OUR MISSION IS TO BE THE LEADING ORGANIZATION IN THE FIELD OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE WORLDWIDE

eNewsLetter

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EDITORIAL: 'FROM THE PRESIDENT"

Contributed by Dr. Graham Beastall, President IFCC 2009

Introduction:

This report coincides with my first four months 'in the job'. It has been a busy but stimulating time. I have attended the Executive Committees of both the Scientific Division and Education and Management Division and I am better informed as a result. I have travelled extensively, participated in conference calls and dealt with thousands (yes really!) of e-mails. It is great to be able to report

contact with dozens of wonderful people who are working hard on behalf of the IFCC family.

Membership:

We have welcomed three new national society members into IFCC during the past four months:

- Sudanese Society of Clinical Biology
- Asociación Peruana de Profesionales del Laboratorio Clínico
- Ethiopian Medical Laboratories Association

This takes our national membership to a record high of 82. It also has enabled us to take the first steps in the direction of an African regional organization and I hope that this will thrive and develop in years to come.

Executive Board:

The first meeting of the new Executive Board was held in a hotel close to London Heathrow airport and the historic town of Windsor –home to the British Royal family. The Board addressed a large number of routine and special items some of which are listed below. The Board also approved the audited accounts for the year 2008. In common with most organizations 2008 was a difficult year but we now have a detailed understanding of the finances for the years ahead.

Strategic Direction:

The Executive Board spent the first morning of its meeting considering a wide range of possible projects for the next three years. These are being collated and prioritised before being shared with a wider audience. A common theme running through many of the suggested projects was that IFCC should look outwards and try to add value to laboratory medicine. A meeting is being held in Innsbruck on Sunday 7th June to further develop this thinking. Representatives of National Members in Europe and all Corporate Members have been invited to participate along with IFCC Divisions, Committees and Working Groups. Similar opportunities for engagement will be available during the AACC meeting in Chicago in July.

Young Scientists:

In response to a request from young scientists IFCC conducted a survey of its members to assess the level of interest in engaging more positively with younger

members of the profession. There was a record return to this survey and a strong wish for this initiative to be developed. The Executive Board is working on practical ways of involving younger scientists without cutting across national initiatives. One positive development is the announcement of a new IFCC Award for young scientists, generously sponsored by Roche Diagnostics. The terms of reference for this new award are being developed.

Awards:

Congratulations to Professor Eleftherios Diamandis from Canada for winning the 2009 IFCC-Abbott Distinguished Award for Significant Contributions in Molecular Diagnostics, which he will receive at EuroMedLab 2009 in Innsbruck. Several Roche/IFCC travel scholarships have been awarded to enable individual scientists to attend the Innsbruck congress and other scientific meetings and a number of professional scientific exchange programmes have been approved to allow scientists to acquire new skills and participate in collaborative research.

Meetings:

EuroMedlab Innsbruck 2009 promises to be a huge success and there will be a report in the next issue of the IFCC e-Newsletter. The Roche Bergmeyer Conference, which takes as its theme 'Novel biomarkers: from discovery to clinical application', will be held from 8-10th March 2010 in Eibsee in Germany. The next IFCC General Conference will be held in Corfu, Greece in April 2010 – all IFCC functional units will be meeting and national and corporate members have already been invited.

Communication:

The new IFCC website (www.ifcc.org) was finally introduced in February. It represents a significant improvement on the previous website. There is still some tidying up to be done to make best use of the functionality but I am confident that the website will function as we require as a primary means of communication. The new IFCC Task Force on Liaison has also been working on ways to improve communication between members and I hopeful that within the next three months we will be able to encourage much more spontaneous interaction between individuals and members of the IFCC family. And finally, if you want to communicate with me please contact gbeastall@googlemail.com

ACTIVITY UPDATE: IFCC-CPD COMMITTEE ON PUBLIC RELATIONS

Contributed by Dr. Khosrow Adeli, Chair of the Public relations Committee, Vice-Chair of the Communications and Publications Division

C-PR is a Committee of the Communications and Publications Division of the IFCC. The committee was formed in Fall 2007 to assist the IFCC in promotion of both the organization and the discipline of clinical chemistry internationally and to coordinate PR activities of the various IFCC units. The committee is composed of members from IFCC member countries throughout the world. Current membership includes:

Committee Members:

Dr. Susan Matthews (Australia),

Dr. Magdalena Krintus (Poland),

Dr. Monica Spalvieri (Argentina),

Dr. Loralie Langman, (USA)

