**Horizon Scan Report 0011** **1 February 2010**

# **Diagnostic Technology:** Point-of-care test for total white blood cell count

## Clinical Question:

1. In patients undergoing chemotherapy treatment, what is the accuracy and utility of a point-of-care white blood cell counter compared to standard care?
2. In patients receiving immunosuppressive therapy treatment, what is the accuracy and utility of a point-of-care white blood cell counter compared to standard care?
3. In patients with symptoms of acute infection, does a point-of-care white blood cell counter help inform antibiotic prescription by aiding the distinction between viral and bacterial infection?

**Advantages over Existing Technology:**
An elevated white blood cell (WBC) count occurs in bacterial infection, allergy, systemic illness, inflammation, tissue injury, and leukaemia. A low WBC count may occur in viral infections, immunodeficiency states, acute leukaemia and bone marrow failure, post chemotherapy [1]. Chemotherapy patients, for example, regularly have their white blood cell counts checked, particularly prior to each chemotherapy treatment, as neutropaenia is a common side effect of certain chemotherapy treatments. These are currently performed in a hospital laboratory and chemotherapy is delayed if counts are too low. If patients could visit their local general practitioner to have their WBC measured, this would potentially save patients an unnecessary trip to the hospital, should their counts be too low. WBCs have also been shown to aid judicious antibiotic prescribing in, for example, acute respiratory tract infections, thus effectively avoiding unnecessary antibiotic use [2].

**Details of Technology:**
Several point-of-care (POC) white blood cell counters were identified:

1. Chempaq XBC (Chempaq A/S, Denmark) measures haemoglobin concentration (red blood cells are lysed), leukocyte counts and a 3-part differential (lymphocytes, monocytes and granulocytes, concentrations and % of total) [1]. Reagents are contained in a disposable cassette and measurements can be taken from a finger stick or venous sample. Results are available in 3 min.
2. The HemoCue WBC (HemoCue AB, Angelholm, Sweden) is a battery-run device utilising a disposable cuvette pre-loaded with reagent, along with an image detector and an LCD display [3]. The device measures white blood cells only, red blood cells are lysed. Measurements require10 µl (1 to 2 drops) (of capillary or venous blood and are completed in 2 min.
3. The pocH-100i hematology analyser (Sysmex Corporation, Kobe, Japan) provides a full blood count and a 3-part differential leukocyte count [4]. Neutrophils are reported separately [4]. Readings take 2-3 min. per sample.
4. In development: Point-of-care microfluidic single cell impedance cytometer, which performs white blood cell differential count (T-lymphocytes, monocytes and neutrophils) based on inherent electrical properties of cells [5].

**Patient Group and Use:**

- Patients undergoing chemotherapy treatment
- Patients receiving immunosuppressive therapy treatment
- Differentiation between bacterial and viral infection in acutely ill patients to reduce antibiotic prescription for viral infection

**Importance:**
More than 293,000 new cases of cancer are diagnosed each year in the UK (Cancer Research UK), many of whom will receive chemotherapy treatment. Between 2003 and 2007 the amount of chemotherapy delivered has increased by 60%,

indicating an increase from around 40 000 to around 65 000 programmes of chemotherapy per year in England (National Chemotherapy Advisory Group; Chemotherapy Services in England: Ensuring quality and Safety, August 2009).

According to 2008/2009 annual report from the National Institute for Health and Clinical Excellence (NICE), each year one in four people visit their GP because of an acute respiratory tract infection (RTI) [6]. Treatment for RTIs accounts for 60% of all antibiotic prescribing in general practice; however clinical evidence shows that antibiotics have limited effectiveness. The NICE guideline on helping healthcare professionals decide when antibiotics are appropriate is estimated to potentially save the NHS £3.5 million a year.

**Previous Research:**

*Accuracy compared to existing technology*

Five hundred routine blood samples from a hospital were tested in parallel by the HemoCue WBC compared to a reference analyser and data showed that the HemoCue WBC was reliable for white blood cell counts within the analytical range of 0.4-30 x $10^9$/l, except in samples with high numbers of normoblasts or reticulocytes (e.g. in sickle cell anaemia or thalassaemia major) [3]. A total of 95% of the samples were within the acceptable performance limit of 8-10% of the correct measurements as required by the United Kingdom National External Quality Assessment Service. In patients exhibiting symptoms of infection, a low or normal total WBC is usually associated with viral illness [7]. A study comparing HemoCue WBC to an automated counter (Cell-Dyn) in a general practice setting in the USA tested blood samples from 120 acutely ill children and showed a high correlation (r = 0.98) between the two devices. Of the 88 children with low WBC who did not receive an antibiotic, 3 returned within 30 days and received an antibiotic. The device may therefore have utility in targeting antibiotic prescription.

