

# WE NEED TO TALK ABOUT CMV

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## I AM CMV

I have infected 3 out of 5 people you will ever meet  
Yet most don't even know that I am there  
In most people I probably won't have caused  
anything more than a mild sniffle  
before I hide, unnoticed forever  
Yet to an unborn baby I can cause serious harm  
I can cause miscarriages. I can cause stillbirths  
2 or 3 babies are born every single day in the UK  
who have been affected by me  
that's nearly 1000 every year  
These babies can have hearing loss, vision loss,  
cerebral palsy and epilepsy  
At the moment, you cannot vaccinate against me  
and in the UK nobody screens for me  
So you can't stop me  
But with greater awareness, I can be outsmarted  
The more people talk, the more they will know how  
to reduce their risk of exposure to me  
The more they know, the more they can identify  
the babies I have affected  
But until you realise how vulnerable I really am,  
I am the stealth virus



Registered charity no: 1147633

With grateful thanks to Professor Paul Griffiths, author of *The Stealth Virus*,  
available from [amazon.co.uk](http://amazon.co.uk)



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# CONTENTS

Executive Summary	4
Foreword	6
Case Study: Lyra	7
The changing zeitgeist of CMV vaccines	8
Reducing CMV transmission	11
What midwives and childbearing women should know	13
Case Study: Oscar	15
Management in pregnancy	16
What the future holds	18
Conclusion	20

## EXECUTIVE SUMMARY

Around 1 in 5 babies born with cytomegalovirus, or CMV, will suffer serious consequences such as hearing loss, cerebral palsy and epilepsy. Not only does this put a huge strain on the families affected, but also on the NHS.

Currently pregnant women receive no advice about reducing their risk of infection. Educating the general public, as well as health care professionals, is fundamental to winning the fight against CMV. Through education, we can help babies receive an earlier diagnosis which will allow the opportunity for treatment. More research is also needed to develop an effective CMV vaccine.

CMV IS A  
NEGLECTED  
PUBLIC HEALTH  
BURDEN

The 'We need to talk about CMV' expert report is calling for more to be done to tackle CMV which affects more babies every year than Down's syndrome, toxoplasmosis or listeriosis.

CMV is a neglected public health burden despite representing a very real public health concern. Around 1 in 5 babies born with CMV will have problems such as hearing loss, cerebral palsy and physical impairment – placing considerable burdens on families as well as health, social and educational services.

Over past decades, one by one, the scourges of polio, measles, mumps and rubella began to be eliminated in many countries. So why in

the golden era of vaccine research has CMV been left behind? In the past it has been seen as too complex a virus. But the zeitgeist has now changed from 'if we get a CMV vaccine' to 'when we get a CMV vaccine'.

We now know more about how CMV is spread. The main way that pregnant women catch CMV is from the urine and saliva of small children. There is a growing body of research that shows that providing pregnant women with this information can

reduce the risk of acquiring CMV in pregnancy. We also know that pregnant women are highly motivated to follow preventative advice and that British women of childbearing age want to know more about CMV.

In the US, many states are legislating to mandate better education and more rapid diagnostics. Public health and professional bodies in several countries already recommend that health professionals discuss CMV with pregnant patients.

THE GOOD NEWS IS THERE'S PLENTY THAT CAN BE DONE RIGHT NOW

So how can this information be delivered effectively in the NHS? Midwives are perfectly placed to give pregnant women advice about four simple hygiene precautions. However, many will have received minimal education on CMV since their initial training. Midwife educators should prioritise continuing professional development on CMV to equip midwives with the knowledge to make a vital difference.

Even when infection in pregnancy is identified, there are many frustrations in managing it. Unlike many other infectious diseases, there are few prevention and treatment options. There is an urgent need for more research into vaccination and treatment to prevent the devastating consequences of fetal infection. In the meantime, it is important that obstetricians and other professionals involved in antenatal care improve their understanding of susceptibility, infection and transmission.

While research into CMV has traditionally lagged behind other viruses, our understanding is now evolving in more exciting directions than ever before. We also know more about the gaps in research that we need to fill and the UK is at the forefront of finding the answers. So as we near the 65th anniversary of the isolation of the human

form of this virus, might science now be close to pensioning it off?

Given the far-reaching consequences for children, families and public services this is a goal that desperately needs to be achieved. But the good news is there's plenty that can be done right now at little or no cost. GPs and midwives can advise women about reducing the risks of infection. Obstetricians, sonographers, radiographers and neonatologists can be alert to the potential signs of CMV infection in a fetus or newborn so that more newborn babies can be diagnosed and treated within the first four weeks of life. Paediatricians, and other professionals working with families, can understand the guidelines for managing CMV so that more families receive the monitoring and support their child needs.