Dr. Khosrow Adeli (Canada; Chair)

Regional Federation Advisors:

Dr. Endang Hoyaranda – representing APFCB

Dr. Fouad Harb – representing the Arab Federation

Dr. Ana Leticia de Maselli – representing COLABIOCLI

To be Appointed – EFCC

Other Advisors:

Dr. Ozcan Erel – Turkey

Dr. David Holt – UK

Dr. Abdolamir Allameh – Iran

Dr. Chris Lam – Hong Kong

The terms of reference for the C-PR include:

1. Acting as IFCC ambassadors promoting IFCC and the field of clinical chemistry in their country of residence, national society, and region.
2. Identifying key PR tools and make recommendations to the CPD, other divisions and/or EB
3. Developing and updating promotional materials, through the CPD, on the IFCC organization and activities, as well as the discipline of clinical chemistry for distribution worldwide.
4. Acting as a link for distribution of IFCC brochures and other promotion materials to other laboratory professionals in their country of residence, national society, and region
5. Assisting IFCC in improving its visibility in their country of residence, national society, region, as well as internationally
6. Participating in as IFCC ambassadors while attending regional, national, and international conferences
7. Attending occasional conference calls or face-face meetings to discuss the activities of the PR Committee

Recent Activities of the C-PR:

An IFCC promotional brochure was developed and to date has been published in English, Chinese, Italian, Polish, Portuguese and Spanish. It is currently being translated into Arabic, French and German. The IFCC Milestones brochure was updated in late 2007 and distributed at the IFCC-FESCC EuroMedlab Congress in Amsterdam. New posters for the IFCC booth, based on the Milestones Brochure content, were prepared and used for the first time in Amsterdam.

In consultation with the EMD and SD, an IFCC Speakers Bureau has been put together. This includes speakers currently in the Visiting Lecturer Program as well as several new speakers. Other additions have also been made based on specific recommendations received from IFCC members.

An important activity of the C-PR has been the joint IFCC-"Labs are Vital" PR Initiative. Labs are Vital is a "Laboratory Survival Program", sponsored by Abbott Diagnostics but at arms-length. The main goal is the promotion of the laboratory profession. The IFCC was invited to become a partner in this venture. The recommendations for an IFCC and Global "Labs are VitalTM" program include:

1. Reinforcing the importance of IFCC to international members.
2. Developing a Global Website presence.

3. Global Media monitoring and rapid response.
4. Global Lab week initiatives (to promote Labs in many countries – brochures and leaflets).

There were discussions to determine future areas of cooperation and joint activities between the Working Group and this campaign. The "Labs are Vital" campaign is developing several tools including posters, an interactive website, videos, and other promotional materials and the PR WG and the IFCC was invited to provide advice and suggestions to "Labs are Vital" for preparation of future promotional materials.

Other related activities include:

- The "Labs are Vital" program has been launched in several countries in South America as well as in Australia with the help of PR committee members
- **Dr. Susan Matthews helped with the official launch of Labs are Vital™ in Australia at the 2008 Annual Scientific Conference of the AACB in Adelaide on September 15th.**
- A Labs are Vital presentation was prepared and given by the C-PR committee chair to the attendees of the IFCC-WorldLab conference in Fortaleza
- During the Fortaleza conference, the committee chair also attended the launch of Labs are Vital in Brazil and made a short presentation to the South American attendees

Current and Future Plans of the C-PR:

- PR brochure translations: new translations including German, French, Arabic and Japanese.
- A new PR brochure targeted to the general public, governments, industry, etc. The new IFCC-Public brochure will be developed for review at the June 2009 meeting.
- Establish a communication process among PR committee members and regional federation representative so the joint team can most effectively update and work on agreed upon activities and initiatives.
- Prepare and make formal presentations at local and regional conferences (a slide presentation has already been developed for this purpose)
- The PR committee will develop formal recommendations to the EB on the development of practice guidelines on various aspects of laboratory medicine.

These practice guidelines will be very useful and important PR tools that will increase IFCC visibility in the health care community worldwide.

Stay tuned for future news from the C-PR and its members!

Shown is a photo from the last meeting of the C-PR
during the IFCC General Conference in Antalya, Turkey, April 2008.

