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**Blood samples drawn for culture as a surrogate marker for case-mix  
adjustment of hospital antibiotic use**

THESE

Préparée sous la direction du Professeur assistant Giorgio Zanetti

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## Résumé de l'étude

La surveillance de la prescription des antibiotiques en milieu hospitalier est une des mesures recommandées pour prévenir l'émergence de bactéries résistantes. La consommation d'antibiotiques est généralement exprimée en termes de DDD (defined daily dose) rapporté au taux d'occupation (jours patients). Cette mesure ne tient cependant pas compte de la variation de la casuistique d'un service au cours du temps. La consommation d'antibiotiques est influencée par l'incidence des infections, qui peut être saisonnière ou varier selon les circonstances épidémiologiques, ainsi que par les habitudes des médecins en termes de prescription. Une échelle de mesure adaptée à ces paramètres est donc capitale pour rendre compte de la consommation d'antibiotiques au sein d'un service et identifier de possibles dérivations dans les habitudes de prescriptions.

Nous avons émis l'hypothèse que le nombre de demandes d'hémocultures pouvait servir d'indicateur de la charge infectieuse d'un service. Une analyse préliminaire a permis d'établir une bonne relation entre ce paramètre et l'incidence d'événements infectieux en comparaison à d'autres paramètres testés (nombre de prélèvements microbiologiques provenant de sites stériles ou nombre total de prélèvements microbiologiques).

Sur la base de cette hypothèse, nous avons analysé la consommation d'antibiotiques d'une unité de médecine générale (Service de Médecine Interne du CHUV) sur seize trimestres consécutifs en comparant deux échelles de mesures : la méthode standard en DDD par jours patients et une échelle ajustée à la charge infectieuse (DDD par nombre de demandes d'hémocultures). L'échelle ajustée aux hémocultures a permis d'identifier trois trimestres avec une consommation anormalement élevée qui n'avaient pas été classés comme tels par l'échelle standard (consommation dans les normes en DDD par jours patients). Une analyse détaillée d'un de ces trimestres a confirmé une incidence d'infections moins élevée en comparaison à un trimestre de référence (proche de la norme selon les deux échelles), alors que la corrélation entre infections et demandes d'hémocultures était similaire pour les deux périodes. De même, l'échelle ajustée à la charge infectieuse a démontré une consommation dans la norme pour un trimestre avec une consommation en apparence trop élevée selon l'échelle standard en raison d'une incidence d'infections plus élevée pour cette période.

Cette étude a donc permis une identification plus performante et plus précise de périodes avec des dérivations dans la pratique de la prescription des antibiotiques en utilisant une échelle de mesure ajustée à la charge infectieuse d'un service au cours du temps. Nous avons démontré que le nombre d'hémocultures prélevées était un indicateur stable de la charge infectieuse dans un service de médecine générale. Ceci ne permet cependant pas de généraliser l'usage de cet indicateur pour tous les types de service. La pratique des hémocultures peut, en effet, varier d'une unité à l'autre, ou entre différentes institutions. Il convient donc de tester la validité de ce paramètre dans un service avant de l'appliquer.

## RESEARCH NOTE

**Blood samples drawn for culture as a surrogate marker for case-mix adjustment of hospital antibiotic use**F. Lamoth<sup>1</sup>, P. Francioli<sup>1,2</sup> and G. Zanetti<sup>1,2</sup><sup>1</sup>Service of Infectious Diseases, Department of Medicine and <sup>2</sup>Division of Hospital Preventive Medicine, University Hospital, Lausanne, Switzerland

## ABSTRACT

Hospital antibiotic consumption is generally adjusted to occupancy. This study hypothesised that the number of blood culture samples could be a surrogate marker for case-mix adjustment. Antibiotic consumption was compared over 16 consecutive trimesters in one medical ward in terms of patient-days or blood culture samples. Compared with patient-days, measurement adjusted to blood culture samples detected three trimesters with an unusually high consumption, and one trimester with consumption falsely classified as high because of a high incidence of infections. Blood culture numbers enabled easy and accurate identification of periods with a drift in antibiotic consumption in a medical ward.

**Keywords** Antibiotic consumption, blood cultures, case-mix adjustment, marker, surveillance

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Surveillance of antibiotic use and feedback of the data to prescribers has been recommended as a measure for the containment of bacterial resistance [1–7]. Antibiotic consumption is often reported in terms of defined daily doses (DDD) (<http://www.whocc.no/atcddd/>) and then adjusted

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according to an indicator of hospital occupancy, most often patient-days. One limitation of this measurement scale is its inability to adjust antibiotic use according to variation in the case-mix over time. Antibiotic consumption is driven by the incidence of bacterial infections and by the prescribing practices of physicians. The incidence of infection on a ward may be seasonal, or may vary because of unpredictable political or epidemiological circumstances. Adjustment for these variations is therefore vital for proper identification of possible drifts in prescription practice.

Because blood cultures are often requested in hospitals when an infection is suspected, this study examined the hypothesis that the number of blood samples drawn for culture is a surrogate marker of the burden of infections in a hospital ward. The consumption of systemic antibiotics (J01 drugs in the Anatomical Therapeutic Chemical classification) (<http://www.whocc.no/atcddd/>) was compared in terms of DDD/patient-day or DDD/blood sample drawn for culture (referred to hereafter as blood culture) for accurate detection of periods with high antibiotic consumption.