We realise that it will take time and collaborative working to achieve the vision of fewer babies being born with CMV and better support in place for those affected. But it can and must be achieved if we are to reduce the unacceptable burden on the hundreds of young lives blighted each year through congenital CMV infection.

IT WILL TAKE TIME TO ACHIEVE THE VISION OF FEWER BABIES BEING BORN WITH CMV

## FOREWORD

CMV is a common infection that devastates lives. CMV can infect people of all ages. Most healthy adults and children experience no long-term effects from it. But it is very dangerous to unborn babies and is the most common infection passed from a pregnant woman to her baby.



Every year in the UK, CMV infection affects almost 1000 babies. It places an extra burden on the NHS, social care, welfare and education systems, as well as the children and families who live with the consequences of the virus.

Lyra is my granddaughter and as an educational professional (I am a Teacher of the Deaf) I was shocked that so few of the healthcare professionals we met had heard of CMV. Even fewer knew how to manage it. Yet CMV is not rare: it is more common than Down's syndrome and even infections that all pregnant women are warned about such as toxoplasmosis and listeriosis.

CMV Action is committed to raising awareness of this virus. Our hope is that this report, *We need to talk about CMV*, will alert prospective parents, families, healthcare professionals and those running the health service of the threat of CMV.

*We need to talk about CMV:*

- Brings together evidence demonstrating that CMV is a serious public health issue
- Sets out, for the first time, what different professionals can do now to limit the impact of this virus
- Outlines the research needed now, and in the future, including finding a vaccine for CMV

CMV Action's vision for the future is one where fewer babies in the UK are born with CMV and better support is in place for those who are affected. I hope this report will raise awareness of CMV and inspire readers to support all efforts to educate, vaccinate and eradicate this devastating virus.

We can reduce the impact of CMV. And we need to start now.

**Jan Pearman**  
Trustee and Secretary  
of CMV Action

CMV AFFECTS ALMOST  
**1000**  
BABIES EVERY YEAR

## CASE STUDY



### LYRA

Lyra was born to parents who had never heard of CMV. The pregnancy was straightforward but it was evident at birth that Lyra was a very sick baby; her parents were told she might not survive.

The doctors treating Lyra diagnosed CMV infection quickly but admitted they knew little about the infection and were liaising with specialists in London. They started treatment with anti viral drugs the day after she was born.

Scans and tests showed chronic liver damage, low platelets and extensive brain damage. Lyra's parents were told that it was unlikely she would ever walk or talk and would probably never even know they were her mum and dad. They had to come to terms with the knowledge that their daughter was severely mentally and physically disabled and medically fragile.

Blood tests showed that Lyra's mother had contracted the virus early on during the pregnancy but the infection and resulting damage had not been identified.

Lyra is now nearly 3 years old. CMV has affected her whole body. She has severe cerebral palsy. She can't roll, sit or hold her head up. She has chronic liver disease, epilepsy that is complex and difficult to control, damage to her lungs, kidneys and spleen, scoliosis of the spine, dislocated hips, feeding difficulties and more. She can't fight infection. She is blind. But she can hear and she smiles for her mum and dad. Those smiles are priceless.

**Jan Pearman**

Grandparent

# THE CHANGING ZEITGEIST OF CMV VACCINES

In 1953 a Nobel Prize was awarded for the discovery of cell culture techniques, and from this somewhat obscure and highly technical breakthrough was launched one of the most significant public health interventions in human history – the modern era of vaccination. So why in the golden era of vaccine research was CMV left behind? And how close are we now to finding an answer?



## CMV: A neglected public health burden

CMV represents a very real public health concern. This virus damages more babies than many better known infections and every year one or two in every 200 babies are born with CMV.<sup>1</sup> This makes CMV the most common infection passed from mother to her baby.

Sadly, around one in every five of these babies will have problems as a result of congenital CMV infection.<sup>2</sup> These include vision loss, cerebral palsy, epilepsy, physical impairment, as well as behavioural and learning difficulties. In addition, some 13 per cent of babies born with CMV develop hearing loss,<sup>3</sup> and at a quarter of all cases, CMV infection is the leading cause of preventable hearing loss in childhood.<sup>4</sup>

Clearly these problems can place considerable burdens on the affected child and their family. But they also place burdens on health, social and educational services. The cost to the NHS of hearing loss, for example, is significant; the hearing loss associated with CMV infection is frequently progressive, with the commonest severity being severe-profound, for which the lifelong cost of a cochlear implant is £82,000 – £108,000.<sup>5</sup>

Similarly, the cost of the provision of specialist health care for other conditions caused by CMV can be high. The total cost of care for epilepsy conditions is around £2billion in direct and indirect costs,<sup>6</sup> and

the annual recurrent cost of NICE recommended care for ADHD around £40million.<sup>7</sup> If we add to this the costs of NHS care for vision loss, cerebral palsy, developmental problems and the many other conditions caused by CMV, the total burden rises even further.

