The Golden Hour
Management of neutropenic sepsis

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Nurse Clinician BMT
Background

• UK experience
  • NCEPOD 2008
  • SACT 2008
  • NCAG 2009
  • National cancer action team 2011

• Acute oncology tenets of good practice
  • Patient education
  • Side effects and their management
NCEPOD

- National Confidential Enquiry into Patient Outcome and Death report commenced pilot in 2006 called ‘For better, for worse’
- Deficiencies in care of patients receiving systemic anticancer therapy who then died within 30 days of treatment
- Recommendations were made to improve care clinically and in the organisation
SACT Objectives

- The appropriateness of the decision to treat with SACT
- The process of care in the prescribing and administration of SACT
- The safety of care in the monitoring of toxicity and managing complications
- End of life care
- Communication - patient information, multidisciplinary team (MDT) working, referral pathways;
- Clinical governance, clinical audit and risk management issues
Key Findings Overview

- Hospital Resources
- Decision to treat
- Prescriptions and administration
- Safety of SACT
- Hospital admission during final 30 days of life
- End of life care
NCAG

- National Chemotherapy Advisory Group
- Many recommendations made
- Neutropenic sepsis and the door to needle target of 1 hour most important
- 24 hour chemo hot line
- Currently just Christie but plans to expand
## The Current State of Play

### Table 4. Cause of death, other

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Number (%)</td>
<td>Number (%)</td>
</tr>
<tr>
<td>Acute cardiac event</td>
<td>3 (7%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Acute GI toxicity</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>CVA</td>
<td>(%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td><strong>Neutropenic sepsis</strong></td>
<td><strong>13 (31%)</strong></td>
<td><strong>4 (26%)</strong></td>
</tr>
<tr>
<td>Non neutropenic sepsis</td>
<td>10 (24%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3 (7%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Severe haemorrhage</td>
<td>1 (2%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Thrombo-embolism</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (7%)</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Not answered</td>
<td>8 (19%)</td>
<td>(%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42 (100%)</strong></td>
<td><strong>15 (100%)</strong></td>
</tr>
</tbody>
</table>
What can we do?

• Education
• Patients and carers
• Nursing and medical teams
• Referral centres and local A+E
Sepsis management at Christie

- Guidelines for the management of sepsis (including neutropenic sepsis)
- PGD training manual
- PGD gentamicin
- PGD piperacillin/tazobactam
- PGD meropenem
- Door to needle SOP
- Door to needle profoma
- Door to needle algorithm
Management of febrile cancer patients

- Acute Oncology teams
- All Christie-registered
- Dual care
The Christie NHS Foundation Trust

Febrile neutropenia 1

- 60% of febrile neutropenic patients prove to have infections
- 16-20% patients with neutrophils <100/mm³ have a bacteraemia
- Fever probably a result of bacteraemia
- Gram positive cocci or Gram negative bacilli
- Fungal infections tend to occur after patients have received broad-spectrum antibiotics and have had prolonged periods of neutropenia but may present as primary infections
Febrile neutropenia 2

• Response
• Fever
• The possibility of infection must be considered in any patient undergoing treatment for cancer who is unwell and particularly in those who are neutropenic.
• Other causes of fever
Sepsis or Systemic Inflammatory Response Syndrome (SIRS)

• Patients are often described as being "septic" or having "septic shock".
• Systemic inflammatory response syndrome (SIRS)
  • Temperature > 38°C or < 36°C
  • Heart rate > 90/min
  • Respiratory rate > 20/min or PaCO2 < 4.3kPa
  • White cell count > 12 x 10^9/l (in those with normal bone marrow activity)
• Sepsis is defined as SIRS in response to infection.
• Severe sepsis is sepsis associated with:
  • organ dysfunction (altered organ function such that normal physiology cannot be maintained without support)
  • hypotension (systolic blood pressure < 90mmHg or a reduction of > 40 mmHg from the patient's normal in the absence of other causes of hypotension)
  • organ hypoperfusion (revealed by signs such as lactic acidosis, oliguria, acute alteration of mental status).
• Septic shock describes sepsis with hypotension despite adequate fluid resuscitation.
• Multiple organ dysfunction syndrome (MODS) describes a state where dysfunction is seen in several organs.
Neutropenia

• Increased susceptibility to infection is likely when the neutrophil count falls below $1.0 \times 10^9$ with escalating risk at $<0.5 \times 10^9$ and at $<0.1 \times 10^9$

• The risk of infection is greater the faster the rate of decline of the neutrophil count and the longer the duration of neutropenia especially if neutropenia lasts for $>10$ days.

