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A working group for electron microscopic viral diagnostics

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Introduction

More than 60 years ago poxviruses were shown for the first time by electron microscopy (EM) [5, 10]. Since then the potential of EM as a tool in basic research and for the rapid diagnosis of viruses has been recognised and widely used in the diagnosis of infections [1]. In 1967, the Public Health Laboratory Service (PHLS) in Great Britain was the first to introduce the Quality Control and Assessment (QCA) of diagnostic methods in microbiology, which included an External Quality Assurance (EQA) Programme for EM viral diagnosis (EQA-EMV) [9]. Between 1977 and 1993 the PHLS sent out a total of 20 EQA-EMV distributions after which the programme was discontinued.

In Germany, around 40 institutions in universities, public health authorities, industry and the Armed Forces provide EM viral diagnostic services for human and veterinary medicine [2, 8]. In the early 1990s, with the help of the Institut zur Standardisierung und Dokumentation im medizinischen Laboratorium (INSTAND), the Deutsche Gesellschaft für Elektronenmikroskopie (DGE), and the German Scientific Societies, the Robert Koch Institut (RKI) brought together interested working groups and re-established the EQA-EMV programmes. The first two runs of the new scheme took place in 1994 and were limited to participants in Germany, of which there were 28 in total. Ever since, the number of participating countries has been increasing, and in the present run of the programme, EQA-EMV 10, 93 laboratories from 27 countries are taking part (Figure 1). In 1999, at the Meeting of the European Society for Clinical Virology (ESCV) in Budapest, there was a discussion and assessment of all Europe's EQA schemes, and the group from the Robert Koch Institut was the only one dealing with EM diagnostics. Its achievements have recently been acknowledged by INSTAND, which gave its 1999 Förderpreis (Scientific Award) to Stefan Biel in recognition for his activities in the worldwide expansion of the EQA-EMV programmes.

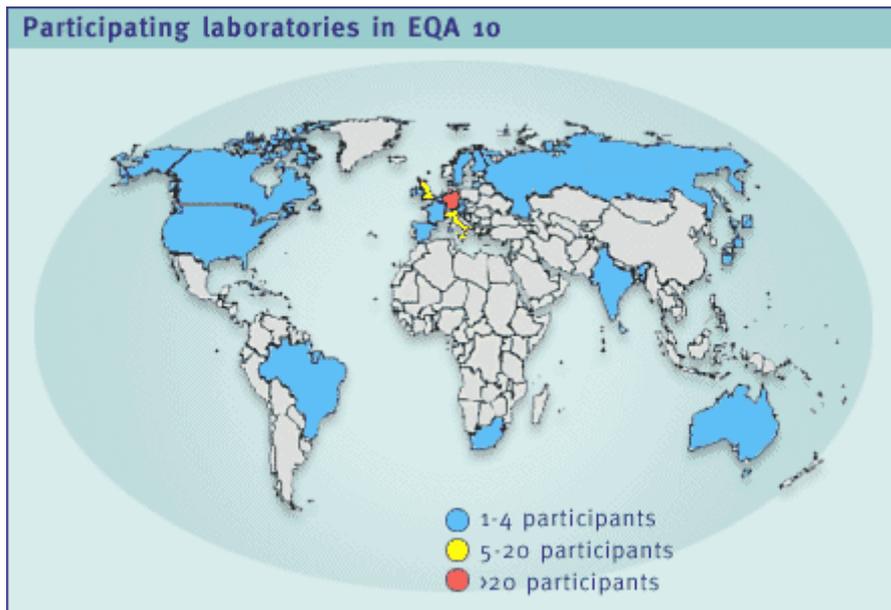


Figure 1. Map showing the worldwide distribution of the 93 participants in the 10th External Quality Assurance Programme for Electron Microscopy Viral Diagnosis (EQA-EMV 10). Participants come from a total of 27 countries.

The programme is supported by the European Society for Clinical Virology (ESCV), European Society for Veterinary Virology (ESVV), the Institut zur Standardisierung und Dokumentation im medizinischen Laboratorium (INSTAND), the Deutsche Gesellschaft für Elektronenmikroskopie (DGE), the Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten (DVV) and the Deutsche Gesellschaft für Hygiene und Mikrobiologie (DGHM).

