Glucose, bronchial secretions and MRSA

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Association of MRSA infection with abnormal glucose levels in respiratory tract secretions

Strains of Staphylococcus aureus resistant to first line antibiotic therapy (the penicillinase resistant penicillins cloxacillin, flucloxacillin and methicillin), termed methicillin resistant S aureus (MRSA), first appeared in 1961 and are now widespread worldwide. In the UK MRSA is particularly prevalent, especially on intensive care wards, causing a variety of important nosocomial infections. Infection with MRSA usually requires parenteral therapy with a glycopeptide antibiotic and frequently substantially prolongs the patient’s hospital admission. Isolation of carriers places considerable stress on available bed resources and local outbreaks can even result in temporary ward closures. As a consequence, the human and financial burden of MRSA is significant, and this is reflected by the adoption of improved control of hospital acquired infections by a major political party as a major election “pledge”.

The paper by Philips et al in this issue of Thorax reports a possible association between a positive culture for MRSA from bronchial aspirates from patients in an intensive care ward and abnormally high levels of glucose in the bronchial aspirates (ranging from 2.7 to 4.4 mmol/l). MRSA infection was just over twice as likely in patients with abnormal glucose levels in bronchial aspirates, but the overall incidence of 45% for isolation of MRSA from the respiratory tract is surprisingly high and may limit the applicability of these results to other hospitals. However, if the association of MRSA with abnormal glucose levels in respiratory secretions is reproducible, it does offer a potential way of identifying patients at risk of MRSA infection. Hyperglycaemia is associated with both an increased severity of pneumonia and with death from sepsis for twice as likely in patients with abnormal glucose levels in bronchial aspirates, providing support for a relationship between infection and high levels of glucose in respiratory secretions. However, many questions remain about the role of glucose in bronchial secretions and a possible increased risk of infection.

Firstly, what is the mechanism by which high glucose levels occur in bronchial secretions? The very low concentration of glucose in normal respiratory airway surface fluid (<0.5 mmol/l) is thought to be actively maintained by reabsorption of glucose by an epithelial sodium glucose co-transporter. In a previous study increasing hyperglycaemia was associated with increasing glucose levels in respiratory secretions. All subjects with a blood glucose level of >10.1 mmol/l had abnormal glucose levels in respiratory secretions. This suggests that at a threshold level of hyperglycaemia there is “overflow” into bronchial secretions, perhaps because active reabsorption of airways fluid glucose by sodium glucose co-transporters is saturated or inefficient in the presence of hyperglycaemia. In addition to “leakage” due to hyperglycaemia, glucose could also enter bronchial secretions via the breakdown of the integrity of endothelial and epithelial layers as a result of local or systemic inflammation. This possibility is supported by earlier work by Philips et al which found that non-diabetic subjects with acute viral rhinitis have abnormal levels of glucose in their respiratory tract secretions.

Secondly, is the association of abnormal glucose levels and infection in bronchial aspirates causally related? Rather than increasing the risk of infection, the association of MRSA with abnormal glucose levels in bronchial aspirates could reflect the effects of a third confounding factor. Alternatively, abnormal glucose levels in bronchial secretions could just be a marker for hyperglycaemia and it is the blood glucose level that affects susceptibility to respiratory infection. Corticosteroid therapy and illness severity are the two most obvious confounding factors that are known to influence the levels of infection and glucose, but neither was significantly different between patients with abnormal or normal glucose levels in bronchial aspirates. Diabetes could also be an independent risk factor for infection irrespective of hyperglycaemia, but in this study most of the patients had raised blood glucose levels due to stress hyperglycaemia rather than diabetes. Antibiotic use could also be increased in patients with hyperglycaemia and lead to higher levels of MRSA infection, but unfortunately data on antibiotics was not provided in the study by Philips et al. The proportion of patients with infiltrates on the chest radiograph and the C reactive protein level were both increased in patients with abnormal glucose levels in bronchial aspirates, and the authors have interpreted this as evidence for pneumonia due to MRSA in this group. However, this would give an implausibly high incidence of MRSA pneumonia in these patients. It is more likely that the pulmonary infiltrates in these patients had many different causes, and the presence of lung shadowing could be another possible confounding factor associated independently with abnormal glucose levels and increased infection in bronchial aspirates.