• Do not delay administration of antibiotics whilst awaiting WCC results
Initial assessment

• Immediate assessment
• A brief history
• Limited examination
• Monitoring
• Secondary assessment
• Plan
• MEWS
• Surviving sepsis
History and examination

- Mouth
- ENT
- Eyes
- GI
- Respiratory
- Perineum
- Diarrhoea
- Skin lesions
- Genito-urinary
- Vascular access
Investigations

- Bloods
- ECG
- CXR
- Cultures
- Stool microscopy
- Urinalysis and culture
- Blood cultures
- Respiratory
- Clotted blood
- *Varicella zoster* or *Herpes simplex* is being considered
- Swabs and blood for viral PCR
Who to Treat

- All febrile patients with neutrophil counts $<0.5 \times 10^9$ and those whose counts are $<1.0 \times 10^9$ but are falling rapidly.
- Afebrile patients with neutrophil counts $<0.5 \times 10^9$ should also be treated if they have symptoms compatible with infection.
High risk patients

- In-patients
- Outpatients
- Outpatients +
- Patients on immunosuppressive agents
- Patients with specific foci of infection
- Presence of.........................
- Neutropenia likely to last for more than 10 days
- Recent fludarabine treatment
- Phase I or II clinical trial patients (inform investigator)
Empirical treatment

- First line therapy
- Piperacillin/Tazobactam
- Second line
- Meropenem
- Vancomycin if
Surviving sepsis

- Resuscitation
- Resuscitation goals
- Central venous pressure
- Mean arterial pressure
- Urine output
- Central venous (superior vena cava) oxygen saturation
- If venous O2 saturation target not achieved
**Diagnosis**

- Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration. (1C)
- Obtain two or more blood cultures (BC)
- One or more BC should be percutaneous
- One BC from each vascular access device in place > 48 hours
- Culture other sites as clinically indicated
- Perform imaging studies promptly in order to confirm and sample any source of infection; if safe to do so. (1C)
Antibiotic therapy

- Antibiotics
- Broad-spectrum
- Reassess
- Consider combination
- Duration
- Stop
Source identification and control

- Site
- Evaluate
- Implement
- Exception
- Choose
- Remove
Fluid therapy

- Fluid-resuscitate using crystalloids or colloids. (1B)
- Target a CVP of ≥ 8mmHg (≥12mmHg if mechanically ventilated). (1C)
- Use a fluid challenge technique while associated with a haemodynamic improvement. (1D)
- Give fluid challenges of 1000 ml of crystalloids or 300–500 ml of colloids over 30 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion. (1D)
- Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent haemodynamic improvement. (1D)
Vasopressors

- Maintain MAP ≥ 65mmHg. (1C)
- Norepinephrine or dopamine centrally administered are the initial vasopressors of choice. (1C)
- Epinephrine, phenylephrine or vasopressin should not be administered as the initial vasopressor in septic shock. (2C)
- Vasopressin 0.03 units/min maybe subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone.
- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine. (2B)
- Do not use low-dose dopamine for renal protection. (1A)
- In patients requiring vasopressors, insert an arterial catheter as soon as practical. (1D)
Inotropic therapy

• Use dobutamine in patients with myocardial dysfunction as indicated by elevated cardiac filling pressures and low cardiac output. (1C)
• Do not increase cardiac index to predetermined supranormal levels. (1B)
Steroids

- Consider intravenous hydrocortisone for adult septic shock when hypotension remains poorly responsive to adequate fluid resuscitation and vasopressors. (2C)
- ACTH stimulation test is not recommended to identify the subset of adults with septic shock who should receive hydrocortisone. (2B)
- Hydrocortisone is preferred to dexamethasone. (2B)
- Fludrocortisone (50μg orally once a day) may be included if an alternative to hydrocortisone is being used which lacks significant mineralocorticoid activity.
- Fludrocortisone is optional if hydrocortisone is used. (2C)
- Steroid therapy may be weaned once vasopressors are no longer required. (2D)
- Hydrocortisone dose should be < 300mg/day. (1A)
- Do not use corticosteroids to treat sepsis in the absence of shock unless the patient’s endocrine or corticosteroid history warrants it. (1D)
Recombinant human activated protein C (rhAPC)

- Consider rhAPC in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE II ≥ 25 or multiple organ failure) if there are no contraindications. (2B, 2C for post-operative patients)

- Adult patients with severe sepsis and low risk of death (eg: APACHE II<20 or one organ failure) should not receive rhAPC. (1A)
Blood product support

• Give red blood cells when haemoglobin decreases to <7.0 g/dl (<70 g/L) to target a haemoglobin of 7.0 – 9.0 g/dl in adults. (1B)
• A higher haemoglobin level may be required in special circumstances (eg: myocardial ischaemia, severe hypoxaemia, acute haemorrhage, cyanotic heart disease or lactic acidosis)
• Do not use erythropoietin to treat sepsis-related anaemia. Erythropoietin may be used for other accepted reasons. (1B)
• Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures. (2D)
• Do not use antithrombin therapy. (1B)
• Administer platelets when: (2D)
  Counts are 5 X 10⁹/L regardless of bleeding.
  Counts are 5–30 X 10⁹/L and there is significant bleeding risk.
  Higher platelet counts 50 X 10⁹/L are required for surgery or invasive procedures
Glucose control