Of course, eradication of CMV will not completely remove all of these costs—since they can all be caused by other diseases—but they would at least remove an important preventable component of the overall total. Health economic assessments are needed to more accurately determine some of these burdens.

THE FUTURE MAY NOT BE NOW, BUT IT'S GETTING VERY MUCH CLOSER.

## The search for a vaccine

One by one, the scourges of polio, measles, mumps and rubella began to be eliminated in many countries. In terms of public health, CMV was an obvious early candidate for a vaccine. It damaged many more babies each year than did rubella for example, and the costs of treating the consequences are high. Unfortunately, for various reasons, a suitable vaccine was not quickly identified and researchers turned their attention to making successful vaccines against viruses like hepatitis A, hepatitis B, rotavirus and chickenpox.

Over the decades few researchers showed enthusiasm for tackling the problem of CMV. It was seen as too complex a virus because it infected each person more than once and can lie dormant or latent for years before reawakening to cause recurrent infections in some. The molecular biology of the virus itself showed it to be adept at evading the human immune system and many argued it would simply be "impossible" to make a vaccine against CMV.

Nevertheless, some investigators persisted, citing the need for evidence before giving up on such an important cause of disease. And their persistence is showing encouraging signs of being rewarded.

CMV REPRESENTS A VERY REAL PUBLIC HEALTH CONCERN

## Signs of progress

The results of three studies in particular have been reported in recent years<sup>8,9,10</sup> and, while none of the vaccines was good enough to yet offer to the general public, there are at least some signs now that there is the potential for making improvements through further development and additional clinical trials. Some of these are so-called 'Phase 1' (very early) studies, but there is now at least one vaccine in 'Phase 3' trials—the type of large-scale study from which regulatory bodies are able to determine whether the vaccine should be made available to the general public. So it seems that some progress is being made.

So is there anything that the public can do to help? The good news is that they can get involved with family members, friends and neighbours to take part in randomised controlled trials. Tens of thousands of volunteers will eventually be needed including toddlers, teenagers of both sexes and women of childbearing age. These studies take time but they will provide the best way of ensuring that a CMV vaccine is being given a fair chance to demonstrate its safety and efficacy.

How long will it take before we have a vaccine to routinely protect against the terrible effects of congenital CMV, just as we now routinely protect against the effects of measles, mumps, rubella and polio? Realistically, it will need years or even decades, and we don't know how many vaccine candidates will have to be evaluated before one is found that is good enough to be licensed. But the zeitgeist has definitely changed from when it was deemed "impossible", we now talk not of "if we get a CMV vaccine" but "when we get a CMV vaccine". The future may not be now, but it's getting very much closer.

**Professor Paul Griffiths**

Professor of Virology, University College London

**Table 1: The Zeitgeist extends beyond vaccines: key international differences between UK and the rest of the world**

## Key differences in practice in CMV between the UK and other countries

### Public education

- In the US, the Centers for Disease Control and Prevention (CDC) recommends doctors tell pregnant women about CMV and is investing in a public education programme
- The state of Utah have made CMV education mandatory and Hawaii's legislature recently took the first step in passing their proposed law on communicating the dangers of CMV to pregnant women. Similar legislation is being considered in a number of other states including Connecticut, Illinois, Tennessee and Texas
- Professional and Public Health bodies across several other countries recommend that health professionals educate women about CMV. For example, The Australian Society for Infectious Diseases (ASID) recommends CMV counselling at prenatal and antenatal appointments. In France, the ANAES (Agence Nationale d'Accréditation et d'Evaluation en Santé) and CSHPF (Conseil supérieur d'hygiène publique de France) also recommend giving information to pregnant women about CMV infection
- There are no recommendations in the UK for antenatal education

### Antenatal screening

- Testing of pregnant women is controversial and its use is not recommended in the UK or US
- However, Israel and eight European countries (France, Belgium, Spain, Italy, Germany, Austria, Portugal and the Netherlands) routinely screen the majority of pregnant women serologically for CMV.<sup>11</sup> This routine serologic screening occurs without the recommendations or guidelines of any governmental agency, authority or professional medical society

### Screening of neonates

- Screening programmes for newborns have not yet been implemented at national level in the US or Europe but there is increasing enthusiasm for this among health care professionals
- In the US, a large study is evaluating whether CMV screening should be routinely implemented and the feasibility of such a programme
- In the state of Utah CMV testing is mandatory for newborns who fail their hearing screen and other states are planning a similar approach

### Other healthcare guidelines

- In the US, the Institute of Medicine has ranked the development of a CMV vaccine as one of their highest priorities because of the lives it would save and the disabilities it would prevent. However, it may be a number of years before there is a Food and Drug Administration-approved CMV vaccine
- In the UK, health technology assessment bodies such as the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC) have no current plans to update guidelines involving CMV

## REDUCING CMV TRANSMISSION



If you were to ask people what poses the most risk to a pregnant woman and her baby out of a dirty cat litter tray, an unpasteurised cheese or a drooling toddler, most would pick the litter tray or the cheese. And yet they would be completely wrong.

