



AMMF

THE CHOLANGIOCARCINOMA CHARITY

Cholangiocarcinoma Awareness Month
February 2013

“Facctoids”

posted daily on AMMF’s Facebook page
throughout the month

www.ammf.org.uk

CC DAY 1 Facctoid: *What is it?*

Cholangiocarcinoma (which may be abbreviated to CC, or more frequently in the US, CCA), is a cancer that arises in the bile ducts in or around the liver. Diagnoses fall into 2 main categories:

Intrahepatic – affecting bile ducts within the liver

Extrahepatic – affecting bile ducts outside the liver

Hilar (or Klatskin tumours) arise at the junction of the left and right hepatic ducts, and are therefore anatomically extrahepatic, although these were reclassified in 1995 as intrahepatic, which has caused some debate.

The incidence of CC is rising, with intrahepatic seeming to show the largest increase –currently it is not known why this is happening.

CC DAY 2 Facctoid: *Cholangiocarcinoma by numbers: the epidemiology*

Worldwide, CC is the second most common cancer arising in the liver. The numbers of new cases per year and annual deaths from CC have risen steeply and steadily across the world over the past few decades. Latest available figures (CRUK 2009) show that CC is now the cause of some 1800 deaths per annum in the UK alone, with approx equal numbers of men and women.

Although published statistics show this disease occurring mostly in those over the age of 60, it seems to be increasing across all age groups including much younger people. The cause of this ongoing rise is currently unknown and is not explained by improvements in diagnosis techniques.

CC DAY 3 Facctoid: *The cause of CC is unclear ...*

In the western world the exact cause of CC is unclear – most cases of CC are sporadic. Established risk factors, including some illnesses that cause chronic damage to the liver and/or bile ducts, and possibly a small genetic predisposition, are thought to account for less than 30% of all cases. Primary Sclerosing Cholangitis (PSC), is the commonest known predisposing cause.

Other recognised risk factors include gallstones which have remained in the bile ducts for a long time; cysts in the bile ducts; and exposure to certain toxins. Newly discovered likely risk factors include obesity, diabetes and fatty liver disease.

However, most of the people with CC have none of the risk factors mentioned, so studies into the causes are a vital area of research.

FIND OUT MORE...

CC DAY 4 Facctoid: *Thailand has the world's highest CC incidence*

Cholangiocarcinoma is particularly prevalent in South East Asia, with Thailand having the world's highest incidence. Unlike in the western world where the cause is generally unknown, here the cause is the wide spread consumption of raw fish infected with a liver fluke (*Opisthorcis*). Once eaten, the flukes accumulate in the bile ducts of the human host, causing infection and the onset of cancer.

Researchers from Imperial College London are collaborating with Khon Kaen University, Thailand, on the exciting idea that a test to diagnose CC from checking the urine alone may be found. Initial results are looking very promising and this work is to continue.

To read more about Imperial's work in Thailand, and AMMF's involvement, see the section, "Biomarker Work/Thailand" under the following link:

FIND OUT MORE...

CC DAY 5 Facctoid: *CC's symptoms can be vague ...*

Because cholangiocarcinoma (bile duct cancer) arises from the bile ducts, either within the liver or after the main bile duct leaves the liver and links the liver to the duodenum, the commonest symptoms are due to blocking of the flow of bile in the bile ducts – jaundice (yellowing of the eyes and skin), often in association with dark urine or pale stools, a pain or ache under the right ribs, and sometimes itching. There may also be unexplained weight loss, general malaise and fatigue.

Whilst several of these symptoms can be non-specific and could be caused by benign conditions, they do require urgent assessment (especially where jaundice is present).

CC DAY 6 Facctoid: *CC can be very difficult to confidently diagnose ...*

Currently there is no single simple test that conclusively proves a diagnosis of cholangiocarcinoma. Even with a combination of patient's history, clinical examination, blood tests for cancer "markers", imaging scans (ultrasound, CT and MRI), and endoscopy techniques (ERCP) being used, CC can still be very difficult to confidently diagnose.