- Use IV insulin to control hyperglycaemia in patients with severe sepsis following stabilisation in the ICU. (1B)
- Aim to keep blood glucose <150 mg/dl (8.3 mmol/L) using a validated protocol for insulin dose adjustment. (2C)
- Provide a glucose calorie source and monitor blood glucose values every 1-2 hrs (4 hrs when stable) in patients receiving intravenous insulin. (1C)
- Interpret with caution low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values. (1B)
Renal replacement

- Intermittent haemodialysis and continuous veno-venous haemofiltration (CVVH) are considered equivalent. (2B)
- CVVH offers easier management in haemodynamically unstable patients. (2D)
Bicarbonate therapy

• Do not use bicarbonate therapy for the purpose of improving haemodynamics or reducing vasopressor requirements when treating hypoperfusion-induced lactic acidaemia with pH $\geq 7.15$. (1B)
DVT prophylaxis

- Use either low-dose unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), unless contraindicated. (1A)
- Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated. (1A)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (2C)
- In patients at very high risk LMWH should be used rather than UFH. (2C)
Stress ulcer prophylaxis

- Provide stress ulcer prophylaxis using H2 blocker (1A) or proton pump inhibitor (1B). Benefits of prevention of upper GI bleed must be weighed against the potential for development of ventilator-acquired pneumonia.
Consideration of limitation of support

• Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations.(1D)
**Management of patients with signs of sepsis following Chemotherapy treatment or with a possibly infected Central Venous Catheter (CVC)**

**WARNING SIGNS**
- Rigors / Fever >37.5°C Diarrhoea / Mucosits

Patient referred to A&E via The Christie Hotline

**TRIAGE AS URGENT**
- Urgent FBC
- Biochemistry
- Blood cultures (peripheral and from CVC as applicable)
- Full infection screen (refer to neutropenic guidelines)
- Regular monitoring of vital signs
- CXR

**POSSIBLE NEUTROPENIC PATIENT**

If neutrophil count is \(<1.0\) in conjunction with signs of sepsis (fever, focal or systemic signs) commence IV antibiotics **DOOR TO NEEDLE 1 hour** in the A&E Department.

*NOTE* if FBC results not available within 1 hour start antibiotics anyway.

For all patients give:
- Piperacillin / Tazobactam (Tazocin) 4.5g TDS (3 times a day) and Gentamicin 5mg per kilogram OD (once daily)
- Maximum dose 500mg.

Stabilise & admit

If the patient is stable, all cultures negative and their neutrophil count is \(>1.0\) then it may be appropriate to discharge the patient with a 5 day course of oral Ciprofloxacin 750mgs bd or Co-Amoxiclav 625mgs tds

**WARNING**

Initial treatment with these antibiotics should be adequate for most patients. If penicillin allergic (non anaphylaxis) or renal failure give Meropenem 1g TDS. Please note, many chemotherapy regimens contain platinum agents, if received in the last 7 days avoid aminoglycosides and give Meropenem 1g TDS instead. Ensure renal function is regularly monitored and reviewed.

*Please note:* All patients on chemotherapy at The Christie receive 24 hour access to advice and support through The Christie Hotline. Where appropriate acute admission will be offered at The Christie. If this is not appropriate, patients will be referred to their local A&E under current acute oncology arrangements with each Trust. Please contact The Christie Hotline (0161 446 3658) to discuss further management.
Pathway for patients with suspected sepsis – to achieve one hour to antibiotics administration.

Patients who have received systemic anticancer treatment in the last 6 weeks and has one of the following:
- Temperature >38°C
- Temperature <36°C but unwell i.e. sign of infection, rigors, acutely altered mental status

Patients presenting with systemic inflammatory response syndrome (SIRS) characterised by a sign of infection and two or more of the following:
- Temperature >38°C or <36°C
- Heart rate > 90/min
- Respiratory rate > 20/min
- White cell < 4 or > 12 x 10⁹/L
- Acutely altered mental status
- Hyperglycaemia (>6.6 mmol in the absence of diabetes)

Suspected neutropenic sepsis

Commence the one hour to antibiotic proforma.

Medical review a priority. Care of the patient to be managed in accordance with the Guidelines for the Management of Sepsis 2010.

Patients who are not proven to be neutropenic may be converted to alternative antibiotics as clinically appropriate (Antimicrobial Guidelines for Common Infections, v2.4, 2010).
## One hour to antibiotic proforma - for suspected sepsis

| Date: ................................................. | □ Potential neutropenic sepsis □ Suspected sepsis |
| Time assessed & sepsis suspected .................. | Point of entry: □ A&E □ OP Area □ Ward |
| Patient ID Label | Diagnosis: |
|                  | □ Other (Solid Tumours) ................................ |
|                  | □ Haematology ........................................ |
|                  | Chemotherapy regimen (if known) ....................... |
|                  | Date of day 1 of last cycle .......................... |
|                  | Suspected platinum chemotherapy in last 7 days □ Yes □ No |
|                  | Central line in situ □ No □ Yes (See CVC Infection Guidance) |
| HR ...................... Temp .................... | |
| BP ..................... SaO2 ...................... | |
| RR ..................... AVPU ...................... | |
| MEWS ............... Urine Output ............. | If MEWS ≥ 4 (or 3 in single category) Contact Outreach/Primary Responder |
| □ IV access | □ Blood cultures and sampling | □ Record Weight .............................. |
| Record drug allergies /hypersensitivity ................. |