When researchers first identified CMV in the 1950s—the same decade as the chickenpox and measles viruses were discovered—it heralded a golden era of viral research. But whilst this research has led to effective treatments and vaccines that are now routinely used to combat many viral illnesses, research into CMV has often lagged behind. And perhaps most worryingly, only 14 per cent of British women know what CMV is.<sup>12</sup>

So how is a virus that three in every five people<sup>13</sup> have caught at some point in their lives, actually spread?

THE MAIN WAY PREGNANT WOMEN CATCH CMV IS FROM THE URINE OR SALIVA OF YOUNG CHILDREN

Surprisingly, CMV is not that easily transmitted as it is spread only through close contact with bodily fluids. In fact, the main way pregnant women catch CMV is from the urine or saliva of young children. Younger children pose a greater transmission risk than older children: there are higher levels of virus found in their bodily fluids and they are more likely to spread these around, through drooling, mouthing toys and so on. And the virus can remain present in a child's bodily fluids for many months or even years after they have recovered from the initial infection.<sup>14</sup>

CMV can be spread through all bodily fluids—including sexual contact and medical treatments such as blood or organ transplantation—however, saliva is a particular risk. This is because CMV is present at higher levels in saliva than urine. Also, many of the behaviours that increase exposure—such as sharing food and utensils, kissing on the mouth, and wiping the face—are very common practice among mothers and their young children. And these activities also allow for direct transfer of CMV to mucous membranes.

Exposure through contact with urine mainly occurs during nappy changing. However, it is less likely to be transmitted this way than via saliva, as most women say they already clean their hands after a nappy change.<sup>15</sup>

Aren't all the people who've caught it already immune from it? Unfortunately, people who have already caught CMV do not have guaranteed protection. You can still catch a different strain or have a flare-up of the virus that's already in your body.

So how does this knowledge of the rather messy transmission of CMV help us? Although there is as yet no vaccine against CMV infection, there is a growing body of research that suggests risks can be reduced.

Research studies from the US, France and Italy have all provided evidence that providing pregnant women with counselling and clear information can reduce the risk of acquiring CMV in pregnancy – in some cases reducing the risk of acquiring CMV by up to 85 per cent.<sup>16,17,18</sup> Despite this, information about avoidance of CMV infection is not routinely provided in the NHS.

There is a long history of evidence that educational interventions can prevent congenital diseases. For example, efforts aimed at preventing fetal alcohol syndrome have reduced maternal alcohol consumption in pregnancy,<sup>19</sup> prenatal vitamin and folic acid supplementation have lowered rates of neural tube defects,<sup>20</sup> and antiviral use in pregnancy has been shown to reduce mother to child transmission of HIV.<sup>21</sup>

We also know that pregnant women are a highly motivated group who are more likely to follow CMV preventative measures than non-pregnant women,<sup>16</sup> and that women of childbearing age in the UK want to know more about CMV: in a survey of over 1,000 British women aged between 18 and 44 9 out of 10 (91 per cent) think that pregnant women should be given advice about CMV infection during pregnancy.<sup>12</sup> And after reading advice about how to prevent infection, three quarters (75%) of British women of childbearing age think that it is easy to prevent CMV.<sup>12</sup>

CMV can be prevented. While we wait for vaccines and other interventions to become available, we have evidence that CMV education may be able to effectively prevent CMV infection in pregnancy. We know that pregnant women want this information and are willing to take appropriate measures to reduce their risk of acquiring CMV infection. Our immediate priority therefore, should be finding ways in which this education can be effectively delivered to pregnant women in the NHS, at the point at which they most need it.

#### **Professor Paul Heath**

Professor of Paediatric Infectious Diseases,  
St George's University Hospitals  
NHS Foundation Trust

# 14%

ONLY 14 PER CENT OF BRITISH WOMEN KNOW WHAT CMV IS

OUR IMMEDIATE PRIORITY SHOULD BE TO EFFECTIVELY EDUCATE PREGNANT WOMEN

# WHAT MIDWIVES AND CHILDBEARING WOMEN SHOULD KNOW



The risks of childbearing women contracting CMV raises significant responsibilities for health and social care professionals in terms of prevention and management. Humans are desirable hosts and bodily fluids are a keen source of transmission of CMV.