Research work is now underway looking for new and specific markers of the cancer in CC patients' urine, blood and bile, and into newer types of scans and endoscopy that will allow closer examination within the bile ducts.

For an update on the work on biomarkers in bile and blood click on the link:

FIND OUT MORE...

CC DAY 7 Facctoid: *Surgery is the only potential cure for CC*

Surgery to totally remove the cancer is currently the only curative treatment for patients with CC and is only successful if performed when the CC is confined to a small area. Unfortunately, by the time most patients are diagnosed, the cancer is too advanced. For this reason fewer than one third of those diagnosed with CC will be able to undergo surgery.

Professor Brian R Davidson (Consultant HPB and Liver Transplant Surgeon, University Department of Surgery, Royal Free Hospital and Professor of Surgery, Head of HPB and Liver transplant Research, UCL) recently wrote an article for AMMF giving his viewpoint on the current situation re surgery for CC and his hopes for the future.

To read this, go to the link:

FIND OUT MORE...

CC DAY 8 Facctoid: *PVE may be used before surgery ...*

A major aim of the surgery for CC is to obtain complete cancer resection (called an R0 resection), as this gives the best possible chance of cure. One of the important developments regarding liver surgery is individualising the surgical approach dependent on the extent of an individual patient's cancer. This individualised plan allows safe surgery, whilst giving the best possible chance of achieving a complete resection.

As part of this planning, the volume of liver which will be left after surgery is measured by a special computer programme. If there will be a low volume left, then pre-operative occlusion (blocking) of a branch of the vein supplying blood to the part of the liver to be removed can be done by the radiology team through a small skin puncture. This is a safe method for allowing the future liver remnant to grow prior to the surgery, and is known as portal vein embolisation (PVE).

FIND OUT MORE...

CC DAY 9 Facctoid: *There are other treatments ...*

Stents:

If surgery is not an option, there are several other types of treatment which, although not curative, can help control symptoms and delay progression of the cancer and/or its effects on the body. These include placing a "stent" into the bile duct to hold it open and relieve the blockage to the flow of bile.

According to the recommendations of the recently published "Guidelines for the Diagnosis and Treatment of CC in the UK", initial stent insertion should be the plastic or covered SEMS* type, and if the initial stent becomes blocked then replacement with a metal stent is favoured. For full, up to date information on stents (including metal v plastic, covered v uncovered and complications), see pages 8/9 of the Guidelines.

* SEMS – self-expanding metal stent

FIND OUT MORE...

CC DAY 10 Facctoid: *There are other treatments ...*

Chemotherapy:

If surgery is not an option, there are several other types of treatment which, although not curative, can help control symptoms and delay progression of the cancer and/or its effects on the body. These include chemotherapy.

The Gemcitabine/Cisplatin combination for those with inoperable CC, (locally advanced or metastatic inoperable CC) – Following the success of the ABC range of trials here in the UK, the combination of the chemotherapies Gemcitabine and Cisplatin showed significant survival advantage without the addition of substantial toxicity. This combination has now been established as the standard of care in unresectable CC.

There have been encouraging reports of several patients being successfully downstaged with neoadjuvant chemotherapy and so becoming operable.

There is detailed information re the Gem/Cis combination in the new Guidelines (available as a download from AMMF's website). And to hear Dr John Bridgewater, lead on the ABC trials, talk about the Gem/Cis combination, go to the video link on AMMF's website:

[FIND OUT MORE...](#)

CC DAY 11 Facctoid: *There are other treatments ...*

The BILCAP trial:

Although there is currently no published evidence to support chemotherapy treatment following surgery for CC, the long running BILCAP trial is currently underway, and is expected to report in 2014.

The primary aim of the trial, involving people who have had surgery for biliary tract cancer (CC or gallbladder carcinoma), is to see if the chemotherapy capecitabine will extend survival compared to surgery alone, the effect of the treatment on the percentage of people surviving for five years or more after their diagnosis, and on the length of time before the cancer returns. If it can be shown that the drug treatment has a positive effect on any of these, it could lead to a change in the way CC patients are treated here in the UK and internationally.