□ Proceed to PGD for first line antibiotics

Time to antibiotic < 60 minutes? □ Yes □ No

**Comments:**

Outcome to be completed by Doctor/ Nurse clinician

WCC ........................ Neuts ........................
Outcome ..................................................
...........................................................................
...........................................................................

**PLEASE FILE A COPY OF THIS PROFORMA IN PATIENT NOTES.**
• Northern Ireland Cancer Network
24-Hour Help-Lines For Chemotherapy Advice For Acute Hospitals With Sussex Cancer Network:

Royal Sussex County:
Sussex Cancer Centre: (Mon-Fri 9.00-5.00) 01273-696955 ext 4799.
A Chemotherapy nurse will always be available to talk to.
Howard 1 (Out of Hours) 01273 696955 ext 4051, staffed by Oncology nurses - ask for the nurse in charge of the unit
Haematology Ward: 01273-696955 ext 7413, direct line 01273-664771 – ask for nurse in charge of ward

Worthing Hospital:
Medical Day Case Unit: (Mon-Fri 8.00-6.00) 01903-205111 ext 5450.
A Chemotherapy nurse will always be available to talk to.
Erringham Ward (out of hours) 01903 205111 ext 5510, staffed by medical and haematology nurses - ask for the nurse in charge of the unit

Eastbourne District General Hospital:
Pevensey Day Unit: (Mon-Fri 8.00-5.00) 01323-417400 ext 3020.
A Chemotherapy nurse will always be available to talk to.
Pevensey Ward (out of hours) 01323-435866, staffed by haematology nurses who have experience in chemotherapy - ask for the nurse in charge of the unit

Conquest Hospital:
Mc Cartney Day Unit (Mon-Fri 9.00-5.00) direct line 01424-757030
A Chemotherapy nurse will always be available to talk to.
Pevensey Ward (out of hours) 01323-435866, staffed by haematology nurses who have experience in chemotherapy - ask for the nurse in charge of the unit

www.sussexcancer.net
Signs and symptoms of neutropenic sepsis:

Chemotherapy can result in a life threatening side effect of neutropenic sepsis.
Early diagnosis will prevent death.

**Early signs:**
- Feeling generally unwell with or without a temperature
- T 38°C and slight hypotension or slight tachycardia
- Symptoms of infection
- Shivering, hot and cold, spontaneous rigor
- Diarrhoea
- At the early stage the patient will be warm and alert and not look unwell. However, they can deteriorate rapidly and death can follow

**Late signs:**
- Cold and clammy
- Restless, anxious or confused
- Hyperthermic
- Hypotensive, tachycardic

**Patients at risk:**
- Post chemotherapy 7-10 days is a classic time for neutropenia following chemotherapy, however delayed neutropenia can occur with some regimes
- Haematology patients
- Elderly
- Heavily pre-treated
- Any indwelling line
- Co-morbid conditions e.g. advanced cancer
- General poor health

**What to do:**

**History** – Are they on chemotherapy? When did they last have treatment? How have they been feeling? Are there any specific symptoms of infection.

**Examine** - Temperature, pulse, blood pressure and respiration.

**Action** – Urgent full blood count is required, therefore refer urgently to local acute provider.

**Treatment** - On diagnosis of neutropenic sepsis, urgent intravenous antibiotics must be administered within one hour of admission time.

**HEAT**

**MANAGEMENT OF NEUTROPENIC SEPSIS**

**REMEMBER NEUTROPENIC SEPSIS CAN BE FATAL** Symptoms may be vague and often there is no obvious focus of infection

**HISTORY**

Is the patient on chemotherapy?

Greater 21 days

When did patient last receive chemotherapy?

Less 21 days

**EXAMINE**

- How are they feeling?
- TPR and BP
- Presence of 1 -3 symptoms of SIRS?

In the community

- Urgently refer to acute trust

At the acute trust

- Urgent full blood count and white cell differential

**TREAT**

- SIRS - Systemic Inflammatory Response Syndrome
- Symptoms
  - Fever or hypothermia
  - Shaking, chills
  - Tachycardia
  - Tachypnoea
  - Hypotension

IF NEUTROPENIC SEPSIS IS DIAGNOSED:

- URGENT IV ANTIBIOTICS WITHIN 1 HOUR
- FOLLOW NEUTROPENIC SEPSIS POLICY
Febrile Neutropenia Admission Assessment Proforma

<table>
<thead>
<tr>
<th>Name</th>
<th>DOB</th>
<th>Hospital No.</th>
<th>Consultant</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date:</th>
<th>Time:</th>
</tr>
</thead>
</table>

Diagnosis
Chemotherapy regimen (if known) ...........................................
Date of last chemo & where given (if known) ................................
Cycle no. and day (if known) .............................................
Previous episodes of febrile neutropenia? Y / N
If Y, no. of previous episodes ...........................................
Are they a triage patient? Y / N

Presenting history of this episode
Did patient take temp at home? Y / N
If Y, approx time and value ...............................................

