Literature Review and Practice Recommendations:

Monitoring the effectiveness of decontamination of the healthcare environment

ATP Bioluminescence and Fluorescent Markers

Contents

Topic

The use of adenosine triphosphate (ATP) bioluminescence and fluorescent markers to monitor the effectiveness of decontamination of the healthcare environment and reusable non-invasive patient care equipment.

Background

There is strong evidence that contaminated environmental surfaces contribute to the transmission of pathogens in healthcare settings.[1-4] As such, environmental decontamination has an important role to play in the control and prevention of healthcare associated infection.[1-4]

The management of effective decontamination should involve a monitoring component, as more cleaning is often equated with better cleaning but this is difficult to ascertain in the absence of appropriate monitoring methods.[5] Visual assessment tends to be the standard method used to assess efficacy of decontamination in the healthcare environment and this can provide an incomplete picture.[5] Microbial testing is a useful measure of decontamination effectiveness as it detects the presence of residual microorganisms which should decrease as a result of effective decontamination. ATP bioluminescence is a measure of cleanliness that detects organic soiling (microbial and non-microbial ATP) that is increasingly used to assess decontamination effectiveness.[6]

Fluorescent marking is also increasingly being used to assess decontamination effectiveness. It involves the application of a fluorescent marker to high touch surfaces and detecting the fluorescence after cleaning in order to assess cleaning efficacy.[7]

Aim

To review the evidence for the use of ATP bioluminescence and fluorescent markers to monitor the effectiveness of decontamination of the healthcare environment and reusable non-invasive patient care equipment.

Objectives

- To provide a description of how ATP bioluminescence and fluorescent markers can be used to monitor the effectiveness of decontamination of the healthcare environment.

- To assess the scientific evidence for effectiveness of ATP bioluminescence and fluorescent markers.

- To explore practical and safety considerations related to the use of ATP bioluminescence and fluorescent markers.

- To explore the costs associated with using ATP bioluminescence and fluorescent markers.

- To produce an evidence sheet to assist the Environmental Decontamination Steering Group in making practical recommendations on the use of ATP bioluminescence and fluorescent markers for NHSScotland.

Research questions

The following research questions will be addressed for each of the technologies under review:

1.   Are ATP bioluminescence and fluorescent marker monitoring systems currently used in UK healthcare settings? If not, are they used in healthcare settings outside the UK?

2.   How do ATP bioluminescence and fluorescent marker monitoring systems work?

3.   What is the procedure for using ATP bioluminescence and fluorescent marker monitoring systems?

4.   What is the scientific evidence for effectiveness of ATP bioluminescence and fluorescent marker monitoring systems for monitoring the effectiveness of decontamination of the healthcare environment?

5.   Are there any safety considerations associated with using ATP bioluminescence and fluorescent marker monitoring systems in the healthcare setting?

6.   Are there any practical or logistical considerations associated with using ATP bioluminescence and fluorescent markers in the healthcare setting?

7.   What costs are associated with using ATP bioluminescence and fluorescent markers in the healthcare setting?

8.   Have ATP bioluminescence and fluorescent marker monitoring systems been assessed by the Rapid Review Panel?

Methodology

Search Strategy

The following databases and websites were searched to identify relevant academic and grey literature:

- MEDLINE

- CINAHL

- EMBASE

- NHS Evidence (http://www.evidence.nhs.uk/)

- Health Technology Assessment (HTA) Database (http://www.crd.york.ac.uk/CRDWeb/)

- Database of Abstracts of Reviews of Effects (DARE) (http://www.crd.york.ac.uk/CRDWeb/)

- National Patient Safety Agency (http://www.npsa.nhs.uk/)

- NICE (http://www.nice.org.uk/)

- MHRA (http://www.mhra.gov.uk/)

- Rapid Review Panel Reports Archive (http://www.hpa.org.uk/ProductsServices/MicrobiologyPathology/RapidReviewPanel/ReportsArchive/)

Search terms were developed and adapted to suit each database or website. Literature searches were run on 8/02/2016. See Appendix 1 for an example search run in the Medline database.

Exclusion criteria

Academic and grey literature will be excluded from the review on the basis of the following exclusion criteria:

- Item was published before 2005
- Item is not in English
- Item does not concern either ATP bioluminescence and fluorescent marker monitoring (off topic)
- Item is an opinion piece or non-systematic review
- Item does not assess the effectiveness of ATP bioluminescence and fluorescent marker monitoring systems against the microbiological gold standard of aerobic colony counts (ACC)/cm^2

Manufacturer information will not be subject to the exclusion criteria outlined above, as it is sought primarily for information about the procedure for using the technology in question.

Screening

There was a two-stage process for screening the items returned from the literature searches. In the first stage, the title and abstract were screened against the exclusion criteria by the lead reviewer. Items that were not excluded at the screening stage progressed to the second screening stage. In the second stage of the screening process, the full text of remaining items was screened against the exclusion criteria by the lead reviewer. Items that were not excluded at the second screening stage were included in the review.