In response to demands for further education in the field of viral diagnostics the working group organises annual workshops (every second year during DGE meetings), the first of which took place in 1995 in Leipzig; the following ones were in Regensburg (1997) and Dortmund (1999). Independent workshops are also organised every other year and are held at the Heimvolkshochschule Jagdschloss Glienicke in Berlin (1996, 1998 and 2000). There are also Basic Laboratory Courses held in the RKI, which have provided an increasingly effective information network. In 1997, as a direct result of these and other activities, the German Scientific Societies suggested establishing the Konsiliarlaboratorium (Expert Laboratory) for the rapid diagnosis of viruses by EM, based at the Robert Koch Institut. Professor Hans R. Gelderblom is the head of this laboratory. By popular request, international workshops in EM viral diagnostics have also taken place in Hamburg (1998) during the ESCV annual meeting, in Bergen, Norway (1999) in connection with SCANDEM-99, in Brno (2000) at EUREM2000, and in Glasgow (2000) at European Virology 2000.

Potential of EM in viral diagnosis

What does electron microscopy have to offer today compared to other highly sensitive and specialised methods used for the diagnosis of infectious diseases? With the simple negative staining preparation available, EM allows the rapid and direct detection of an etiological agent on a sample from a patient, or from diagnostic cell cultures. Compared to other methods, EM benefits from an "open view", which means that as a catchall method it also reveals double infections and the presence of agents that clinicians might not otherwise have considered. EM diagnosis follows taxonomically fixed criteria on morphology, which results in the classification of suspect structures into specific virus families. In most instances this morpho-diagnosis is sufficient to make a therapeutic decision. It can also be cost-effective - for urgent clinical or epidemiological situations, or for clinical syndromes (e.g. acute gastroenteritis) caused, for example, by members of at least five different virus families, all of which can be clearly

discerned by EM [6]. If necessary, immuno-EM can be of further assistance in the pursuit of identifying an isolate using morpho-diagnostic analysis. The advantages and disadvantages of EM diagnostics, and the current indications, are discussed in detail elsewhere [1].

Activities of the Working Group for EM Viral Diagnostics (AK-EMED)

During the DGE Meeting in Dortmund, 1999, the hitherto informal group of scientists interested in EM viral diagnostics created the official DGE Working Group for EM Viral Diagnostics (AK-EMED). Professor Hans R. Gelderblom, from Berlin, and Karl-Friedrich Reckling, from Stendal, were elected as speakers and Stefan S. Biel as the group's secretary. The objectives of AK-EMED are focused on promoting EM diagnostic expertise through continuous education, regular quality control of the programme and its related educational courses, and the timely development of diagnostic indications.

The topics of the associated workshops range from discussions on methodology, such as the favoured surface properties of EM grids, the ways in which particle numbers on the grid can be enriched and effective routine negative staining techniques, to the use of the electronic communication medium for the more efficient and wider ranging flow of information, and for the provision of help on diagnostic problems to laboratories ("tele-diagnosis, tele-microscopy"). Another workshop covers the themes of "Viral diagnostics in out-of-area operations", and the diagnosis of orthopoxviruses (*Variola major*) as a possible pathogen in bio-terrorism [4]. Because of its rapidity, EM is the preferred method for the diagnosis of suspected primary and secondary cases of variola. In the workshop the inherent biosafety problems raised by the preparation of pathogens, and the necessary safety measures associated with each, e.g. the inactivation of potential infective agents on the grids using, for example, exposure to UV irradiation, immersion in glutaraldehyde and exposure to formalin vapour, are discussed. The importance of correct specimen collection for EM analysis was emphasised recently [3]. EM diagnosis can also be applied in bacteriological and parasitological studies to give a first and rapid indication to a problem, which will then speed up the subsequent fine diagnostic procedures that might be required [7]. Another way to learn EM viral diagnostic techniques is provided in the form of a diagnostic slide test, or quiz, and is provided as an integral part of the workshops.

Future Events

1. An International Workshop on EM viral diagnosis will be held in Innsbruck, Germany on 13 th September, 2001 and will be organised by Professor H.R. Gelderblom, Berlin and Wolfgang Muss, Salzburg. The Workshop will form an official part of the Joint Meeting of the Austrian-German-Swiss Societies for Electron Microscopy.
2. The next Basic Laboratory Course on EM viral diagnosis will be organised in October or November of 2001, to be held once again at the RKI provided there is sufficient demand. The course, supported by the DGE, will be open to both technical and scientific staff, the official language will be German, and no more than 10 registrants will be admitted onto the course. Possible candidates for the course, either individuals or groups, are invited to contact H. Gelderblom directly (see below).
3. Specimens for EQA-EMV 10 were sent out on January 16, 2001 to the 92 registered participants. Spare specimen sets are left over from this latest EQA run and are available for distribution, free of charge, to any laboratories interested in participating in the programme of quality control in EM viral

diagnosis. Further information on participation and other activities can be obtained from the Internet, at the homepage of the [Working Group](#), which also has links to the DGE and ESCV.

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