## Don't Share, Wash with Care

- 1 Avoid placing objects in your mouth that have previously been in an infant's mouth e.g. avoid food, cup and utensil sharing, or sucking a child's dummy to clean it after it has been dropped.
- 2 Avoid kissing young children on the mouth or cheek. Instead, kiss them on the head or give them a big hug.
- 3 Wash your hands thoroughly with soap and water after coming into contact with any bodily fluids. This includes after a nappy change, or after wiping a toddler's nose or mouth.
- 4 Thoroughly cleanse items that have been in contact with bodily fluids and may have become contaminated.

So, what should health and social care professionals be doing to play their part in reducing the number of infants affected by the virus? Given the devastating consequences for the neonate from contracting congenital CMV in utero, it is imperative that both health care professionals and women receive education about reducing the risks of transmission.

## Education

Routine provision of health information is a pivotal step in encouraging childbearing women to understand how to avoid CMV transmission. Transmission of CMV occurs via bodily fluids, e.g. urine, saliva, vaginal secretions, semen, breastmilk, blood transfusions and organ transplants. Primary infection of childbearing women occurs in around 0.15–2.0% of all pregnancies<sup>22</sup> and can lead to catastrophic consequences for the infant who contracts CMV in utero. Hence, as part of routine preconception and antenatal care, midwives must provide childbearing women

with advice to reduce their risk of contamination by CMV. The simple and most effective education that midwives can offer couples planning or already pregnant involves four very simple hygiene precautions.

Education costs little and is key to reducing the spread of CMV. Education regarding CMV is aimed at reducing infant risk of developing Intrauterine Growth Retardation (IUGR), hyperbilirubinemia, hepatosplenomegaly, thrombocytopenia, and microcephaly, all of which cause serious morbidity problems and often death.

Discussing CMV with childbearing women may make some feel anxious. Nevertheless, given the catastrophic consequences for the infant of contracting congenital CMV in utero, it is imperative that both health care professionals and women receive carefully measured educational messages about its prevention.<sup>23</sup>

Education could be further strengthened by widening general public health messages about how to prevent the spread of CMV infection. For example, by teaching adults and older children thorough methods of hand hygiene and how to avoid spread between children in day care facilities. Education programmes that extend midwives knowledge about CMV are clearly required, e.g. organising study sessions for all grades of staff and increasing the amount and level of CMV education in the midwifery curriculum. Further training in prevention and management of CMV would profoundly improve long-term infant mortality and morbidity.

It is the responsibility of midwives to deliver information about CMV in a balanced way so as not to cause alarm. The spread of CMV can be avoided and whilst it is hard for busy women to avoid every potential exposure, simply improving hygiene measures can markedly reduce the risk of transmission. To this effect, CMV Action has developed a range of educational literature for childbearing women ([cmvaction.org.uk](http://cmvaction.org.uk)).

EDUCATION PROGRAMMES THAT EXTEND MIDWIVES KNOWLEDGE ABOUT CMV ARE CLEARLY REQUIRED

## Midwife education

The midwife is perfectly placed to increase delivery of CMV education to both staff and childbearing families, yet many have received minimal education on the topic since their initial training. Despite the growing body of published evidence that emphasises the importance of increasing health education in attempts to reduce CMV transmission<sup>2,11,22,23,24, 25,26,27,28</sup>, in many countries there lacks provision of directives to vital health care professionals, such as general practitioners, midwives, neonatal paediatricians and nurses about this subject. This finding sharply contrasts with education designed for delivery in relation to other teratogenic infections in pregnancy, e.g. listeriosis and toxoplasmosis, which represent far less danger to the infant. Improving education that teaches people how to avoid contamination

is key to reducing CMV spread. With this in mind, midwifery educators in the UK should consider advancing education for midwives as part of continuing professional development. For example, content of curriculum should include:

- How to prevent CMV infection spread (Don't Share, Wash with Care)
- Provide a clear definition and description of CMV signs and symptoms
- Discuss prevalence of CMV
- Discuss brutal consequences for a fetus who has contracted congenital CMV

CMV Action and The Royal College of Midwives have developed an e-learning training module to promote support further education for midwives on CMV. ([ilearn.rcm.org.uk](http://ilearn.rcm.org.uk)). It is aimed at enhancing

midwives understanding as well as increasing their confidence to counsel women about CMV and its serious consequences. Evidence supports that high quality training in prevention and management of CMV markedly reduces mortality and morbidity of fragile infant lives.

To conclude, educating women to diminish CMV risk is enormously important if midwives are to make a difference. Clearly a lot is yet to be tackled if we are to eradicate CMV risk and spread. In essence, the key variable for reducing CMV transmission involves straightforward hygiene measures.