Critical appraisal

Critical appraisal of the studies included in this review and considered judgement of the evidence was carried out by the lead reviewer using SIGN methodology.[8]

Results

The searches found 872 articles in total (815 from ATP searches, 57 from ATP bioluminescence and fluorescent marker searches). After the first stage of screening using the title and abstract this was reduced to 57 articles in total (45 from ATP searches, 12 from ATP bioluminescence and fluorescent marker searches), and after stage 2 screening using the full text there were 11 articles that fulfilled the exclusion criteria and were critically appraised for inclusion in this review. Of the included articles 8 concerned ATP bioluminscence[9-16] and 3 concerned both ATP bioluminescence and fluorescent marking[17-19]; no studies were identified that concerned ATP bioluminescence and fluorescent markers only. One systematic review was identified; this was comprised primarily of low level studies and was classed as level 2+ evidence; the remaining 10 studies were experimental studies classed as level 3 evidence. All of the studies were carried out in hospital settings (typically general medical or surgical wards). 2 studies were carried out in the UK (1 in Scotland[10] and 1 in England[9]), of the remaining studies 5 were carried out in the US,[13;16-19] 1 in Italy,[12] 1 in Taiwan[14] and 1 in the Republic of Ireland.[15]

The included studies were generally consistent in their objectives and methodology, however, as shown in table 1 there was considerable variation in the acceptable limits set for ATP (≥ 1 to ≥ 15.6 (relative light unit) RLU/cm^2); there was less variation in acceptable ACC (aerobic colony counts) limits with the majority of studies setting a threshold of ≥ 2.5 (colony forming units) CFU/cm^2. Two of the three studies that assessed removal of fluorescent markers considered complete removal of the marker as an indicator of effective decontamination;[18;19] however, one study also accepted partial removal of the marker.[17] To facilitate comparisons between studies RLU measurements have been converted to RLU/cm^2 to account for any difference in size of sampling areas between studies, this does not apply to the systematic review by Amodio et al.[11]

The most commonly used ATP bioluminescence monitoring system was the 3M Clean-Trace ATP System used in 6 studies,[13-18] followed by the Hygiena system used by 2 studies[9;10] and the Accupoint Healthcare (HC)[19] and Lumicontrol II systems[12] each used in 1 study. One of the studies assessed fluorescent marker removal using DAZO (Ecolab) only[19] and two used a variety of markers[17;18] (Glo Germ gel, Glo germ and DigiGlo, (Ecolab) Glitterbug (Brevis) or The Inspector (Creative solutions)).

The cleaning methodology was typically poorly reported in these studies, 5 of the included studies did not state what products were used and it was not always clear whether the cleaning undertaken was routine, post-discharge or terminal. One study used detergent for routine cleaning and 0.6% hypochlorite for patients with MRSA but did not break down the results according to cleaning methodology.[15]

Table 1 adjusted outcome measurements for included studies

Study	ATP bioluminescence	ATP limit (RLU/cm^2)	ACC limit (CFU/cm^2)	Fluorescent marker
Amodio et al.[12]	1	<1	<2.5	N/A
Mulvey et al.[10]	2	<1	<2.5	N/A
Smith et al.[13]	3	-	<2.5	N/A
Smith et al.[16]	3	<2.5/8	<2.5	N/A
Sherlock et al.[15]	3	<5	<2.5	N/A
Huang et al.[14]	3	<5	<2.5	N/A
Boyce et al.[17]	3	<9.7	<2.5	Complete or partial removal
Snyder et al.[18]	3	<9.7	<5	Complete removal
Willis et al.[9]	2	<10	<10	N/A
Luick et al.[19]	4	<15.6	<2.5	Complete removal

1= Lumicontrol II (PBI International, Milano, Italy

2= Hygiena system (Hygiena® International Ltd., Watford, UK.)

3=3M clean-trace system (3M Co., St Paul, MN)

4=Accupoint Healthcare (HC) system (Neogen, Lansing, MI)
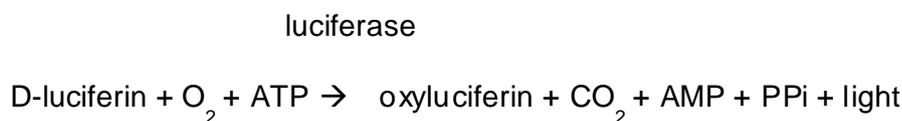
Research Questions

1. Are ATP bioluminescence and fluorescent marker monitoring systems currently used in UK health settings? If not, are they used in healthcare settings outside the UK?