IFCC CHAIR PUBBLICATIONS / DISTANCE LEARNING COORDINATOR

It is with great pleasure that we announce the appointment of Dr. Ta Van Thanh as the IFCC Publications and Distant Learning Coordinator. Dr Thanh is currently Vice Chair of the Department of Chemistry and Biochemistry, Director of Center for Gene-Protein Research at the Hanoi Medical University, and Deputy Director of the Department of Science and Training at the Ministry of Health, Hanoi.

Dr Thanh received his medical degree form the Hanoi Medical University with a specialty in Obstetrics and Gynecology in 1987. He pursued graduate studies in the Department of Applied Biology of the Kyoto Institute of Technology where he obtained his PhD. He then went on to perform 2 Postdoctoral

fellowships, one at the Department of Biological Sciences at the University of Delaware and the other at the Department of Medical Chemistry and Molecular Biology of the Kyoto University Faculty of Medicine. Dr Thanh received several honors and awards throughout his training. He has extensive experience in carbohydrate chemistry, protein characterization as well as molecular biology techniques.

Dr. Thanh is a member of Executive Board of Biochemistry and Molecular Biology Association of the North Vietnam, and of the Molecular Biology Association of Vietnam.

We welcome Prof Thanh to the IFCC Communications & Publications Division and look forward to his contributions.

NEWS FROM NATIONAL ASSOCIATIONS AND FEDERATIONS

ASSOCIATION OF CLINICAL CHEMISTS OF NIGERIA (ACCN)

Contributed by Dr. Mabel Charles-Davies, Department of Chemical Pathology, College of Medicine, University College Hospital, Ibadan, Nigeria.

An executive meeting of the Association of Clinical Chemists of Nigeria (ACCN) preceded its Annual Scientific Seminar. The theme of the Seminar- Immunological Basis of Human Diseases was well addressed at 4 plenary sessions.

Prof. Claude Muller, a renowned immunologist from the Institute of Immunology, a World Health Organization (WHO) collaborating Centre for Measles located in Luxembourg, speaker of the first plenary session, presented a conference on cellular aspects of antibody production.

Prof. G.O.Oyeyinka, the second plenary speaker from the University of Ilorin, Ilorin, Nigeria presented a talk on issues in immune status monitoring in a resource-poor environment.

Immune Deficiency Syndrome, the topic of the third plenary session, was masterly handled by Dr L. Salawu from Obafemi Awolowo University, Ile-Ife, Nigeria.

The fourth and last session was steered by Mr A.A. Odewunmi from Ahmadu Bello University, Zaria, Nigeria. His topic bore on clinical immunology and his talk entitled: From bench to bedside: The contribution of Clinical Bacteriology.

The South-West Zone of the ACCN, chaired by Prof. F.A.A. Adeniyi, hosted the Scientific Seminar at the School of Nursing Auditorium, University College Hospital, Ibadan, Nigeria. The seminar was well attended by members and guests and was honored by the presence of the executive members of the ACCN, including the President-Prof. A.B. Okesina, Past President- Dr P.H.O. Amodu, and Prof. O.A. Dada, member of the Board of Trustees of ACCN.

Left to Right: Dr Mabel A.Charles-Davies (ACCN Secretary / National Representative) discussing with members of the local organising committee - Mr.M.O. Akiibinu, Mrs O.D. Ogundipe and Dr O.M.Akinosun.

Left to right: Prof. O.A. Dada (member of ACCN board of trustees) with Prof. A.B. Okesina(President of ACCN)

Edited by Edgard Delvin PhD, FCACB, FACB

Editor

CATALAN ASSOCIATION FOR CLINICAL LABORATORY SCIENCES

Contributed by Dr. Xavier Filella and Xavier Fuentes-Arderiu, Department of Biochemistry and Molecular Genetics Hospital Clínic, Barcelona, Catalonia, Spain

The V Clinical Laboratory and *in vitro* Diagnostics European Symposium on Standardization and Tumor Markers was held 16-17 April at the Institut d'Estudis Catalans, in Barcelona (Catalonia, Spain). The Catalan Association for Clinical Laboratory Sciences, under the IFCC auspices and IUPAC sponsorship, organised this event. Dr. Xavier Filella (Hospital Clínic, Barcelona) was the chairman and Dr. Àngels Bosch (Consorci Laboratori Intercomarcal, Igualada) was the technical secretary of the Symposium.

The main subject of the symposium was the present and the future of standardization of the measurement of tumour markers, and particularly its incidence in their clinical usefulness. More than 100 participants took part in the meeting that was based on real experiences from laboratory professionals and industry, including members of Abbott, Beckman-Coulter, Olympus, Roche Diagnostics and Siemens.