Additional prospective detailed studies are required to evaluate in more detail the relationship between glucose levels and infection in bronchial aspirates before the association can be confirmed to be clinically important. Laboratory studies suggest that it is biologically plausible that high glucose levels in bodily fluids can lead to an increased risk of infection. Glucose is an excellent source of nutrition for many bacteria, and it is also an environmental signal that can modulate bacterial gene expression and therefore potentially affect virulence. Furthermore, glucose can inhibit various aspects of the immune system including phagocyte and T cell function. However, these effects usually require much higher levels of glucose than those observed in bronchial secretions in this study. At present there are few data on the effects of glucose on physical lung defences such as mucociliary function, but the increased osmolality of airways fluid could adversely affect mucus clearance. Hyperglycaemia may also have a “hangover” effect on the function of migrating white cells, in which case abnormal glucose levels in the respiratory tract would be a marker—but not necessarily a cause—for impaired respiratory immunity.

The third question this article raises is whether abnormal glucose levels in bronchial aspirates is only associated with S aureus infection, as the incidence of other pathogens was too low for any conclusions to be drawn. If respiratory host defences are impaired by abnormal levels of glucose, this would increase infection by other pathogens in addition to MRSA. In addition, many bacterial and fungal species, including the important respiratory tract pathogens Streptococcus pneumoniae, Pseudomonas aeruginosa, and...
Aspergillus fumigatus, can use glucose as a carbon source. Therefore, if abnormal glucose levels in respiratory secretions do lead to an increase in infection, the pathogens affected will probably not be limited to MRSA. This may have implications in controlling infection in other patient groups—for example, patients with cystic fibrosis who frequently have co-existent diabetes and chronic bronchial suppuration, or patients on long term corticosteroid treatment for chronic lung conditions such as pulmonary fibrosis and asthma.

The novel observation by Philips et al. that MRSA infection is associated with abnormal glucose levels in respiratory tract secretions may eventually lead to improved control of MRSA and potentially other respiratory tract infections in high risk patients. However, further research is needed to evaluate the potential mechanisms underlying this observation to confirm whether abnormal glucose levels in respiratory secretions cause the increased risk of infection, and whether intervention to lower blood glucose levels will reduce the incidence of respiratory infection.


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Impact factors for 2004

Journal impact factors for 2004: another rise for Thorax

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The impact factor for Thorax continues to rise

The journal impact factors for the year 2004 have recently been announced. The impact factor reflects the number of citations in 2004 to the number of original papers and reviews published in Thorax in 2002 and 2003. We are very pleased to let all our readers know that the impact factor for Thorax has risen from 4.188 in 2003 to 5.040 in 2004. Thorax is the second highest ranked respiratory journal in terms of impact factor, behind the American Journal of Respiratory and Critical Care Medicine. The impact factors for the main respiratory journals are listed in table 1.

The impact factor for Thorax has risen over the last few years and this reflects the high quality original papers and reviews we have received for publication. In 2002 and 2003 we also published useful management guidelines for common conditions including the new British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guidelines for the management of asthma in February 2003, and BTS guidelines for the management of community acquired pneumonia in children, the use of non-invasive ventilation in acute respiratory failure, guidelines on air travel, the management of pulmonary embolism, the management of pleural disease, and on respiratory aspects of fitness for diving. Over the past few years we have seen a marked rise in submissions to the journal, especially of high quality original papers, and we very much urge you to continue to send us your best papers. The increase in the impact factor reflects the success of the journal, and the future for Thorax is very good indeed.


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