This review identified two UK based studies where ATP bioluminescence monitoring systems were being tested, including one in NHSScotland.[9;10] In addition NHSScotland (Health Facilities Scotland) undertook a visit to North Tees Hospital Trust in England to produce a report on their use of ATP bioluminescence as a tool for monitoring environmental cleanliness. [20] The report found that ATP monitoring had been used effectively as 'a platform for promotion of hospital hygiene' and had been useful for monitoring environmental cleanliness, as a training tool and to promote public confidence. ATP monitoring was introduced in this Trust alongside a number of other measures to improve environmental cleanliness and as such it is not possible to derive the impact that ATP monitoring has had on rates of HAI. The report also highlights that ATP monitoring should not be used as a standalone measure for hospital hygiene.

2. How do ATP bioluminescence and fluorescent marker monitoring systems work?

ATP bioluminescence monitoring systems

Adenosine triphosphate (ATP) is present in all plant and animal cells and all microorganisms; it is necessary for transporting chemical energy within these cells for metabolism. ATP can be used as an indicator of organic soil (shed skin cells, microorganisms etc) on surfaces. ATP reacts with firefly luciferase to produce light in the following reaction:[20]

$$\text{D-luciferin} + O_2 + \text{ATP} \xrightarrow{\text{luciferase}} \text{oxyluciferin} + CO_2 + \text{AMP} + \text{PPi} + \text{light}$$

Under optimum conditions this reaction is linear and 1 relative light unit (RLU) is equivalent to 1 molecule of ATP. The emitted light from this reaction can be measured using a luminometer.

Fluorescent marker monitoring systems

Fluorescent markers are clear and colourless but fluoresce under a blacklight and so should not be visible during cleaning. By placing these products on surfaces in healthcare settings before cleaning takes place the effectiveness of cleaning can be inferred by assessing whether or not the mark has been removed.[7]

3. What is the procedure for using ATP bioluminescence and fluorescent marker monitoring systems?

Procedure for using ATP bioluminescence monitoring systems

ATP monitoring systems are designed to be simple to use and require minimal training.[21;22] The systems consist of a single-use pre-moistened swab contained within a sealed tube and a device for detecting and measuring bioluminescence (a luminometer). To perform the test the pre-moistened swab is removed from its sealed tube and the test area is swabbed in one direction, then the other direction using a rotating motion to ensure good coverage of the swab. The swab is the replaced in its tube, at this point an activating reagent is released from within the tube by puncturing the compartment it is stored in (this is typically done by clicking or snapping the top of the tube). The tube is shaken to mix the reagents, after the required time (5s) the swab is removed and placed into the luminometer which provides a reading, typically in less than 30 seconds.

Procedure for using fluorescent marker monitoring systems

Fluorescence marker monitoring systems are designed to be simple to use and require minimal training. These products are placed in a specified area, typically a high-touch surface, before cleaning takes place. After cleaning a blacklight is shone on the area where the mark was placed to determine whether the mark was removed (successful cleaning) or not (cleaning not successful).

4. What is the scientific evidence for effectiveness for ATP bioluminescence and fluorescent marker monitoring systems?

Evidence for effectiveness of ATP monitoring systems

All studies were of **level 3 (low-quality) evidence**, with the exception of the systematic review which was designated **level 2+ (moderate-quality) evidence**.

The systematic review by Amodio et al identified 12 studies for inclusion, no meta-analysis was performed, instead the review systematically summarised the available literature on the effectiveness of ATP assessment as a monitoring tool for environmental cleanliness in the hospital setting.[11] ATP thresholds for cleanliness in the included studies ranged from 100 to 500 relative light units (RLUs), actual ATP measurements reported ranged from 0 to >500,000RLU before cleaning and from 3 to >500,000RLU after cleaning. The failure rates (% of surfaces that exceeded the acceptable limits for ATP) in the included studies varied from 21.2% to 93.1% before cleaning and from 5.3% to 96.5% after cleaning. The authors conclude that while ATP bioluminescence is a quick and objective method for monitoring hospital cleanliness, the methodology and acceptable limits are still poorly standardised both nationally (UK) and internationally. The authors also note that the variability seen between studies is likely due to the

differences in materials, methods and bioluminescence tools employed, and that this makes comparisons between studies difficult.

Another study by Amodio et al aimed to investigate the association between relative light units measured by ATP assay and aerobic colony counts (ACC/cm^2) on hospital surfaces.[12] The study took place in a 500 bed University hospital in Italy. 193 samples sites were randomly selected and swabbed 2 hours after cleaning to assess presence of ATP using the Lumicontrol II ATP system. Swabs were taken at adjacent sites to assess ACC/cm^2 and to screen for the presence of *Staphylococcus aureus.* Sites sampled included tables, lockers and furnishings (bed, chair etc.). Of the 193 surfaces tested 44% exceeded the acceptable microbiological limit of ≥2.5CFU/ cm^2. The authors found that higher RLUs were significantly associated with failing the acceptable microbiological limit (p=<0.001). The analyses performed for this study were not clearly presented, it appears as though the correlation between RLU and CFU/cm^2 is minimal when assessed by Pearson's correlation coefficient (R^2=0.29). However, none of the surfaces that achieved an ATP reading of <1RLU/cm^2 failed the microbiological standard suggesting that for this model of luminometer, in this setting, an acceptable ATP limit of <1RLU/cm^2 may be an accurate measure of surface cleanliness rather than the manufacturer's suggested limit of <5RLU/cm^2. This is a small study and wider testing of this acceptable limit would be required.