**Professor Caroline Hollins Martin**

Professor in Maternal Health, Edinburgh Napier University

## CASE STUDY



### OSCAR

After trying for a baby for two years, we luckily became pregnant with our first child just two days before we signed the paperwork to undergo IVF treatment. A lucky miracle I called it.

I'd spent so much time looking into fertility and how difficult getting pregnant can actually be!

I'm also a midwife of eleven years, with experience mostly on the labour ward but also in teaching and more recently community, so seeing people everyday and them telling me their 'lucky' stories of falling pregnant made my two years very long indeed.

However, we were lucky, we had no bleeding, no blood pressure issues, the Down's syndrome screening came back very low and, despite sickness that lasted until 22 weeks and horrendous heartburn, I couldn't complain!

My midwife started measuring me at 26 weeks when she picked up that I was SFD (small for dates.) I also never felt my baby move.

I started undergoing serial growth scans. I send my own patients for these all the time and they generally come back fine, so I wasn't worried. My consultant did a TORCH blood screen for infections. The TORCH screen is a group of blood tests that check for several different infections in a newborn. TORCH stands for toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and HIV, but it can also include other newborn infections.

Well I knew I was fit and healthy and didn't have any infections, but it's only a blood test, so why not?

That's when my world crumbled. I had contracted CMV at some point during the first trimester, meaning my baby could be infected, although the doctors reassured us our baby may not be 'affected'. Whilst I'd heard of it, I had never known anyone who had had CMV. How on earth had I picked this up? Where had it come from? This was my fault. Of course I've since gone on to read about how it is contracted and with all my work with families and children, who knows where it came from?

We started googling and found that he may have some learning disabilities or mild hearing loss, not a problem we thought.

The consultant suggested an amniocentesis, which we had at 33+1 weeks. We also had a brain scan which now showed ventriculomegaly, some brain abnormalities. We then went onto have an MRI scan at the John Radcliffe Hospital in Oxford. Our baby was diagnosed with severe CMV, there was poor growth, enlarged liver / abdomen, a small head and no brain activity at all.

Our beautiful baby, Oscar William, was stillborn at 33+6 weeks, on 9th March 2015, my shining star.

His death is still, obviously, fresh and everyday is a struggle, from simply watching baby adverts on TV, to seeing friends with babies or looking through Oscars' photos.

I'm now on maternity leave and want to raise more awareness and support CMV Action as much as I can.

**Sharon Robinson**

Midwife

## MANAGEMENT IN PREGNANCY

Clearly there is a need for more research into vaccination and treatment to prevent the devastating consequences of this infection to the unborn baby. In the meantime it is important that obstetricians and other professionals involved in antenatal care improve their understanding of this infection, and counsel pregnant women accordingly.



There are many frustrations in the management of CMV infection in pregnancy. Unlike many other infectious diseases—such as rubella (German Measles), toxoplasmosis and chickenpox—there are few prevention and treatment options for CMV.

CMV is the largest of the Herpes virus family. Like all Herpes viruses, a first or 'primary' infection can occur at any time, but it may also remain 'latent' to be re-activated later in life. This can happen for example in someone whose immune system is suppressed, or if they have experienced a stressful stimulus, in which case it is known as a 'secondary' infection.

Estimates vary by ethnic group, but overall around three out of every five people<sup>13</sup> in the UK have been infected with CMV at some point in their life, usually early on.

This leaves around two in every five pregnant women susceptible to a primary infection, and between one and four out of every hundred pregnancies will see a mother infected by CMV for the first time.<sup>29</sup> Of those who become infected when pregnant, almost a third (32 per cent)<sup>30</sup> will transmit the infection to their unborn baby. Once infected, up to 15 per cent<sup>2</sup> of unborn babies will show signs of disease, and a similar proportion of babies who have no symptoms at all will go on to develop permanent problems,<sup>2</sup> of which the most common is hearing loss.

# 32%

WILL TRANSMIT THE INFECTION TO THEIR UNBORN BABY.

PUBLIC HEALTH MEASURES ARE URGENTLY NEEDED TO REDUCE THE RISKS OF INFECTION

CMV infection during pregnancy is most often suspected and diagnosed when an ultrasound scan shows suspicious features. These include the baby being small, with low amniotic fluid (oligohydramnios), echogenic (bright) kidneys and in some cases brain abnormality (usually water on the brain or hydrocephalus). Such cases are usually referred to a specialist fetal medicine centre where a detailed scan can be performed by an expert. Since testing the mother's blood can produce inconclusive results, the majority of experts will want to perform an amniocentesis test to identify CMV DNA, and also look for other signs such as a low platelet count in the baby's blood.