Participants discussed the state of art of the standardization in four round-tables, that included the following topics: "It is necessary to obtain the standardization of tumour markers, but what are the problems? "; "The industry and the standardization of tumour markers: why are our results so different? "; "The clinical usefulness of tumour markers"; and finally "The interpretation of results: standardization and cut-off values".

Difference between methods for the measurement of prostate specific antigen (PSA) with the adoption of the International Reference Preparation WHO 96/670 was one

of the highlights of the meeting. The acceptation of this reference material by clinical laboratories supports the adoption of a new cut-off value at 3.1 mg/L instead of 4.0 mg/L. On the other hand, the experts indicated that, in addition to the reference material, there are other factors such as incubation time, matrix effect and the platform used also influence the results.

Another conclusion of the symposium was that, although major advances had been made for the measurement of many tumour markers (e.g.: carcinoembryonic antigen, a-fetoprotein or choriogonadotropin), their complexity impedes the inter-changeability of the results between different methods.

Edited by Edgard Delvin PhD, FCACB, FACB
Editor

THE CANADIAN SOCIETY OF CLINICAL CHEMISTS (CSCC)

Contributed by Dr. Raymond Lepage, President of the CSCC

It is my great pleasure and privilege to inform you that Dr. Eleftherios P. Diamandis has been awarded the 2009 IFCC/ Abbott International Award for Significant Contribution to Molecular Diagnostics.

This award is sponsored by Abbott Molecular Diagnostics. It is conferred annually and honours an individual who has made a unique contribution to the promotion and understanding of molecular biology and its applications in clinical chemistry and laboratory medicine throughout the world.

Dr. Diamandis was nominated by both the Canadian and Greek national societies. He was selected unanimously from a strong field of candidates by the IFCC Awards Committee, under the chairmanship of Professor Christopher Lam.

The Award comprises an honorarium of €5000 plus travel expenses to receive the award. It will be presented during the Opening Ceremonies of EuroMedLab 2009 taking place in Innsbruck, Austria coming June 7 to 11.

Congratulations to Dr. Diamandis on behalf of all the membership of CSCC

IFCC – ABBOTT VISITING LECTURER PROGRAM

Contributed by Rosa Sierra-Amor, National Representative IFCC, Member of the eNewsletter Working Group

Prof. Cas WEYKAMP recently visited Mexico as part of the IFCC VLP –ABBOTT program where he lectured at different sites. The first visit was the University of Tamaulipas Campus Reynosa. He then lectured at the XXXII National Congress in Clinical Biochemistry and Lab EXPO 2009; and finally gave a talk at the Medical Specialties Center of the State of Veracruz in Xalapa, capital city of the State of Veracruz. All activities where coordinated in conjunction with the Mexican Association of Clinical Biochemistry, the University of Tamaulipas Campus Reynosa, the College of Clinical Chemists of the State of Veracruz, the Minister of Health of the State of Veracruz and the University of Veracruz Campus Xalapa.

During his visit to REYNOSA, Prof. WEYKAMP had a morning meeting at the University of Tamaulipas (UAT) with faculty members of the Chemistry Sciences Department where he learned about the projects that are being conducted at the UAT, which is rated among the first 20th best qualified of the 43 public universities in the country. He visited the teaching university laboratory, and answered to questions that students had on HbA1c. He met with the career coordinator of QFB and director of the master program in clinical analysis, Rosa Issel ACOSTA-GONAZALEZ, MS, and two of the researches, Anabel BOCANEGRA, PhD, and Virgilio BOCANEGRA, PhD; later on he had a meeting with the Director of the Multidisciplinary Academic Unit, UAT Campus Reynosa Aztlan, Juan Jose GONZALEZ MS, and Eduardo ROJANO, MS, a former graduated student of the UT

((http://www.medigraphic.com/espanol/e-htms/e-bioquimia/e-bq2007/e-bq07-3/em-bq073c.htm).

Dr Cas Weykamp also met with a group of clinical laboratory directors, from different healthcare organizations in REYNOSA (IMSS, ISSSTE, PEMEX, SSA), and with owners of clinical private laboratories. During the afternoons of Thursday and Friday, he lectured first to the faculty members and to the students; and second, to the laboratory professionals, directors and clinical chemists of the State of Tamaulipas, the north of the State of Veracruz, the State of Tlaxcala and other cities of the surroundings.