Similarly, Mulvey et al also found that an acceptable ATP limit of <1RLU/cm^2 was optimum. This study assessed ATP and ACC/cm^2 before and after detergent cleaning in two 4 bedded bays (one surgical, one medical) in the Southern General Hospital, Glasgow.[10] 10 surfaces were tested - 5 clinical surfaces (bedside locker; bedframe (left side); overbed table; floor under bed; and bedframe (right side)) and 5 surfaces not included in routine domestic cleaning (bedside curtain; patient notes; computer keyboard; nurses' desk; and toilet door pushplate). The study did not initially set an acceptable limit for ATP; ACC were categorised as no growth (0 CFU/cm^2), scanty growth (<2.5 CFU/cm^2), light growth 2.5-12 CFU/cm^2), moderate growth 12-40 CFU/cm^2) or heavy growth 40-100 CFU/cm^2), only no growth or scanty growth were considered acceptable. The study assessed 270 paired data points for ATP and ACC/cm^2. ATP data were further stratified into acceptable limits of 0.25RLU/cm^2, 1 RLU/cm^2 and 2.5RLU/cm^2 and the proportion of surfaces failing the ATP test were calculated for each microbial growth category. Sensitivity and specificity for each growth category were calculated, there was weak evidence for ATP as an indicator of microbial contamination and that an acceptable ATP limit of <1RLU/cm^2 was optimum (sensitivity 57%, specificity 57%). The authors concluded that ATP monitoring could be a useful indicator of surface cleanliness provided that an appropriate benchmark was used and that the results were 'collected systematically over time and interpreted accurately'. The authors also highlight that there are limitations to ATP monitoring, for example, there was variation between triplicate samples

that could not be explained and *S. aureus* was identified on 7 sites that had been deemed clean by ATP monitoring.

Smith et al measured ATP and ACC/cm^2 on bisected hospital surfaces before and after cleaning and assessed whether there was an association between these two methods.[13] The study took place in a 650-bed acute care, tertiary referral centre. A convenience sample of ten patient rooms were selected post-discharge. 18 surfaces within each room were sampled, these were; bedrail control panel, nurse call light, sink faucet handle, bedside table hi/lo control, patient phone, bedrail, toilet flush handle, stethoscope diaphragm, room chair arms, patient lounge chair, bedside table surface, exterior door handle, soap dispenser, sink light switch, toilet seat, main light switch, mattress, bathroom interior door handle. Higher RLU readings were observed for surfaces with CFU counts ≥2.5CFU/cm^2 (n=76) versus those with counts <2.5CFU/cm^2 (n=94) (p<0.001).   In addition the three surfaces with the lowest RLU readings were ranked identically in order of CFU counts (main light switch, mattress and interior door handle) and four surfaces were ranked in the top 6 for contamination by both ATP and CFU counts. In this study mean colony counts of ≥2.5CFU/cm^2 were associated with mean RLU readings ranging from 3.5-34.4RLU/cm^2, the authors have not suggested an ATP threshold based on their data.

A second study by Smith et al attempted to identify an optimum acceptable ATP limit by drawing a ROC curve of false positives and true positives determined using an acceptable ATP limit of ≤2.5RLU/cm^2 and ACC limit of ≤2.5CFU/cm^2. [16] This study took place in 10 rooms of a 698-bed tertiary referral hospital in Nebraska, US. 10 surfaces were sampled before and after discharge cleaning, these were; top of mattress, mattress side, bed head/foot board, bedrail (top), bedrail (inner panel), overbed table, commode seat, room chair arms, call light and patient telephone. The percentage of surfaces deemed 'dirty' by ATP and ACC before cleaning were 76% and 53%, respectively. The percentage of surfaces deemed dirty by ATP and ACC after cleaning were 48% and 10%, respectively. A chi-squared test showed a positive association between pre-clean results for ATP and ACC (P=0.001) but not after cleaning (p=0.51). Analysis of false positives and true positives as determined by ACC demonstrated that a cut-off value of 8.0RLU/cm^2 had the optimum sensitivity and specificity. ATP assay sampling results were assessed again using the optimum RLU threshold and using these values, before cleaning 47% of the surfaces were deemed dirty and after cleaning 20% of the surfaces were deemed dirty. After recalculating results using the adjusted ATP limit a chi-squared test showed positive association between ATP and ACC (P=0.01).