Summary of Symptoms

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Mod</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucoedema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Productive cough</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Examination on admission
Temp ............ Pulse ............ BP .............
Respir rate ............ O2 sats .............
MEWS score ............
Is there a clear clinical focus of infection? Y / N
If Y, where?
Cellulite
Abscess
Central line
Pneumonia
Other

Any Significant PMH?
e.g. COPD/ DM/ HT/ IHD

Medication
Antibiotics in last 7 days? Y / N
If Y, which?

Any allergies to antibiotics? Y / N
If Y, which?
Definite
Probable
Possible
Other allergies?

The Christie NHS Foundation Trust
Febrile Neutropenia Admission Assessment Proforma

<table>
<thead>
<tr>
<th>Initial investigations on admission for <strong>all</strong> patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC □</td>
<td>Hb □</td>
</tr>
<tr>
<td>U + E □</td>
<td>WCC □</td>
</tr>
<tr>
<td>Blood cultures □</td>
<td>Pla □</td>
</tr>
<tr>
<td>Nasal/throat MRSA screen □</td>
<td>Neuts □</td>
</tr>
<tr>
<td></td>
<td>Cr □</td>
</tr>
</tbody>
</table>

**Other investigations as clinically indicated**

- LFTs □
- Ca²⁺ □
- CXR □
- Result □
- MSU □
- Stool culture □
- Sputum culture □
- Wound swabs □
- Line site swabs □

**ASSESSMENT:**

1. **Does patient have febrile neutropenia?**
   - i.e. Neuts ≤ $1 \times 10^9/l$
   - AND
   - Y / N
   - Temp ≥ 37.8°C on at least 1 occasion
   - **Temp ≥ 37.8°C on at least 1 occasion**
   - **(Include pt reading at home if reliable)**
   - **IF PATIENT DOES NOT FULFIL THESE CRITERIA FOR FEBRILE NEUTROPENIA TREAT ACCORDING TO STANDARD ANTIBIOTIC FORMULARY**
   - **If febrile neutropenia,**
   - 2. **Is this episode “low-risk”?**
     - Score
     - Please assess by following scoring system
     - a. Age of patient
       - □ ≥ 60y = 0
       - □ < 60y = 2
     - b. Is patient dehydrated, requiring iv fluids?
       - □ No = 3
       - □ Yes = 0
     - c. Is patient hypotensive?
       - □ Systolic BP <90 = 0
       - □ ≥ 90 = 5
     - d. Does patient have COPD?
       - □ Yes = 0
       - □ No = 4
     - e. Does patient have symptoms related to this febrile neutropenia episode?
       - □ No symptoms = 5
       - □ Mild symptoms = 3
       - □ Severe symptoms = 0
     - f. Was the patient already an in-patient before this episode of febrile neutropenia?
       - □ Already an in-patient = 0
       - □ Admitted with this episode = 3

**Total Score**

| Score 17 or more = Low-risk |
| Score less than 17 = High-Risk |

The Christie NHS Foundation Trust
# Febrile Neutropenia Admission Assessment Proforma

## Antibiotic Treatment

### Please circle intended treatment

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Line:</strong></td>
<td><strong>First Line:</strong></td>
</tr>
<tr>
<td>► Oral Augmentin 825mg tds + Ciprofloxacin</td>
<td>► I.V. Piperacillin/Tazobactam 4.5g tds plus I.V. Gentamicin for 48hrs.</td>
</tr>
<tr>
<td>750mg bd</td>
<td>If clinically well continue on Piperacillin/Tazobactam only.</td>
</tr>
<tr>
<td><strong>If Unable to Tolerate Oral Medication</strong></td>
<td><strong>If Penicillin Allergy</strong></td>
</tr>
<tr>
<td>(e.g. Mucositis/Vomiting)</td>
<td>► I.V. Ciprofloxacin 400mg bd plus I.V. Gentamicin for 48hrs.</td>
</tr>
<tr>
<td>► I.V. Ceftazidime 1g bolus dose then 2g/24hrs</td>
<td>If clinically well, continue on Ciprofloxacin only.</td>
</tr>
<tr>
<td>continuous infusion</td>
<td></td>
</tr>
<tr>
<td><strong>Or, if Patient is Already on Antibiotics</strong></td>
<td><strong>If Evidence of Central Line Tunnel Infection</strong></td>
</tr>
<tr>
<td>► Continue oral quinolone (increase to levofloxacin 500mg bd or ciprofloxacin 750mg bd if necessary), add oral Augmentin 625mg tds</td>
<td>► Add I.V. Vancomycin (see antibiotic formulary for dosing)</td>
</tr>
<tr>
<td><strong>Or, if Already on Antibiotics &amp; Penicillin Allergy</strong></td>
<td>Also refer to “High Risk Febrile Neutropenia Guidance” (overleaf)</td>
</tr>
<tr>
<td>► Continue oral quinolone (increase to levofloxacin 500mg bd or ciprofloxacin 750mg bd if necessary), and add oral doxycycline 200mg od (patient to remain in hospital for at least 48 hours)</td>
<td></td>
</tr>
<tr>
<td><strong>Or, if Penicillin Allergy</strong></td>
<td></td>
</tr>
<tr>
<td>► Oral Doxycycline 200mg od + oral ciprofloxacin 750mg bd</td>
<td></td>
</tr>
<tr>
<td><strong>Or, if Evidence of Central Line Tunnel Infection</strong></td>
<td></td>
</tr>
<tr>
<td>► I.V. Ceftazidime as above + I.V. Vancomycin (see antibiotic formulary for dosing)</td>
<td></td>
</tr>
</tbody>
</table>