AMMF has given several grants to help support this important trial. For a more detailed explanation of the BILCAP trial, and AMMF's involvement, click on the 'Find out more' link:

[FIND OUT MORE...](#)

CC DAY 12 Facctoid: *There are other treatments ...*

Radiotherapy:

If surgery is not an option, there are several other types of treatment which, although not curative, can help control symptoms and delay progression of the cancer and/or its effects on the body. These include stenting, chemotherapy and radiotherapy.

Whilst there is currently no published evidence to support the routine use of radiotherapy for inoperable CC, nor for its use post operatively, it may have important palliative value, eg for localized metastases.

(Comment on treatments such as Radiofrequency Ablation (RFA), Photodynamic Therapy (PDT), Cyberknife and NanoKnife to come ...)

See “Guidelines for the diagnosis and treatment of CC in the UK: An update”

[FIND OUT MORE...](#)

CC DAY 13 Facctoid: *There are other potential treatments ...*

Radiofrequency Ablation (RFA):

Surgeons and engineers at Imperial College London have devised a new device which can deliver radiofrequency ablation (RFA) within the bile ducts of patients with advanced CC.

Recent small studies have been promising – showing this is safe and potentially effective in keeping the bile ducts open longer, and may improve longevity and symptoms. Imperial College has now entered into a collaboration with the Mayo Clinic in the US to develop this further.

For more information on RFA, click on the link.

[FIND OUT MORE...](#)

CC DAY 14 Facctoid: *There are other treatments, but ...*

Photodynamic Therapy (PDT):

The current situation with PDT is somewhat confusing. In an early trial in Germany, 39 patients with inoperable CC were randomized to stenting alone or stenting and PDT – the PDT group showed significantly better results. However, when this was further evaluated in a larger UK trial (Photostent-02), those early results were not borne out.

Based on that evidence, the recommendation in the recently published updated Diagnosis & Treatment Guidelines is, “Photodynamic therapy cannot be recommended for routine use based on the most recent data.” (The Guidelines are available to download from AMMF’s website.)

AMMF asked Dr Shahid Khan of Imperial College London, lead on the Guidelines, to comment on this decision:

“The PDT trial is an example of why it takes a long time to make significant advances in clinical research ... This is why it is absolutely crucial that any new diagnostic test or therapy is robustly validated by other groups before being allowed to become mainstream. ...”

(It has to be remembered that here in the UK, the use of treatments/drugs is only allowed based on hard evidence following properly formulated clinical trials.)

Link to Photostent-02 trial report:

FIND OUT MORE...

CC DAY 15 Facctoid: *Other potential treatments, but ...*

CyberKnife (stereotactic radiotherapy):

This recent development in radiotherapy technology works very differently from conventional radiotherapy machines. The robotic arm and image sensors can track a moving target allowing for hundreds of beams of radiation from a wide variety of angles to be delivered with pinpoint accuracy.

This equipment is now being installed in several private and NHS locations* in the UK and there are plans for it to be available for patients with hard-to-treat tumours in the prostate, pancreas, lung, spinal cord, head and neck, and liver.

We understand it has been used in the Mayo Clinic in the USA to treat cholangiocarcinoma, but we are still awaiting news on whether this will be available to suitable cholangiocarcinoma patients in the UK.

(Currently, where it is recommended, CyberKnife treatment on the NHS is provided on a case-by-case basis only, with an application having to be made to each patient’s local primary care trust (PCT) for individual funding. CyberKnife treatment is available privately.)

*eg Barts, The Royal Marsden, Mount Vernon

FIND OUT MORE...

CC DAY 16 Facctoid: *Other potential treatments, but ...*

NanoKnife:

This is described as “focal treatment for advanced tumours”. It is being pioneered at Imperial College London as a treatment of advanced cancers unsuitable for conventional ablation techniques. The Nanoknife applies electricity through needles inserted into the tumour under image guidance. It's precise in its area of tumour destruction and does not damage nearby important structures, making it a promising treatment for tumours close to blood vessels and bile ducts.