Sherlock et al aimed to evaluate the potential use of ATP monitoring in the hospital environment. This study assessed environmental cleanliness on the surgical and medical wards of a 700 bed tertiary care hospital in Dublin, Ireland.[15] One room on each ward was selected and 10 surfaces were assessed before and after cleaning, these were; door handle/pushplate, patient table, patient

locker, window ledge, a random area in a treatment room, a random area on the nurse's desk/station, the toilet floor, patient bedframe and the handle rail in the toilet. Acceptable limits were set at <5RLU/cm^2 and <2.5CFU/cm^2 for ATP and ACC, respectively. In total, across both wards 28.5% of samples exceeded acceptable ATP limits, in comparison 7.9% exceeded acceptable ACC limits. Fail rates for ATP assay and ACC were 15% and 5%, respectively on the medical ward before cleaning whereas 3% and 0.8% failed after cleaning. On the surgical ward, fail rates for each method before cleaning were 22.5% and 6.6% and after cleaning were 16.6% and 2.5%; no association was found between ATP and ACC.

Huang et al assessed the ability of ATP monitoring to detect clean surfaces before and after terminal cleaning (disinfection with 600ppm av.cl.) as compared to the microbiological gold standard of ACC. [14] The study took place on the surgical and medical wards of a 2200 bed tertiary hospital in Taiwan. 8 rooms were selected and 10-12 high touch surfaces in each room were sampled including; the door knob, light switch, windowsill, bedside rails, bedside cabinets, couch, toilet seats and hand rails, refrigerator, kettle, and closet handles. Acceptable limits were set at <5RLU/cm^2 and <2.5CFU/cm^2 for ATP and ACC, respectively. Before cleaning, the overall fail rates by ATP and ACC were 50.6% and 20.0%, respectively. After cleaning, the fail rates were 21.2% and 5.9%, respectively. The fail rate using ATP monitoring was significantly higher than that of ACC (p=<0.05). If adopting a reference of <2.5 CFU/cm^2 as adequate cleanliness, the sensitivity and specificity of ATP monitoring were 63.6% and 68.2%, respectively. A ROC curve of the ATP data indicated that the optimal ATP cut-off value was estimated to be 5.57 RLU/cm^2.

Boyce et al assessed the ability of ATP monitoring and ACC to detect clean surfaces before and after terminal cleaning with a quaternary ammonium compound. [17] This study took place in a 500 bed community teaching hospital, a convenience sample of 100 rooms on medical and surgical wards were selected and 5 high touch surfaces were assessed, the surfaces were; bedside rails, overbed tables, television remote controls, bathroom grab bars and toilet seats. Surfaces were considered clean if they yielded ACC of <2.5CFU/cm^2 or ATP values of <9.7RLU/cm^2. Of the 500 surfaces sampled after terminal cleaning 384 (77%) were classed as clean according to ACC and 225 (45%) were classed as clean according to ATP monitoring. No correlation was found between the number of surfaces found to be clean by ATP monitoring and ACC.

Snyder et al assessed the ability of ATP monitoring to detect clean surfaces before and after post-discharge cleaning using a quaternary ammonium compound as compared to the microbiological gold standard of ACC.[18] This study took place in 661-bed tertiary care hospital in the US. A convenience sample of 20 rooms was selected and 15 surfaces within each room were assessed, these were; bed rail, overbed table, call button, bedside telephone, bedside table, chair, room sink, light switch, inner door knob, bathroom light switch, bathroom hand rail, bathroom sink, toilet seat and bedpan cleaner. Surfaces were considered clean if they yielded ACC of <5CFU/cm^2 or ATP

values of <9.7RLU/cm^2. Of the tested surfaces 72.1% (209) were microbiologically clean with ACC ≤5CFU and 66.2% of surfaces were determined to be clean by ATP monitoring. The sensitivity of ATP to detect clean surfaces was 70.3%, the specificity was 44.4%, and ATP monitoring was poorly correlated to microbial contamination (or lack of) on tested surfaces.

Willis et al assessed the ability of ATP monitoring to detect clean surfaces as compared to the microbiological gold standard of ACC.[9] The cleaning methodology for this study was not described. This study took place across three wards of an English hospital, 108 sites were sampled including 54 floor areas under patient beds, 17 commode seats, 19 pieces of patient equipment (e.g. sphygmomanometers and volumed pumps) and 18 clinical workstations. Surfaces were considered clean if they yielded ACC of <10CFU/cm^2 or ATP values of <10RLU/cm^2. In total 36% of sites sampled were considered unsatisfactory by ACC and 37% by ATP testing. ATP and ACC data were not correlated (correlation coefficient = 0.15), however, there was no significant difference in the proportion of pass/fails between the two methods. Of the sites deemed clean by ATP assay 1 tested positive for MRSA, 2 for *Enterococci* and 3 for *Enterobacteriaceae.*

Luick et al assessed the ability of ATP monitoring to detect clean surfaces as compared to the microbiological gold standard of ACC before and after post-discharge cleaning.[19] This study took place in a 580 bed community hospital in England. A convenience sample of 50 rooms were studied, samples were taken from 5 surfaces in each room (call button, telephone, bed rail, table and toilet rail) before and after terminal cleaning. Surfaces were considered clean if they yielded ACC of <2.5CFU/cm^2 or ATP values of <15.6RLU/cm^2. Before cleaning, 53% of surfaces were classed as clean by ATP assay and 59% by ACC. After cleaning, 76% of surfaces were classed as clean by ATP assay and 87% by ACC. Compared to ACC, ATP found significantly fewer surfaces considered clean after terminal cleaning (p<0.001). The sensitivity of ATP to detect clean surfaces was 78% and the sensitivity was 38%.