### Additional Management Plan / Other Comments

nb. Consider IV fluids/ antiemetics/ management of co-existing morbidities eg DM/ COPD etc.
High Risk Febrile Neutropenia Guidance

Job 1: Blood Cultures (peripheral and line)

Within 1 hour of admission

Job 2: Administer antibiotics

Job 3: Fluid Resuscitation (see below)

**Fluid Resuscitation** To be give only if a patient's systolic BP is below 90 and/or their heart rate is greater than their systolic BP.

Use 500mls NSaline 0.9% over 10–15 mins or 250mls Colloid over 30 mins (consider reduced doses in patients with renal or heart failure).

A strict fluid balance chart must be maintained.

Can give up to three subsequent fluid challenges in order to keep a patient's systolic BP above 90 and/or to also keep the systolic BP recording above the patient's heart rate (as per the Portsmouth ALERT sign guidelines).

If MEWS score 4 or above

Job 4: Take ECG

Within 6 hours of admission

Job 5: Monitor Blood Glucose levels - keep below 8 mmol/L

Job 6: Check Serum Lactate (should be less than 4 mmol/L)
Spreading Improvements for Neutropenic sepsis

Blackpool, Flyde & Wyre Hospitals NHS Trust

**Background**
Blackpool, Fylde & Wyre Hospitals NHS Trust serves a population of approximately 330,000 residents and the 16 million visitors who visit the area every year. The A&E department sees 85,000 patients per annum, there are 1,195 beds and more than 85,000 day case and inpatients and 300,000 outpatients are seen every year.

Blackpool Victoria Hospital currently provides level 1, 2 and 3 haematology services and became the haematology centre for Lancashire & South Cumbria in September 2007. Visiting Oncologists from Lancashire Teaching Hospitals provide oncology support, and the haematology ward provides inpatient care for oncology patients for cases such as neutropenic sepsis.

**Aim:** Tested multiple approaches involving patients and clinicians to reduce mortality and length of stay through developing an emergency pathway for the management of emergency patients with neutropenic sepsis.

Our testing has now been imbedded into practice.

<table>
<thead>
<tr>
<th>Late emergency presentation</th>
<th>Tested Solution</th>
<th>Impact</th>
<th>Baseline 2007</th>
<th>Sustained 2008</th>
<th>Sustained 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk of mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Save Lives</td>
<td>Promote self management and patients' confidence in the system</td>
<td>Cancer Partnership Group undergoing audit of patient views – positive feedback</td>
<td>2 deaths</td>
<td>0 deaths</td>
<td>0 deaths</td>
</tr>
<tr>
<td></td>
<td>• Patient held alert card</td>
<td>Divisional audit on neutropenic sepsis to include presentation times</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 24 hour help line</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Patient experience SVO created by patients for patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multiple emergency access points</th>
<th>Tested Solution</th>
<th>Impact</th>
<th>Baseline 2007</th>
<th>Sustained 2008</th>
<th>Sustained 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right place first time</td>
<td>One entry point</td>
<td>• Increased patient awareness</td>
<td>60% of patients direct referral to correct ward</td>
<td>43% of patients direct referral to correct ward</td>
<td>75% of patients direct referral to correct ward</td>
</tr>
<tr>
<td>Improve patient, primary and secondary care awareness</td>
<td>• Direct admission to ward</td>
<td>When to act, who to contact and where to go</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Awareness campaign to GPs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Press release</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Direct admission policy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutropenic sepsis management policy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Delay in treatment</th>
<th>Tested Solution</th>
<th>Impact</th>
<th>Baseline 2007</th>
<th>Sustained 2008</th>
<th>Sustained 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve door to treatment time for 100% of patients</td>
<td>Patient group directive for antibiotics given at point of entry by nurse</td>
<td>8% receive antibiotics within an hour of arriving at hospital</td>
<td>55% receive antibiotics within an hour of arriving at hospital</td>
<td>77% receive antibiotics within an hour of arriving at hospital</td>
<td></td>
</tr>
</tbody>
</table>
Neutropenic Sepsis