The study was performed retrospectively over 16 consecutive trimesters in a 50-bed general

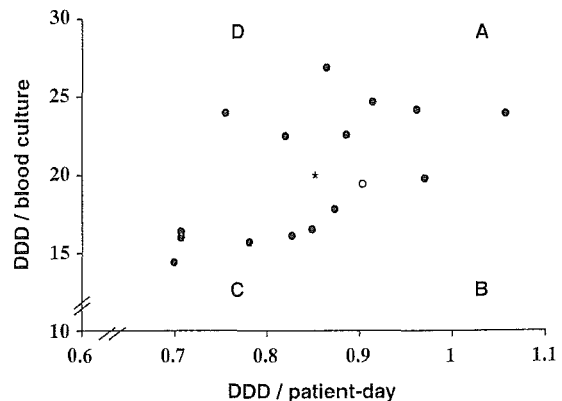


Fig. 1. Four-year quarterly use of antibiotics in a medical ward reported in defined daily doses (DDD) per patient-day (*x*-axis) or per the number of blood samples drawn for culture (*y*-axis). The line at one standard deviation above the mean on each axis divides the plot into four quadrants: quadrant A, high use on both scales; quadrant B, high use only when reported per patient-day; quadrant C, low use on both scales; quadrant D, high use only when reported per blood sample for culture. The open circle represents the reference trimester (see text). The star represents the mean use on both scales.

medical ward of a Swiss university hospital. Delivery data were obtained from the pharmacy electronic database. The quarterly number of blood cultures was obtained from the microbiology electronic database. Trimesters were chosen as time units, because these data were updated every 3 months.

Fig. 1 shows the quarterly antibiotic consumption data. The Spearman correlation coefficient was 0.64 ( $p$  0.007) between both measurement scales. Two trimesters had a rate of consumption that was more than one standard deviation above the mean according to the two measurement scales (quadrant A). Three trimesters were found that had a high rate of consumption only when reported per blood culture (quadrant D). To determine whether this discrepancy was caused by a difference in the use of antibiotics or in the use of blood cultures, a computer-generated random sample of 50 patients from one of these trimesters (arbitrarily chosen) was compared with patients from a reference trimester (identified mathematically by minimising the sum of the relative distance to the mean on both scales). These samples were analysed for any correlation between the occurrence of infection (based on the judgement of the clinician, as reported in the patients' medical records) and the taking of blood cultures. Blood cultures drawn within 48 h of the onset of an infection were considered to be related to the infection. The proportion of infections that motivated blood cultures was 15/24 (63%) in the reference trimester and 12/19 (63%) in the trimester in quadrant D. The proportions of blood cultures performed in the context of an infection were 15/24 (63%) and 12/16 (75%) in the reference trimester and the trimester in quadrant D, respectively. The incidence of infection was indeed lower in the sample from the trimester in quadrant D (36/1000 patient-days) than in the reference trimester (46/1000 patient-days). Thus, measurement of antibiotic use per blood culture appeared to detect three trimesters with an unusually high use of antibiotics relative to their burden of infection that would not have been suspected on a per-patient-day scale.

In contrast, one trimester showed a high antibiotic use per patient-day, but not per blood culture (quadrant B). Detailed analysis of a random sample from this trimester revealed a high incidence of infection (55/1000 patient-days) com-

pared with the reference trimester (46/1000 patient-days). Thus, high antibiotic use in this case could be attributed to a high incidence of infection that, appropriately, resulted in a normal consumption when measured per blood culture. It therefore seems that measurement of antibiotic use per blood culture provides additional information at no cost, given that the number of blood cultures taken is information that is available readily in most hospitals. This information helps in the identification of trends that may motivate a more detailed investigation in order to audit the appropriateness of use and evaluate the need for intervention [8].

This method has several limitations. Stability over time in the practice of blood cultures is a prerequisite for their use as surrogate markers of the case-mix for adjustment of antibiotic consumption. In the present study, the correlation between the practice of blood cultures and infections was stable over time in the medical ward investigated. Implementation of institutional guidelines for the practice of blood culture could help to ensure the stability of this correlation. However, the correlation between infection and the number of cultures from any body site, or any normally sterile site, was poorer than with the number of blood cultures.

It is also uncertain whether the results of this study, which was limited to one ward in one hospital, can be generalised to other settings. The same correlation between blood cultures and infections was found in another general medical ward and in an intensive care unit of the same hospital, but the correlation was poor in a general surgery ward (data not shown). The practice of blood cultures may actually vary among wards with different patient populations and among hospitals, thus precluding comparisons.

A consequence of these limitations is the need to assess how the practice of blood cultures correlates with the incidence of infections in a given setting before using blood cultures as a surrogate marker. Following the proportion of positive blood cultures over time may be a simple way to assess this correlation. Nevertheless, it seems that the number of blood cultures taken can be used as a marker of the burden of infection in patients of a medical ward, provided that a stable policy exists. Reporting antibiotic use according to the num-

ber of blood cultures allows accurate identification of periods with an unexplained high rate of antibiotic consumption that deserve further detailed investigation.

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