In such cases, treatment options are limited, and even when treatment is administered it may not prevent damage to the baby. The use of antiviral medicines such as ganciclovir (either by treating the mother or directly into the baby by in-utero transfusion) may reduce the amount of circulating virus, and improve platelet count and liver function tests in the baby. However once damage has occurred it is unlikely to be reversed. Currently there is little high quality or definitive evidence on the most effective ways to treat CMV infection in pregnancy. There have been no randomised controlled trials proving that antiviral treatment works and reduces handicap rates, and more research studies are urgently needed.

Routine screening for CMV during pregnancy is not performed in the UK. The National Screening Committee has recommended against CMV screening in the antenatal period, because there is uncertainty about the risk to the baby when maternal infection is diagnosed and because the effectiveness of treatment has not been confirmed. However, the consequences of this infection in pregnancy can be devastating. Public health measures are urgently needed to reduce the risks of infection in high risk individuals in particular (for example pregnant health care workers, teachers, and women with young children), and all pregnant women should be routinely counselled about the need for hygiene and avoidance of contact with small children's saliva and urine during pregnancy.

In reality, however, it is hard to avoid every possible exposure, and there is certainly a need for more research into the development of vaccines which could be safe and effective in women of reproductive age. In the meantime, more understanding of the pathogenesis of susceptibility, infection and transmission to the unborn baby during pregnancy can only help in improving outcomes in this little-known but potentially devastating disease process.

### Professor Mark Kilby

Clinical Scientist and Honorary Consultant in Fetal Medicine, Birmingham Women's Foundation Trust

## WHAT THE FUTURE HOLDS

While research into CMV infection has traditionally lagged somewhat behind that of other viruses, our understanding is now evolving in more exciting directions than ever before. In addition, we know more about the gaps in research that we need to fill. So as we near the 65th anniversary of the isolation of the human form of this virus, might science now be near to pensioning it off?



Recent years have seen important steps forward in CMV research, both in the UK and around the world, with studies planned or underway across the entire spectrum of the infection, from diagnosis and screening, through to transmission, treatment and prevention. Yet important gaps in our understanding still exist and the UK is very much at the forefront of finding the answers.

### Identifying and treating CMV infection

Much of the research in the UK has focussed on diagnosis and treatment. Hearing loss at birth is one of the most common symptoms of CMV. Yet some CMV babies who fail their newborn hearing screen are not diagnosed with CMV in time to start antiviral treatment, which must happen in the first month of life in order to limit further deterioration of hearing.

To address this issue, a series of studies in the UK (BEST1 and BEST2) has explored the benefits and feasibility of

integrating testing for CMV within the existing newborn hearing screening programme. Results from these studies have shown that testing for CMV is both acceptable to 97 per cent of parents, and feasible in 'real life' practice.<sup>31</sup> Newborn hearing screeners felt confident in performing the tests and were able to screen around eight out of every ten babies referred for further hearing assessment.<sup>32</sup>

Research in this area is emerging in ever more innovative directions, including development of an easy to use test to diagnose CMV that

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uses nanotechnology – a high tech yet low cost device that could enable even more babies to be tested and diagnosed.

The picture on CMV treatment for newborns is evolving rapidly. A US/UK collaboration reporting in 2013 published evidence on the benefits and risks of oral antiviral medicines and showed that longer treatment could result in improved outcomes compared to shorter treatment.<sup>33</sup> In addition, further research is now underway that will explore the benefits of oral antiviral treatment for children with sensorineural hearing loss and congenital CMV up to the age of 4 years. This could mean that more children have the option of treatment, which is especially important for those who develop hearing problems later on.

### Where to next?

Research has come a long way in recent years, yet some important knowledge gaps remain. Currently several early studies are looking at new approaches in treatment, such as immunoglobulins and antiviral medicines,<sup>34,35,36</sup> as well as the ways of reducing transmission from an infected mother to her unborn child.<sup>34</sup> Clearly, while some of this research appears promising, we need results from larger randomised studies to confirm initial findings.

In addition, we need to know more about the overall impact of this infection and where we should focus our efforts in combating it. The Life Study—the largest ever UK-wide cohort study of babies and young children—will look at the burden of disease of congenital CMV and assess which women get infected

or re-infected. We also need to know which babies with infection at birth are more likely to have long-term disease, can we predict those destined for hearing loss? And do babies with less severe symptoms of disease receive the same benefits from treatment as those who do not?

We know that, ultimately, preventing CMV depends on developing a vaccine. There is a clear need for more clinical trials of potential vaccine candidates.

So while we wait for the answers to these questions, our focus should be on two things: diagnosis and education.

First, we have shown that babies who are at risk of CMV-related hearing loss can be tested for CMV quickly and easily within the NHS. We now need a larger-scale implementation study to fully assess the potential costs and savings, so that NHS commissioners have the information they need to make decisions about improving neonatal pathways.