Three questions:

1. Could your patient be neutropenic?
   - Chemo in the last 2 months
   - Active cancer
   - Yes
   - No
   - Assess as per hospital sepsis protocol

2. Is your patient infected?
   - Fever at home or in hospital of 38°C or 2 x 38°C within an hour
   - Violent shivering
   - Unwell/Unconscious
   - Yes
   - No
   - Signs and symptoms can be subtle, if the Neutrophil result comes back as <1 x10⁹l

GIVE ANTIBIOTICS IMMEDIATELY
   - Tazocin 4.5g TDS
   - Gentamicin 1mg/kg or Meropenem 1g TDS if penicillin allergic.
   - Always inform Microbiology On-Call of patient and review previous culture results.
   - They must not be moved from admitting department until antibiotics have been given.
   - Cultures should be taken prior to antibiotics. For help with Hiclen line cultures contact 3403.

3. Is your patient septic?
   - Assess BP, HR, cap refill, GCS
   - Yes
   - Reassess frequently: neutropenic patients may deteriorate rapidly
   - Urgent resuscitation as per Sepsis policy
   - No
   - If in any doubt speak to on-call Haematologist for advice

Additional progress:
There is still work to be done in encouraging patient self-management and in educating staff especially in emergency access. We will continue to use the DVD and continue to audit the outcomes to present to staff groups.

For further information contact:
Kathryn Jones
Service Improvement Facilitator
Kathryn.jones@bfwhospitals.nhs.uk
Antimicrobial Guidelines for Common Infections

**Sepsis**
- Take Blood Cultures immediately & initiate antibiotics within 1 hour

**Urinary Tract Infection**
- If suspected central line infection, add gram positive cover
  - Piperacillin/Tazobactam (Tazocin) 4.5g TDS plus Gentamicin 5mg/kg (max. 500mg)
  - Tetracycline 200mg BD
  - 3 days in females
  - 7 days in males

**Cellulitis**
- SIMPLE UTI
  - Trimethoprim 200mg BD
  - 3 days in females
  - 7 days in males
  - Add metronidazole

**Hospital Acquired Pneumonia**
- More than 5 days in hospital
  - Piperacillin/Tazobactam (Tazocin) 4.5g TDS IV
  - Penicillin allergic
  - Clindamycin 450mg QDS IV
  - Add metronidazole

**Community Acquired Pneumonia**
- Less than 5 days in hospital or new admission
  - Co-amoxiclav 1.2g TDS plus Clarithromycin 500mg BD IV

**Bacterial Meningitis**
- Take Cultures immediately
  - Ceftriaxone 2g 12 hourly
  - Modify treatment according to sensitivities

**Fungal Infection**
- For Candida
  - Fluconazole or caspofungin if already on antifungal prophylaxis
- For Aspergillosis
  - Voriconazole or Anidulafungin, see policy

**Alternative if Penicillin allergic (non anaphylaxis)**
- Vancomycin 1gm BD
- Meropenem 1g TDS
- Reduce dose if creatinine clearance under 50mll/min

**Complex UTI**
- Refer to Policy

The Christie NHS Foundation Trust
SACT Definition

• Systemic Anti-Cancer Therapy (SACT) includes all cytotoxics and biological agents such as interferon, monoclonal antibodies or tyrosine kinase inhibitors.

It does not include:
- hormonal therapies or
- intrathecal chemotherapy

• 30-day defined as 30 days from Day 1 of SACT cycle immediately prior to death.
  - where SACT continuous - 30 days from date of last prescription
Results

- 8 of 20 received antibiotics in 1 hour
- 60% patients did not have in 1 hour
Results

- 9 different malignancies
- Breast cancer most common type
Results

- 20 of 22 received antibiotics
- 10 Tazocin and Gent, 10 meropenem

![Graph 6]

**Antibiotics given**

- 10 Piperacillin/Taz+gent
- 10 Meropenem
- 2 Not given
Results

- 6 of 20 patients were not given correct first line antibiotic
Results

- Third of patients had haematological malignancy
- 20 patients had a MEWS of at least 1
- 8 patients had MEWS of 4 or more
- 1 patient had MEWS of 8
- 20 of the 22 episodes resulted in IV antibiotics being given
- 2 that did not, one had been on oral a/b for a couple of days and was left on them
- 1 was given oral a/b with symptoms of nausea with a tachycardia and pyrexial
Conclusion

• Less than half of patients in this audit received antibiotics within 1 hour
• This is not in line with current recommendations and is not good medical practice
• Meropenem is being given inappropriately
Recommendations

• Immediate assessment at point of entry
• Identify if high risk of sepsis (chemo in last 4 weeks) promptly and initiate treatment
• Staff education (nurses and doctors) re sepsis management
• Develop PGD for first dose antibiotic
• Repeat audit
Audit question MAU

