and develop jaundice, he explained.

As adults, they are also more likely to suffer from obesity, diabetes, heart attacks and strokes.

It is cheaper to give specially tailored multivitamins to mothers-to-be than look after a baby in intensive care, added Mr O'Brien.

The study, from the Institute of Brain Chemistry and Human Nutrition at London Metropolitan University and the Homerton University Hospital, is published today in the British Journal of Nutrition.

Pregnacare, made by Vitabiotics, costs £4.95 for a month's supply.

Mothers-to-be are not generally advised to take supplements, with the exception of folic acid.

The UK has one of the worst records in Western Europe for babies of low birthweight relative to time spent in the womb.

It is worse than Cuba and on a par with Romania at 8 per cent.

j.hope@dailymail.co.uk

'All this fish oil and I can't even remember my own name'

FISH OILS 'DON'T HELP ELDERLY'

ALL the fuss over fish oil as brain food may be unjustified.

There is no evidence that the supplements offer benefits for brain function in older people, a two-year study found.

This contradicts previous surveys on the wonders of omega-3 fatty acids.

Researcher Alan Dangour, a senior lecturer at the London School of Hygiene and Tropical Medicine, studied 900 volunteers aged 70 to 80 from England and Wales.

They were all considered to have 'good mental health' and were split into two groups. The first group received fish oil supplements, while the others had a placebo.

Two years later, each of the elderly volunteers was given a series of memory and concentration tests.

Those who took fish oil had far greater levels of omega-3 in their bloodstream but did no better in the tests.

But Mr Dangour said: 'Although this is the longest trial of its kind ever conducted, it may be that it was not long enough for any true beneficial effects to be detected.'

The study is reported in the American Journal of Clinical Nutrition.

Daily Mail

Vitamins' tot hope

TAKING multi-vitamin pills during pregnancy **HALVES** the risk of having an underweight baby, a study claimed yesterday.

Just nine per cent of women given tablets had low-weight kids compared to 20 per cent of those given a placebo, the study of 402 mums-to-be found.

Smaller babies face obesity and diabetes in later life, said professors who carried out the study in Hackney, East London.

The Sun

MULTIVITAMUMS

Supplements can halve risky low birth weights

EMILY COOK
HEALTH CORRESPONDENT
emily.cook@mirror.co.uk

GIVING mums-to-be a multivitamin could boost their health AND halve the number of low birth-weight babies.

In the first major trial of its kind, a UK study found that pregnant women who took a supplement increased their levels of iron, folate and vitamin D – all vital in helping a foetus develop.

Taking a Vitabiotic Pregnacare tablet also cut the number who gave birth to tiny babies by more than half.

Small babies are at risk of jaundice and breathing complications and, later, obesity, diabetes and heart disease.

Research by the Institute of Brain Chemistry and Human Nutrition, based at London Metropolitan University, suggests that a poor diet in pregnancy could result in children getting health problems later in life.

Despite being one of the wealthiest countries in Europe, the UK has one of the worst rates for low birth-weight babies. In 1973 the incidence here was 6.6% but by 2005 it was 8%.

Lead researcher Dr Louise Brough said: "A baby's health can be adversely affected if it is too small at birth... supplementing with a specific multivitamin may help to reduce this."

The team followed 400 women from Hackney, East London – 55% taking a placebo pill were anaemic in late pregnancy compared with 36% on the supplement; and 32% were deficient in vitamin B1 compared with 20%.

The study is published in the British Journal of Nutrition.

▶ **HEALTHY** Vitamins good for baby

Daily Mirror

Omega 3

- Essential fats are vital for health, and play a role to support fertility and pregnancy
- Omega-3 essential fats support blood flow and so **oxygen and nutrient delivery to the body cells**, support sperm motility and are needed to build baby's brain, eyes and nervous system as well as for healthy cell structure throughout the body
- Research has shown that omega-3 fatty acids may provide an effective and practical avenue for **delaying ovarian aging** and **improving oocyte quality** at advanced maternal age
- Omega-3 fatty acids help **control inflammation** which may interfere with getting and staying pregnant
- Before and during pregnancy it is recommended to limit intake of oily fish due to potentially detrimental levels of mercury and pollutant contamination. A purified fish oil supplement is a good solution
- Once a woman becomes pregnant Omega-3 has a continued role to play: Omega-3 provides DHA . Maternal intake of DHA contributes to normal **eye and brain development of the foetus†**

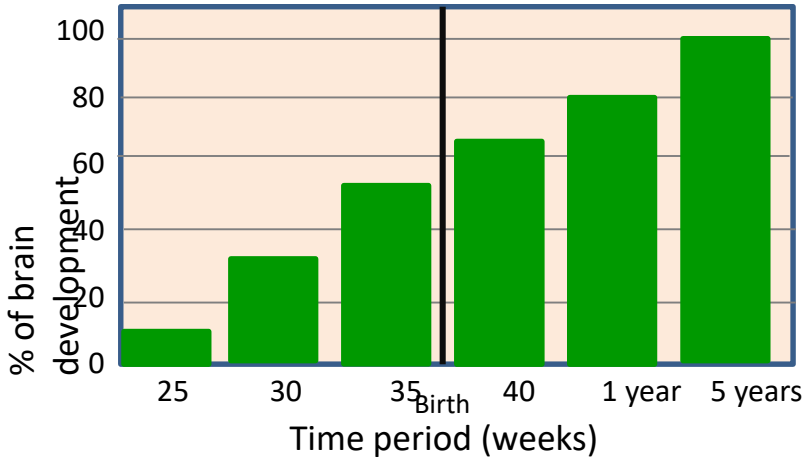
†A daily intake of 200mg DHA is required in addition to the recommended daily intake of 250mg DHA / EPA for adults.

Each Omega-3 capsule provides **300mg DHA** (docosahexaenoic acid); the exact level recommended by international experts*

- Provides a direct source of Omega-3

- Maternal intake of DHA contributes to normal **eye and brain development of the foetus†**
  - 60 % of the foetal brain is fats – 40% of which is DHA
  - 60% of the retina is made up of fatty acids

Normal brain growth during foetal life and pre-school years



*ISSFAL (International Society for the Study of Fatty Acids and Lipids) Workshop on the Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids. National Institutes of Health (NIH) April 1999

†A daily intake of 200mg DHA is required in addition to the recommended daily intake of 250mg DHA / EPA for adults.

VITABIOTICS
SCIENCE OF HEALTHY LIVING

Thank you.

Q/A will be held later in the day.

Pregnacare