Evidence for effectiveness of fluorescent marker monitoring systems

All studies were of **level 3 (low-quality) evidence**.

Boyce et al assessed the ability of fluorescent marker removal to detect clean surfaces before and after terminal cleaning with a quaternary ammonium compound compared to the microbiological gold standard ACC. The study was carried out as described above; a fluorescent marker was applied to the 5 selected high touch sites before cleaning commenced. In the first 24 rooms surfaces were marked with Glitterbug (Brevis) or The Inspector (Creative solutions), surfaces in the remaining 76 rooms were marked with DAZO (Ecolab). Surfaces were considered clean if they yielded ACC of <2.5CFU/cm^2 or if the fluorescent marker was completely or partially removed. Of the 500 surfaces sampled after terminal cleaning 378 (76%) were classed as clean using fluorescent markers and 384 (77%) were classed as clean according to ACC. The proportion of

surfaces considered clean was similar for ACC and fluorescent markers except for samples taken from bathroom grab bars where the proportion deemed clean by ACC was significantly more than by fluorescent marker removal (p=.007). The study did not stratify the data by brand of fluorescent marker.

Snyder et al assessed the ability of fluorescent marker (Glo Germ gel, Glo germ and DigiGlo, Ecolab) removal to detect clean surfaces before and after post-discharge cleaning using a quaternary ammonium compound as compared to the microbiological gold standard of ACC.[18] The study was carried out as described above; a fluorescent marker was applied to the 15 selected surfaces before cleaning commenced. Surfaces were considered clean if they yielded ACC of <5CFU/cm^2 or if the fluorescent marker was completely removed. Of the tested surfaces 72.1% (209) were considered clean by ACC and 49.3% by Fluorescent marker removal. The sensitivity and specificity of fluorescent marker removal to detect clean surfaces were 51% and 55.6%, respectively. The authors found that fluorescent marker removal was poorly correlated to ACC and is more likely to falsely report a surface as dirty.

Luick et al assessed the ability of fluorescent marker removal to detect clean surfaces as compared to the microbiological gold standard of ACC before and after post-discharge cleaning.[19] The study was carried out as described above; a fluorescent marker (Dazo, Ecolab) was applied to the 5 selected surfaces before cleaning commenced. Surfaces were considered clean if they yielded ACC of <2.5CFU/cm^2 or if the fluorescent marker was completely removed. Compared to ACC, significantly fewer surfaces were considered clean by fluorescent marker removal after terminal cleaning (p<0.001). The sensitivity of fluorescent marker removal to detect clean surfaces was 68% and the sensitivity was 50%.

5. Are there any safety considerations associated with using ATP bioluminescence and fluorescent marker monitoring systems in the healthcare setting?

This review did not identify any safety considerations associated with the use of ATP bioluminescence or fluorescent marker monitoring systems.

6. Are there any practical or logistical considerations associated with using ATP bioluminescence and fluorescent marker monitoring systems in the healthcare setting?

This review did not identify any evidence of practical or logistical considerations associated with ATP bioluminescence and fluorescent marker monitoring systems. In the procedure described for North Tees Hospital Trust[20] it suggests that ATP monitoring is performed on cleaned rooms and that no-one enters rooms between cleaning and ATP assessment, this could potentially be difficult in busy clinical areas.

7. What costs are associated with using ATP bioluminescence and fluorescent marker monitoring systems in the healthcare setting?

This review did not identify any cost analysis regarding ATP bioluminescence and fluorescent marker monitoring systems. However, the North Tees Hospital Trust report states that each swab costs £1 and that 5 swabs are used per room. This does not include the initial cost of the luminometer(s) and it is not clear whether the swabs will continue to be available at this price.

8. Have ATP bioluminescence and fluorescent marker monitoring systems been assessed by the Rapid Review Panel (RRP)?

ATP monitoring systems from 3M healthcare (biotrace) and Hygiena International Limited have both been evaluated by the Rapid Review Panel and both achieved a recommendation level score of 1 (R1). The RRP will award an R1 if '*basic research and development, validation and recent in use evaluations have shown benefits that should be available to NHS bodies to include as appropriate in their cleaning, hygiene or infection control protocols*'.