- How good are we at treating sepsis?
- Do we follow current guidelines/standards of care?
  - Care Bundles, Surviving Sepsis Campaign
  - NICE TA84 & CG50
  - NPSA PSO/5
- Focus on a specific group
  - Line sepsis – culture positive
  - 30 patients admitted to MAU over a three month period. 25 sets of notes found
<table>
<thead>
<tr>
<th>Cause of admission</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia / Fever / Shivering</td>
<td>56%</td>
</tr>
<tr>
<td>Redness / swelling / tenderness around line exit</td>
<td>28%</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>12%</td>
</tr>
<tr>
<td>Positive blood cultures from line</td>
<td>8%</td>
</tr>
<tr>
<td>Other: vomiting, abdominal pain/abscess, unwell/weakness</td>
<td>12%</td>
</tr>
</tbody>
</table>
### Sepsis Criteria

<table>
<thead>
<tr>
<th>Count (%)</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 (56%)</td>
<td>WCC &gt; 12x10 (9/l) or &lt; 4x10 (9/l)</td>
</tr>
<tr>
<td>12 (48%)</td>
<td>Heart rate &gt; 90 bpm</td>
</tr>
<tr>
<td>7 (28%)</td>
<td>Temperature &lt; 36 °C or &gt; 38.3 °C</td>
</tr>
<tr>
<td>3 (12%)</td>
<td>Hyperglycaemia</td>
</tr>
<tr>
<td>1 (4%)</td>
<td>Acutely altered mental state</td>
</tr>
</tbody>
</table>
## Process of Care

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>88%</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>88%</td>
<td>Blood Cultures</td>
</tr>
<tr>
<td>52%</td>
<td>I.V. Fluids</td>
</tr>
<tr>
<td>4%</td>
<td>Urine Catheter</td>
</tr>
</tbody>
</table>
## Timings of care

### Junior Doc review

<table>
<thead>
<tr>
<th>Mins</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>20</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>35</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>50</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>60</td>
<td>3</td>
<td>12.0</td>
</tr>
<tr>
<td>70</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>90</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>100</td>
<td>1</td>
<td>4.0</td>
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<tr>
<td>150</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>210</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>Data</td>
<td>15</td>
<td>60.0</td>
</tr>
<tr>
<td>Missing</td>
<td>10</td>
<td>40.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

### Antibiotic first dose

<table>
<thead>
<tr>
<th>Time (mins)</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>-105</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>-45</td>
<td>1</td>
<td>4.0</td>
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<tr>
<td>5</td>
<td>1</td>
<td>4.0</td>
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<tr>
<td>20</td>
<td>1</td>
<td>4.0</td>
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<tr>
<td>30</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>80</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>140</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>145</td>
<td>2</td>
<td>8.0</td>
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<tr>
<td>150</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>165</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>180</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>250</td>
<td>1</td>
<td>4.0</td>
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<tr>
<td>255</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>270</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>Data</td>
<td>17</td>
<td>68.0</td>
</tr>
<tr>
<td>Missing</td>
<td>8</td>
<td>32.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

### Senior Review

<table>
<thead>
<tr>
<th>Day</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same day</td>
<td>6</td>
<td>24.0</td>
</tr>
<tr>
<td>Next day</td>
<td>17</td>
<td>68.0</td>
</tr>
<tr>
<td>Not documented</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>Data</td>
<td>24</td>
<td>96.0</td>
</tr>
<tr>
<td>Not reviewed</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

- Mean time to Junior review: 67 mins
- Mean Time to first antibiotic: 125 mins
Fate of the line & patient

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hickman</td>
<td>22</td>
<td>88.0</td>
</tr>
<tr>
<td>PICC</td>
<td>3</td>
<td>12.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Removed?</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>19</td>
<td>76.0</td>
</tr>
<tr>
<td>This admission?</td>
<td>8</td>
<td>32.0</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>12.0</td>
</tr>
<tr>
<td>Not documented</td>
<td>3</td>
<td>12.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did they improve?</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes - with oral ABX</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>Yes - with IV ABX</td>
<td>19</td>
<td>76.0</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>92.0</td>
</tr>
<tr>
<td>Not documented</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100.0</td>
</tr>
</tbody>
</table>

76% of total received i.v. antibiotics
76% of lines were removed
But only 32% in this admission

Mean time to get better 5.5 days
Mean length of stay 7 days
Summary – Line sepsis

• May be difficult to diagnose
  • Low grade fever, tachycardia, abnormal WCC
• More consideration for iv fluids & urine catheterisation
• Delays to first antibiotic
  • Other tasks, low priority, primacy of neutropenia
• Relatively low rate of line removal
Suggestions for the future

• “give the dose before you go”

• Formal hospital sepsis guideline
  • Covering both neutropenic and non-neutropenic patients
  • Hospital wide “sepsis six” program & training events