AMMF has been in touch with Professor Edward Leen of the Imaging Department, Hammersmith Hospital, who commented:

“For cholangiocarcinoma there is potential application for small (<3cms) non-surgically resectable cases with no metastases. There is also potential benefit of combination with chemotherapy due to its mode of action – which allows better drug delivery through nanopores.”

Professor Leen further commented, “We have had great results in general ... The limitation is funding ...”

There are currently no clinical trials of NanoKnife treatment for cholangiocarcinoma. The NanoKnife is not available through the NHS, although the Princess Grace Hospital London offers the service privately.

AMMF hopes to meet with Professor Leen soon to discuss this promising treatment further, and the possibility of setting up a clinical trial.

For further details on the NanoKnife, click on the link:

FIND OUT MORE...

CC DAY 17 Facctoid: *Other potential treatments, but ...*

Given the poor prognosis of CC and the lack of curative treatment options, the development of new therapies is clearly an important area of research.

More research is needed here in the UK to further assess the value of therapies for CC such as:

Radioembolisation – this involves the use of radioactive microspheres (Yttrium-90) which are delivered directly to the tumour. The radiation travels only about 4mm in the tissues and does not cause any significant radiation outside the patient. Good results have been shown in other countries ...

TACE (Transcatheter Arterial Chemoembolisation) – this involves chemotherapy being injected into the hepatic (liver) artery that supplies the liver tumour. Again good results have previously been shown elsewhere ...

The recently updated CC Guidelines makes mention of these treatments and their, “emerging role ... in intrahepatic CC...”, and makes the somewhat confusing statement that further clinical trials “should be considered if appropriate.”

FIND OUT MORE...

CC DAY 18 Facctoid: *Liver transplantation for CC ...*

The Mayo Clinic in the US has for some time shown very positive results with their programme of liver transplantation for CC, albeit with very carefully selected patients who are subjected to a stringent pre-transplant treatment protocol. (Five year survivals of over 70% of these patients has now been reported.)

In the autumn of 2011, Dr Shahid Khan and Dr Chris Wadsworth of Imperial College London, visited the Mayo to study this first hand. Although very impressed, Dr Khan commented, “... transplantation for CC is unlikely to be used routinely in the UK or Europe until further studies on its effectiveness have been shown in other centres.”

Later in the summer of 2012, opinion had changed somewhat, with the new Guidelines for the Diagnosis and Treatment for CC (UK) stating in its recommendations, “Increasing data suggest that liver transplantation for CC can be successful in rigorously selected patients undergoing neoadjuvant therapy in highly specialised centres.”

Hopes were then raised that a UK trial for transplantation would be forthcoming. Professor Brian Davidson, in his “Viewpoint” article written for AMMF, expressed the opinion that there is a need for centres of excellence for CC treatments, and that such centres, “... need to be part of or linked with a Liver Transplant Unit as the results for liver transplantation following chemotherapy and radiotherapy for unresectable CC (The Mayo Clinic Protocol) have been improving steadily and require to be evaluated in the UK.”

However, it seems there is still no UK trial on the near horizon. Amongst the reasons given:

- insufficient liver organs for current needs
- no-one outside the US has yet replicated the US data
- the Dublin transplant unit trial showed poor results
- far more expensive than standard transplantation

AMMF will keep asking the questions ...

Click on the link for “Current thoughts ...” as at February 2012:

FIND OUT MORE...

CC DAY 19 Facctoid: *Research is needed ...*

AMMF is committed to encouraging and supporting research into cholangiocarcinoma. Recent grants include:

Research Fellowship – Imperial College London

AMMF agreed to fund a Research Fellowship for Dr Abigail Zabron at Imperial College for a year beginning October 2011, and a further grant was agreed during 2012 to secure a second year.

To read Dr Zabron's CC biomarker research update (2012) click on the link:

[FIND OUT MORE...](#)

Dr Zabron was awarded the Dame Shelia Sherlock travelling fellowship in Hepatology 2012, which enabled her to spend a month at the Mayo Clinic, Minnesota, USA, last autumn.