Discussion

All studies were of **level 3 (low-quality) evidence**, with the exception of the systematic review on ATP bioluminescence which was designated **level 2+ (moderate-quality) evidence**. The systematic review by Amodio *et al.* included 4 of the studies indentified by this review[9;10;15;17] however, complete inclusion and exclusion criteria were not detailed. This systematic review found that comparisons between published studies on ATP monitoring systems were difficult due to the lack of consistency in methodology and acceptable ATP limits set within each study.

This review found the same variation in acceptable ATP limits, there was also considerable variation in the cleaning methodology used in these studies. Reference was made in the identified studies to certain products (e.g. disinfectants) interfering with ATP assays,[10;11] however, it is not clear in what direction this might influence results and it is not possible to take this into consideration without a complete methodology.

The majority of included studies did not find a direct correlation between ATP (RLU/cm^2) and microbial contamination (CFU/cm^2), however, four of the studies found that pass/fail rates between the two methods were similar and/or could be improved by optimising the acceptable limits for ATP.[9;10;12;16] Studies that adjusted their acceptable ATP limits based on actual microbiological contamination were able to find correlation in pass/fails between the two methods suggesting that internal validation may be an important factor in the effectiveness of ATP monitoring. Additionally, studies that included before and after measurements consistently demonstrated that ATP monitoring systems were able to detect improvements in surface cleanliness after decontamantion.[10;13-19] ATP monitoring systems were prone to generating false positive results (assessing a surface as dirty that was microbiologically clean), however, it is important to note that there were instances of microbial contamination with alert organisms (e.g. MRSA) on surfaces that had been deemed clean by ATP monitoring.[9;10]

Only one of the three studies that assessed fluorescent marker monitoring systems found that this method was associated with microbial contamination.[17] In the two other studies fluorescent marker monitoring systems gave a high number of false positives (assessing a surface as dirty that was microbiologically clean).[18;19]

Conclusion

ATP bioluminescence and fluorescent marker monitoring systems are sensitive but generally lack specificity and are more likely to generate false positives (assessing a surface as 'dirty' that is microbiologically clean) than false negatives. However, false negatives were demonstrated in the literature and surfaces that meet acceptable ATP limits may still be contaminated with organisms capable of causing HAI e.g. MRSA. The sensitivity and specificity of ATP monitoring systems may be improved by internal validation of acceptable ATP limits against a microbiological comparator (CFU/cm^2).

There is insufficient evidence to support the use of either ATP bioluminescence or fluorescent marker monitoring systems to infer the microbiological cleanliness of a surface. However, both methods may be useful for training and monitoring purposes provided appropriate benchmarking is implemented.

Implications for research

This review identified research gaps in this topical area. Firstly, as demonstrated in this review there is a lack of consistency in established acceptable limits for ATP (RLU/cm^2), there is also an issue with clear reporting of cleaning methodology used in the included studies which should have been addressed during peer review before publication. The majority of included studies achieved a low grade of evidence when assessed with SIGN50 methodology and there is very limited published evidence on the effectiveness of fluorescent marker monitoring systems. Further studies are required with consistent and clearly presented methodology and which assess the impact of ATP bioluminescence and fluorescent marker monitoring systems on rates of HAI. It will also be necessary to elucidate whether some products (detergent/disinfectants) may interfere with the ATP assay itself and in what direction this may influence results.

Recommendations for practice

This review makes the following recommendations based on an assessment of the extant scientific literature on ATP bioluminescence and fluorescent marker monitoring systems.

If NHS boards use ATP bioluminescence and fluorescent marker products for monitoring decontamination of the healthcare environment and patient care equipment, the following must be considered:

- ATP bioluminescence and fluorescent marker monitoring systems can be used for the purpose of staff training and for monitoring of the healthcare environment.
  (Grade D recommendation)

- There is insufficient evidence to support the use of either ATP bioluminescence or fluorescent marker monitoring systems to infer the **microbiological** cleanliness of a surface.
  (Grade D recommendation)

- Where ATP bioluminescence or fluorescent marker monitoring systems are used, appropriate benchmarking and methodology should be implemented prior to use.
  (Good Practice Point)

- Staff using ATP bioluminescence and fluorescent marker monitoring systems must be fully aware of the benchmarking standards and methodology, and fully trained in the product's use/limitations.
  (Good Practice Point)

Appendix 1: Medline Search

Ovid MEDLINE(R) 1946 to present with daily update

AND

Ovid MEDLINE(R) In-process & other non-indexed citations

Search dates

08/02/2016

Search terms

	AND		AND

1 (all "OR")	2 (all "OR")	3 (all "OR")
ATP.mp. Adenosine/ Adenosine Triphosphate/	clean*.mp. Sterilization/ Decontamination/ Disinfection/ Housekeeping, Hospital/	testing.mp. Equipment Contamination/ Environment/ Monitoring/ Luminescence/ bioluminescence.mp.