A comparison of the Chempaq XBC analyser at different locations (intensive care unit, emergency room, in-patient wards, primary care, paediatric and OB/Gyn clinics) with laboratory measurements showed good correlation at all the locations for WBC, haemoglobin, granulocytes and lymphocytes (r = 0.92–0.96), but not for monocytes (r = 0.88) [1].

Evaluation of the pocH-100i hematology analyser compared to standard methods showed good correlation for neutrophils ($r^2$= 0.996) and lymphocytes ($r^2$= 0.999), but less for the “mixed” population of cells ($r^2$= 0.611) [4]. A study comparing an impedance cytometer with standard laboratory haematology analysis showed good overall correlation (95%) [5]. The covariance (CV) factors between the results obtained from the impedance cytometer and the reference device were: lymphocytes (95%), granulocytes (97%) and monocytes (88%). The simplicity of impedance cytometry has potential application in affordable point-of-care diagnostic systems, but is still under development.

*Impact compared to existing technology*

A study of the effects of immediate testing for C reactive protein (CRP) and white blood cell count (WBC) on physicians’ choices of antibiotic was investigated in patients with acute infection [8]. New outpatients presenting to a regional/community hospital (Japan) with an acutely febrile condition and suspected of having infection were randomised into two groups: Group 1 (147 patients) underwent WBC and CRP testing before initial consultation (advance testing) and antibiotic prescriptions were compared with those in Group 2 (no advance testing; 154 patients). The study showed that the availability of WBC and CRP data greatly reduced prescription of amoxicillin, but had a lesser effect on newer broad spectrum antibiotics. More than 60% of patients with CRP and WBC values lower than 40 mg/litre and $9 \times 10^9$/litre, respectively, received no antibiotics.

No studies on the use of point-of-care white blood cell counters for patients undergoing chemotherapy or immunosuppressive therapy were identified.

*Guidelines and Recommendations*

Guidelines on POCT in haematology have been published by the British Committee for Standards in Haematology [9] and the International Council for Standardization in Haematology [10].

National Institute for Health and Clinical Excellence clinical guideline 69. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care, July 2008 [11].

**Cost-effectiveness and Economic Impact:**
Currently very limited evidence exists on the cost-effectiveness and economic impact of POCT for WBC count. One study has investigated the economic consequence of POC testing for C-reactive protein and WBC count in patients with acute infections [12]. The study was undertaken in Japan and found that immediate testing led to a 30% reduction in the cost of oral and parenteral antibiotics, although these savings were largely offset by the prescription of new antiviral drugs in the immediate testing group. It also led to a non-significant reduction in staff time and additional laboratory use. POC testing for WBC needs to be evaluated to assess whether it potentially delivers a cost-effective alternative to standard care for a group of patients such as those undergoing chemotherapy, those receiving immunosuppressive therapy and those with acute infections.

**Research Questions:**
What is the accuracy, precision and utility of point-of-care white blood cell count devices in the primary care setting?

In patients undergoing chemotherapy or immunosuppressive therapy, how does a monitoring strategy that uses POCT for white cell count(s) compare to current laboratory/hospital based strategies in terms of a) identifying optimal interval for treatment cycles, b) assisting in recognising febrile neutropaenic episodes, c) patient satisfaction, and d) cost effectiveness

What is the utility of point-of-care white blood cell count devices in targeting antibiotic prescription in patients presenting to primary care with acute infections, and how does it compare to inflammatory markers such as C-reactive protein or procalcitonin, and to other strategies to reduce antibiotic prescribing?
Does the use of point-of-care white blood cell count devices affect patient satisfaction regarding decisions on antibiotic prescribing in primary care?

**Suggested next step:**
Studies of the accuracy and utility of point-of-care white blood cell counters in the primary care setting.

Feasibility/pilot studies in patients undergoing chemotherapy or immunosuppressive therapy addressing the questions outlined above.

Comparisons of POCT white cell counts with POCT for other inflammatory markers for patients presenting with acute infections – to include effects on prescribing, patient satisfaction, reconsultation rates, complications (e.g. hospital admission, delayed diagnosis), cost effectiveness.

**Expected outcomes:**
Point-of-care white blood cell counts may provide better coordination of care in patients undergoing chemotherapy, potentially improving patient outcomes and cost effectiveness.
POCT white cell counts either alone or in combination with inflammatory markers may help target antibiotics in patients presenting with infections of unclear aetiology, thus reducing unnecessary antibiotic use.

**References:**

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**Comments:**

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