Whilst there she was able to develop a valuable research collaboration in biomarker research between the Mayo and Imperial College, and she was also able to observe the work being done with the Mayo's successful programme of liver transplantation for carefully selected CC patients.

After her visit, Dr Zabron commented, "... spending time with other doctors determined to beat this insidious disease has only strengthened my resolve to do just that, and my belief that this is achievable."

And that is certainly good to know.

To read Dr Zabron's Mayo visit report, prepared for AMMF, click on the link:

[FIND OUT MORE...](#)

CC DAY 20 Facctoid: *Research is needed ...*

AMMF is committed to encouraging and supporting research into cholangiocarcinoma. Recent grants include:

Biomarker Research / Thai Collaboration

Early in 2013 a grant was agreed and has been allocated, to assist with the continuation of Imperial College London's promising collaborative work with Thailand on the urinary biomarker. (This work, looking at creating a urine dipstick which can detect the presence of CC early and accurately, could have enormous implications worldwide.)

For more information on the urinary biomarker work, see the links to the right:

[FIND OUT MORE...](#)

[FIND OUT MORE...](#)

CC DAY 21 Facctoid: *Research is needed ...*

AMMF is committed to encouraging and supporting research into cholangiocarcinoma. Recent grants include:

BI-010 Biomarker Work / Cambridge Research Institute

During 2012 a grant was made to Dr Hayley Whitaker at the Cambridge Research Institute, to enable the promising work on the BI-010 biomarker to be pursued.

If successful, this would not only provide a diagnostic biomarker but would also offer a way of monitoring response to treatment with a simple blood test.

To read more about this research, click on the link:

[FIND OUT MORE...](#)

CC DAY 22 Facctoid: *Research is needed ...*

AMMF is committed to encouraging and supporting research into cholangiocarcinoma. Recent grants include:

The BILCAP Trial

AMMF has continued to help support CRUK's important BILCAP trial – several grants have been given to date.

BILCAP is a randomised trial open to those who have had a resection – comparing surgery followed by capecitabine chemotherapy with surgery alone for CC or gallbladder carcinoma. It is building on results from other studies in an attempt to give robust, practice-changing evidence for the effectiveness of using chemotherapy after surgery.

For further information on the BILCAP trial and AMMF's involvement, click on the link:

[FIND OUT MORE...](#)

CC DAY 23 Facctoid: *Research is needed ...*

AMMF is committed to encouraging and supporting research into cholangiocarcinoma – to support the researchers working on our behalf to find those desperately needed answers. We know research can be incredibly expensive but, to give a little perspective, here are a couple of examples of the costs involved in current CC research:

£10 to collect and store a biofluid sample

£50 to analyze this for clues to causation and finding new markers

If you would like to help us find those answers, please donate to AMMF

[DONATE
HERE](#)

CC DAY 24 Facctoid: *New Guidelines should improve CC management ...*

For the first time in over ten years a group of experienced liver specialists have pooled their expertise and produced a document based on all available and most up to date evidence based information re CC: “Guidelines for the Diagnosis and Treatment of Cholangiocarcinoma (UK): An Update”

These guidelines are intended to:

- give full details, pros and cons and recommendations, on every aspect of CC from risk factors and diagnosis, through to every available treatment.
- bring about consistency and improvement in the management of CC, from first suspicion onwards
- give those diagnosed with it a more equal chance wherever they happen to live in the UK.

AMMF was extremely pleased to be involved with the guidelines.
To read more about them and to download a copy, click on the link:

FIND OUT MORE...

CC DAY 25 Facctoid: *CC care should be by experienced multi-disciplinary teams (MDT's) ...*

In caring for CC patients, the new Guidelines (available from AMMF's website) state, “A multidisciplinary approach is recommended, and these often complex cases should be managed in specialist centres with the relevant experience.”

And NCAT (National Cancer Action Team) has set out the pathway to diagnosis and treatment of the rare cancers as, “GP for referral – general/district hospital for diagnosis – specialists/specialist centre for treatment”.