Second, there exists a substantial body of international evidence showing that educating pregnant women about CMV can reduce infection in pregnancy. We know education works, we now need to explore how CMV education can most effectively be delivered within the NHS.

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## CONCLUSION

As the evidence in this report shows, the burden of CMV infection is high and the consequences far reaching. There is much that needs to be done if we are to achieve CMV Action's vision of fewer babies born with CMV and better support in place for those affected. But the good news is there's plenty that can be done right now at little or no cost.



CMV Action are recommending a number of minimum standards of care for pregnant women and babies affected by CMV (see box). These minimum standards of care can be introduced as soon as today. Experts attending an international CMV conference in Brisbane in May 2015 agreed unanimously that CMV counseling should be given to all pregnant women. Government and professional bodies in many countries such as the US, France, Australia and the Netherlands already recommend that this happens. However advice on CMV prevention is not routinely given within the NHS.

Most of the minimum standards of care that families with a baby affected by CMV should expect from health professionals can also be introduced immediately.

Over the longer term it is also important to address other aspects of CMV:

- **Managing infection in pregnancy:** The UK National Screening Committee recommends against systematic population screening for CMV in pregnancy. However individual cases will still be identified in the course of routine antenatal care. Each health community should therefore develop and implement local guidelines for:
  - Testing for CMV should there be suspicion of infection.
  - Management and monitoring when infection during pregnancy is detected.
- **Diagnosing CMV in newborns:** Research into treatment and diagnostic technology is underway. As new evidence emerges the National Screening Committee should review its position on universal newborn screening.
- **Managing CMV after diagnosis:** Health professionals such as audiologists, paediatricians and neurologists, who are working with families, should ensure that monitoring appointments occur at recommended intervals.
- **Identifying late-onset problems:** Early years professionals and support workers must be aware of the particular risk CMV brings of late-onset and progressive hearing loss. They need to know how and when to monitor, and how they can assess whether hearing loss is caused by CMV.
- **Tracking longer-term outcomes:** Our understanding of congenital CMV is still limited and there is an urgent need to monitor treatment and longer-term outcomes on a central UK database.

## Minimum standards of care for pregnant women

### GPs should:

- Advise women trying to conceive on how to reduce the risk of CMV infection in the same way as they recommend folic acid before conception
- Advise pregnant women on how to reduce the risk of CMV infection in the same way they give advice on reducing the risk of food and animal-borne infections

### Midwives should:

- Alert all the women booking with them to the dangers of CMV infection: how it spreads and how to reduce the risks, in the same way as they already advise about food and animal-borne infections
- Support women with specific concerns about CMV enabling them to access support locally

### Radiographers, sonographers and obstetricians should:

- Be alert to indicators that suggest a higher risk of CMV, such as fetal anomalies, and take appropriate action

## Minimum standards of care for babies affected by CMV

Local health systems should ensure that guidelines and pathways are in place for testing, diagnosis and management of CMV. These would include:

- Midwives, obstetricians and neonatologists should know the potential signs of congenital CMV in a newborn baby
- A CMV test should take place as soon as hearing loss is confirmed and systems must be in place that make it possible to confirm or exclude CMV diagnosis within the first four weeks of life, so that treatment can be considered
- The standard newborn hearing screen therefore needs to take place within a timeframe which allows diagnosis of congenital CMV within the first four weeks of life
- Following a diagnosis of CMV, families should have access to a paediatric infectious diseases specialist to discuss treatment
- Newborn Screening Laboratories should retain Guthrie cards (dried blood spots) for as long as possible but at least the minimum period of five years. This is to enable the diagnosis of congenital CMV in children who may present with problems during childhood, adolescence and as a young adult
- The healthcare professional that is a family's key point of contact must have knowledge of the evidence-based guidelines for managing CMV

There are also steps that can be taken at a national level. Public Health England should recognise CMV as a serious public health issue and support work on public and professional education, in the same way that the Centers for Disease Control and Prevention (CDC) does in the US.

Research from other countries shows that implementation of guidelines can be hampered by lack of detailed knowledge of CMV. This is why, alongside this report, CMV Action is launching training for midwives and will invest in training for doctors and other professionals in future. Bodies responsible for professional training should also do more to ensure that doctors and midwives are confident in their knowledge of CMV prevention, transmission and management.

The National Institute for Health Research should support research into the prevention, detection and optimal management of congenital CMV.

We would also like to see an increase in research to develop an effective CMV vaccine.

We recognise that our vision cannot be realised overnight, that it will take time and collaborative working to deliver. But it can and must be achieved if we are to reduce the unacceptable burden on the hundreds of young lives blighted each year through congenital CMV infection.

Let's start that process now.

**Caroline Star**  
CMV Action Chair

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