On Monday March 16, Prof. Cas WEYKAMP lectured at the XXXII National Congress in Clinical Biochemistry and Lab EXPO that took place at the Hotel Galeria Plaza. During Monday afternoon, Cas met with BIO RAD LATIN AMERICA: Carlos TENORIO, MS, Mexico Regional representative and Hugo BAEZ, MS, Manager of Quality Systems Division, and from AMBC, Maria Antonieta GARZA-GALINDO, General Coordinator of the EQAS, Eduardo ROJANO, MS, chair of the HbA1c Pilot Proficiency testing program and University of Tamaulipas Campus REYNOSA, and Rosa Isabel SIERRA-AMOR, PhD, IFCC National Representative.

Prof. Weykamp also lectured for the third time at the CEMEV in Xalapa Veracruz; the whole report (in Spanish) is available at: http://www.coquicev.es.tl/CONFERENCIA-HbA1c.htm Health authorities from the Government of Veracruz State gave auspices to this conference. The audience was laboratory professionals from the three Social Security Institutes (IMSS, ISSSTE, and PEMEX), the Civil Hospital, the Faculty of Bioanalysis of the University of Veracruz, from the Minister of Health Clinical Laboratories Office (SESVER), the College of Clinical Chemist of the State of Veracruz (CoQuiVer), and from the CEMEV. Attendees traveled from different cities of the State of Veracruz, and also from Mexico City to listen to Prof. Weykamps' lecture on HbA1c.

We thank IFCC VLP -ABBOTT program for the opportunity to listen to Prof Cas WEYKAMP's expertise on HbA1c and look forward to develop collaboration with other organizations in Mexico to establish a nationwide HbA1c reporting system in the near future.

Eduardo ROJANO, Cas WEYKAMP, Rosa I SIERRA-AMOR, and Rosa Issel ACOSTA-GONZALEZ
at the University of Tamaulipas, Campus Reynosa.

Students participating at the XXXII National Congress in Clinical Biochemistry from the Faculty of Bioanalysis of the University of Veracruz in Veracruz, Veracruz.

Eduardo Rojano MS from the University of Tamaulipas (Campus Reynosa), Cas Weykamp IFCC Abbott-VLP, and Rosa I Sierra-Amor, IFCC NR, Mexican Association of Clinical Biochemistry.

LETTER TO THE EDITOR: YOUR OPINION FOR A BETTER (LAB) WORLD?

Contributed by Dr. Damien Gruson, eNewsletter Working Group Member
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Every morning we look into, not only in our "shaving mirror, but also in front of "the breaking-news" mirror, to be an informed and aware "globalized" citizen. This last mirror provides us with positive or negative thoughts for the beginning of the day, and unfortunately, tells us that we are facing strong economical difficulties, and now experiencing a potential dramatic scenario with the "swine flu".

A recent study, from the Boston Consulting Group (Innovation 2009: Making Hard Decisions in the Downturn), has revealed that, on a worldwide scale, 14% of enterprises will reduce their budget allocated to their Research and Development Department. Dr. B. Gouget, in a recent Editorial published in Labmedica, has highlighted some of the challenges related to our future in this difficult global

context, and has called to our ability to find new solutions and to interact within lab community.

Every day, colleagues, physicians and patients in our laboratory context, challenge us to improve turnaround time, quality of results, processes, productivity and test clinical efficiency. To be successful, we must however be inspired, motivated and supported. Thus, creativity, innovation and exchanges are relevant in maintaining Laboratory Medicine in a positive dynamics. In fact, it seems that these few words are now part of the most important challenge that we ever met: integrate the recent advances from informatics, quality management, molecular medicine, architectural evolution, lab consolidation and fusions (and their human drama) in the strongest economical pressure we have ever encountered.

As we are all involved in this turmoil, I make use of this issue of the eNewsletter to obtain your opinions (left to you imagination) that would enable us to improve everyday laboratory life, and to include a summary entitled "10 ideas for a better laboratory world" in the next issue.

Send your suggestions to gruson_damien@yahoo.fr. Your ideas will be disseminated to our community and will serve to initiate discussions for the upcoming and future EuroMedLab and IFCC events.