In AMMF's experience this pathway is often not followed – many patients diagnosed with cholangiocarcinoma do not get referred to those specialists/specialist centres for their treatment. AMMF feels strongly about this and has raised the issue with Professor Sir Mike Richards. To see the on going series of correspondence, follow the link:

FIND OUT MORE...

CC DAY 26 Facctoid: *CC treatment varies from country to country ...*

There is often considerable confusion over the treatment paths for cholangiocarcinoma that seem to differ from country to country, eg, treatments and drugs used in the US may differ from the UK, perhaps as US clinicians are allowed more freedom to prescribe what they believe is best, at times without an evidence base, whilst here in the UK there is little room for manoeuvre – NICE dictates what may be used based on hard evidence...

We believe CC is a disease that will benefit from cooperation globally. It is, therefore, very welcome news that when The International Liver Cancer Association (ILCA) decided to produce their first ever International Guidelines on liver cancer they chose to do this on cholangiocarcinoma.

The CC International Guidelines have now been prepared by an expert panel including GI specialists from the USA, Korea, Spain, Germany, and from the UK – Dr Shahid Khan, one of AMMF's advisors, and Dr John Bridgewater – and were sent for peer review to the Guidelines Committee of the ILCA a couple of weeks ago.

Once approved and published, a copy of the International Guidelines will be available on AMMF's website.

[FIND OUT MORE...](#)

CC DAY 27 Facctoid: *CC's statistics are tough ...*

- It's the second most common liver cancer in the world
- The incidence is increasing, and we don't know why
- It can be difficult to diagnose clearly and accurately
- Most diagnosed too late for potentially curative surgery
- Chemotherapy is used, but is not curative
- Only 5% will survive one year from CC diagnosis

CC is, in so many cases, a devastating cancer. We know early diagnosis and surgery can give good results, but clearly there is a great need for far more awareness and for ongoing research, especially to find ways to achieve better and clearer early diagnosis. AMMF is currently supporting biomarker research which it is hoped will give us some of the desperately needed answers.

[FIND OUT MORE...](#)

CC DAY 28 Facctoid: *We need to know more ...*

Things are beginning to move in the right direction, albeit slowly. We now know:

- Research is happening
- National Guidelines have been published
- International Guidelines are on their way

But there is a need to know and understand much more about CC, so, working with Dr Shahid Khan of Imperial College London, lead author on the UK Guidelines and one of AMMF's advisors, AMMF is producing an ongoing series of articles written for and contributed to AMMF by leading specialists. These articles are intended to give an up to date viewpoint on CC diagnosis, treatments and research from those at the forefront of each area.

To read the Specialist Viewpoints (or cholangiocarcinoma as they see it) click on the link.

[FIND OUT MORE...](#)

CC Day 28 +1 Facctoid: *CC AWARENESS MONTH IS OVER!*

Cholangiocarcinoma Awareness Month may now be over (and we sneaked in an extra day!) BUT CC awareness raising doesn't end today ...

To quote part of Tom's Guest Post from CC Day 1, "... AMMF has a goal, a goal to reach as many people as possible and make them aware of the devastating disease that is cholangiocarcinoma ..." This month has certainly seen a big step towards that goal.

Huge thanks go to everyone who bravely took part in radio and press interviews during the month (with more to yet come) – such a great way to get the CC message across.

Thanks to all our FB friends, too. There have been days during February when the figures of those reached with AMMF's page were astronomical!

Special thanks, of course, have to go to all those who had the courage to take part in our FB Guest Post feature – we've shed tears over the incredible stories of love, courage and support from those currently undergoing treatment and those who have lost precious people to CC. But we've rejoiced, too, reading our "survivors" stories – who could forget Malcolm's, "Do you want to run, Grandad?", Sandie's French swimming pool adventure, or Helen's tea parties!!

IT DOESN'T END TODAY – for everyone in our CC Family, AMMF will keep working until the answers are found.

[FIND OUT MORE...](#)



AMMF is the UK's only cholangiocarcinoma charity,
and is dedicated to raising awareness, supporting research
and providing information on this disease.



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