HANDLING BCG USED IN THE TREATMENT OF BLADDER CANCER

INTRODUCTION

BCG has been used for the treatment of bladder cancer since the 1970s. In the UK it is given by intravesical administration and until 2000, there was no licensed product available on the UK market. Prior to this, products licensed in ‘third’ (non-EU) countries for this indication were used and dispensed on a ‘named patient’ basis. From the late 1990s onwards the level of use has increased, although still remains relatively low in terms of absolute patient numbers. Increasing risks associated with the safe handling of BCG products started to be highlighted at this time and many Pharmacy departments were asked about the possibility of undertaking the preparation of the product at this time. As highlighted below this generally needed investment in dedicated equipment for this purpose and given the small volume of use this was only ever achieved in a small number of centres.

In 2002, licensed products with effective closed system reconstitution devices were introduced to the UK market allowing the safe preparation of these products in clinical areas, and this then seemed to be an end to the problem.

However supply problems with the licensed products were then seen in 2012 and re-emerged at the end of 2014. There were limited supplies of licensed products in the market and the main source available seemed to be an unlicensed import from India. This product was incompatible with existing closed system devices and as the vial size meant that multiple vials would need to be used in preparation, the maintenance of a true closed system whatever the reconstitution system used will be impossible. In addition, in order to conserve stocks of licensed product, recommendations have been made to use part vials of licensed product. This further complicates matters, as the closed system devices supplied with these products can then no longer be used.

A survey carried out by Regional Quality Assurance in London and the South East found that what limited resources that had existed for handling BCG in pharmacy prior to 2002 had all been lost or reallocated to others uses in the interim period.

REVIEW OF PHARMACY HANDLING OF BCG PRIOR TO 2002

A variety of approaches had been adopted in hospitals, both NHS and Private, across the UK. These varied and include reconstitution and dilution within negative pressure isolators, down-draft laminar flow cabinets, microbiological safety cabinets, glove boxes (with or without air movement and filtration) and on the open bench in preparation rooms. Few hospitals enjoyed the luxury of setting aside an isolator or microbiological safety cabinet reserved solely for BCG because its use is generally low and the ability to outsource these prepared bladder irrigations was somewhat limited because of their short expiry dates - typically 4 hours.
HANDLING CONCERNS RAISED

The concerns that have been raised are:

1. risk to pharmacy and nursing staff involved in preparation activities.
2. cross contamination of other products.
3. microbiological contamination of the BCG with other organisms

The risk to staff is low if they employ safe working practices, are in a good state of health, and have been vaccinated and are not immunocompromised. This risk is further decreased if appropriate equipment is used for the preparation i.e. isolator technology or microbiological safety cabinets.

The risk of contamination of other products is negligible provided that reconstitution is a ‘closed’ procedure, dedicated equipment is used, there are adequate, validated cleaning procedures in place and staff are adequately trained and informed of the potential hazards. However, an American paper describes TB meningitis in two immunocompromised children due to iatrogenic BCG infection. The contamination in this case was thought to have occurred in or near the biological safety cabinet within the hospital pharmacy where BCG and the chemotherapeutic agents the children were being treated with, were prepared. No other contacts with TB were found. This highlights that the risk of cross contamination of other products prepared in the same equipment is a very real one.

The risk of contaminating BCG irrigation microbiologically is small if the precautions outlined above are in place. BCG irrigation is for immediate intravesicular administration so consequently the potential for contamination with other microorganisms is not a prime concern.

It is best practice, and a requirement of EU GMP, that where BCG is handled within a pharmacy then the preparation must be carried out in a dedicated isolator or class 2 microbiological safety cabinet. In this way the risk to the operator and risk of cross contamination is reduced to a minimum. The equipment used must be cleaned with a suitable agent both before and after preparation. Hypochlorite solutions are often used and extremely effective. However there are reports of corrosion of the stainless steel surfaces of equipment cleaned routinely with chlorine based disinfectants. This risk of corrosion can be reduced by removing any residual disinfectant using 70% I.M.S. after an appropriate contact time. All operators involved in such preparation should, via the hospital’s occupational health department, have their immunity to TB checked using the Heaf Test.

BCG PREPARATION ON THE WARD

The following text originally formed part of guidance published on this issue in 2002 by Regional Quality Assurance in London and the South East.

Reports of the Public Health Laboratory (Colindale) being asked to comment on the handling of BCG in hospitals have been followed up. They have been involved in this by hospital cross-infection nurses. The Public Health Laboratory’s response is that
BCG is a category 2 pathogen and can in theory be prepared for administration by nurses alongside the patient, inside the patient’s room. There is probably more risk of their exposure to the organism in giving the irrigation’s than there is in preparing them.

If this stance is still accepted then nurses involved must also have a Heaf test confirming their immunity, be suitably trained to prepare the BCG for irrigation along locally set guidelines, wear such protective clothing as is necessary (a plastic apron, mask and gloves should be the minimum adopted) and there should be in place such cleaning procedures to ensure that the risk of any organisms contaminating anything in the room are dealt with at the end of procedure.

If a hospital adopts this method of preparation and administration of BCG then other issues of risk management must be addressed locally. The movement of other staff and patients through the room while this is going on must be restricted and the room used for other purposes only after satisfactory cleaning has been performed using cleaning agents shown to be effective. The infection control nurses obviously play a very important role in ensuring that the risk to other patients is kept to a minimum. Additionally Occupational Health must check staff immunity using the Heaf test.

**UPDATE IN NOVEMBER 2014**

The current supply situation now appears to place many Trusts back in the position they were in with regards to handling of BCG prior to 2002.

During the initial shortage of BCG in 2012, a number of Trusts experimented with various reconstitution devices on the market and one in particular sourced a combination of components that provided a workable but far from perfect system. It is understood that currently in 2014, some importers are providing these components with the Indian BCG product.

Whilst this offers some help in reconstitution, it cannot be regarded as a true closed system device as it consists of several separate components used together and as stated before, the Indian product requires use of multiple devices.

There have also been anecdotal reports of leakages occurring in use. One possible reason for these could be that these type of devices are not routinely used in clinical areas and so staff there may not be fully trained in and familiar with the principles behind their use.

With regards to good preparation technique and use of such devices, it must be remembered that trained Pharmacy aseptic unit staff (where available) can be a possible source of advice and training to staff in clinical areas.

Few if any Pharmacy aseptic units are likely to have the ability to take on preparation of BCG without significant capital investment.

While the risks of handling BCG in clinical areas can be minimised by using PPE and good techniques it must be stressed that there are risks to staff and patients and these cannot be eliminated.
The current position is far from ideal both from the point of view of patient treatment options and staff safety and ideally, the reconstitution of BCG in clinical areas should never take place in clinical areas using anything other than a true closed system device.

Any final decision on handling BCG must ultimately be made individually at Trust level as the result of a documented risk assessment involving all relevant staff. The residual risks should be formally accepted and where appropriate placed on the Trust Risk Register.

References