Limits

English language

Publication Year 2005-current

Results: 704

Appendix 1: Medline Search

References

(1) Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: norovirus, Clostridium difficile, and Acinetobacter species. AM J INFECT CONTROL 2010 Jun;38(5 Suppl 1):S25-S33.

(2) Weber DJ, Anderson D, Rutala WA. The role of the surface environment in healthcare-associated infections. Curr Opin Infect Dis 2013 Aug;26(4):338-44.

(3) Weber DJ, Anderson DJ, Sexton DJ, Rutala WA. Role of the environment in the transmission of Clostridium difficile in health care facilities. AM J INFECT CONTROL 2013 May;41(5 Suppl):S105-S110.

(4) Boyce JM. Environmental contamination makes an important contribution to hospital infection. J HOSP INFECT 2007 Jun;65 Suppl 2:50-4.

(5) Griffith CJ, Obee P, Cooper RA, Burton NF, Lewis M. Evaluating the thoroughness of environmental cleaning in hospitals. J HOSP INFECT 2007 Dec;67(4):390.

(6) Griffith CJ, Obee P, Cooper RA, Burton NF, Lewis M. The effectiveness of existing and modified cleaning regimens in a Welsh hospital. J HOSP INFECT 2007 Aug;66(4):352-9.

(7) Ecolab. DAZO Fluorescent Marking Gel. 2015 http://www.ecolab.com/product/dazo/ Accessed:28-7-2015

(8) Scottish Intercollegiate Guidelines Network. SIGN 50 A guideline developer's handbook. Scottish Intercollegiate Guidelines Network; 2011.

(9) Willis C, Morley R, Westbury J, Greenwood M, Pallett A. Evaluation of ATP bioluminescence swabbing as a monitoring and training tool for effective hospital cleaning. British Journal of Infection Control 2007 Oct;8(5):17-21.

(10) Mulvey D, Redding P, Robertson C, Woodall C, Kingsmore P, Bedwell D, et al. Finding a benchmark for monitoring hospital cleanliness. J HOSP INFECT 2011;77(1):January.

(11) Amodio E, Dino C. Use of ATP bioluminescence for assessing the cleanliness of hospital surfaces: a review of the published literature (1990-2012). [Review]. Journal of Infection and Public Health 2014 Mar;7(2):92-8.

(12) Amodio E, Cannova L, Villafrate MR, Merendino AM, Aprea L, Calamusa G. Analytical performance issues: comparison of ATP bioluminescence and aerobic bacterial count for evaluating surface cleanliness in an Italian hospital. J OCCUP ENVIRON HYG 2014;11(2):D23-D27.

(13) Smith PW, Gibbs SG, Sayles H, Hewlett A. Observations on hospital room contamination testing. HEALTHC INFECT 2013 Mar;18(1):10-3.

(14) Huang Y-S, Chen Y-C, Chen M-L, Cheng A, Hung I-C, Wang J-T, et al. Comparing visual inspection, aerobic colony counts, and adenosine triphosphate bioluminescence assay for evaluating surface cleanliness at a medical center. AM J INFECT CONTROL 2015;43(8):01.

(15)   Sherlock O, O'Connell N, Creamer E, Humphreys H. Is it really clean? An evaluation of the efficacy of four methods for determining hospital cleanliness. The Journal Of Hospital Infection 2009 Jun;72(2):140-6.

(16)   Smith PW, Sayles H, Hewlett A, Cavalieri RJ, Gibbs SG, Rupp ME. A study of three methods for assessment of hospital environmental cleaning. HEALTHC INFECT 2013 Jun;18(2):80-5.

(17)   Boyce JM, Havill NL, Havill HL, Mangione E, Dumigan DG, Moore BA. Comparison of fluorescent marker systems with 2 quantitative methods of assessing terminal cleaning practices. INFECT CONTROL HOSP EPIDEMIOL 2011 Dec;32(12):1187-93.

(18)   Snyder GM, Holyoak AD, Leary KE, Sullivan BF, Davis RB, Wright SB. Effectiveness of visual inspection compared with non-microbiologic methods to determine the thoroughness of post-discharge cleaning. Antimicrobial Resistance & Infection Control 2013;2(1):26.

(19)   Luick L, Thompson PA, Loock MH, Vetter SL, Cook J, Guerrero DM. Diagnostic assessment of different environmental cleaning monitoring methods. AM J INFECT CONTROL 2013 Aug;41(8):751-2.

(20)   Health Facilities Scotland. Use of ATP as a tool for monitoring cleanliness. Report on visit to North Tees Hospital Trust March 2011. 2015.

(21)   3M. Effective Hygiene Monitoring. 2016 http://solutions.3m.co.uk/wps/portal/3M/en_GB/FoodSafetyEU/FoodSafety/ProductApplications/HygieneControl/CleanTraceATP/

(22)   Hygiena Systems International. Hygiena SystemSURE plus. 2016 http://www.hygiena.com/systemsure-healthcare.html#more