POST MORTEM CHANGES

Contributed by Dr. Bushan Kapur, Ph.D, FRSC, FACB
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One may think of the human body as a static entity after death, it is clearly not so. Although in the living we routinely rely on pharmacokinetics to interpret blood drug concentrations, post-mortem redistribution (PMR) makes this difficult. The complexity of PMR lead Pounder to describe PMR as a toxicological nightmare (1;2). When measuring drug concentrations after death, it is important

to consider the phenomenon of PMR. The properties of drugs (medication) after death change considerably. Postmortem drug concentrations may not be a true reflection of ante-mortem concentrations and as a result, incorrect conclusions could be drawn about the cause of death. Collection and analysis of not only peripheral blood, but also other fluids/tissues is usually important in postmortem work. Various factors such as the site of collection, time elapsed since death also influences the result obtained and subsequent interpretation of postmortem drug concentration (Table 1).

Curry and Sunshine in 1960 were amongst the first to show that there was a difference in peripheral (femoral) blood barbiturate concentration and liver concentrations with liver being higher (3). Initially much attention was paid to barbiturates and this was followed by digoxin and tricyclic antidepressants (TCA). Holt and Benstead found postmortem blood concentrations of digoxin in femoral vein, neck veins and right ventricle were significantly different (4). Femoral blood was the lowest. TCAs, the most studied drugs, post mortem liver concentrations were found to be much higher than blood in TCA and non-TCA related drugs (5). Since the advent of drugs of abuse, a number of abused drugs including cocaine and methamphetamines have recently received attention.

To understand post mortem changes we first need to understand what happens to the cell structure and integrity of its contents upon death. Aerobic respiration, synthesis of enzymatic and structural proteins, and, preservation of the genetic apparatus of the cell are key to the integrity of the cell membrane. Figure 1 shows the mechanisms that take place upon cell injury. Sequences of events depend on the organ involved. Brain neurons show irreversible damage within three to five minutes, myocardium in about 30 to 40 minutes and liver between one to two hours after ischemia.

There are number of pharmacokinetic properties of the drug that affect its postmortem distribution characteristics. Some of these are: volume of distribution, lipophilicity and pKa of the drug in question. The *apparent* volume of distribution (Vd), a significant factor in PMR, is a parameter relating the concentration of a drug in the plasma to the total amount of the drug in the body. It is assumed that the drug is uniformly distributed to reach the concentration that is actually measured in plasma. Vd is the total amount of the drug in body divided by the plasma

concentration and is expressed in liters per kilogram of body weight. Drugs that have a Vd of greater the 3 L/kg are more likely to have PMR characteristics. Many drugs are sequestered in muscle and adipose tissues, thus body composition is an important factor also. Age, gender, and diseases are the other variables that influence Vd. Drugs that are bound to plasma proteins and are not bound to tissue components have a lower Vd, example ethanol; whereas drugs that are sequestered in muscle and adipose tissue and other intracellular components have a large apparent Vd. Table 2 lists a few drugs with their respective Vd.

Many of the highly lipophilic drugs are concentrated in the adipose tissue by simple physical dissolution depending on the concentration gradient and pH on both sides of the membrane. Water-soluble molecules, such as ethanol, diffuse across the lipid membranes through proteic pores because of osmotic and oncotic gradient. Weak acids and bases are transported by active transport that requires energy in the form of ATP and/or a carrier to transport the drug across the membrane. All this stops upon death. Some of the lipophilic drugs have a very wide distribution in tissues due to cellular uptake and accumulation. This most likely happens due to binding to membrane phospholipids and accumulation in acidic compartments.

Lipophilic and organic basic drugs typically concentrate in solid organs such as liver, lungs and myocardium. Thus organs such as esophagus, stomach, lungs and liver, which are proximal to the major blood vessels and heart, are more likely to play an important role in PMR. Upon cell death the aqueous cell contents become progressively acidic (Figure 1). Organic bases, depending on their pKa, are gradually ionized and dissolve in the aqueous medium. Once lysis occurs passive diffusion takes over and they are readily released into plasma. This is a significant contributor to PMR. Lipophilicity influences PMR in a number of anatomical sites such as the stomach, lungs, cardiac muscle, cardiac blood or liver, but does not appear to influence sites such as the brain or the vitreous humor.

Robertson and Drummer showed that putrefaction can lead to bioconversion of various benzodiazepines by enteric bacteria commonly found after death (6;7). The rate of conversion is reduced at 4°C when compared with 22°C to 37°C demonstrating the need to keep cadavers at cool temperatures. These bacteria are known to cross the gastrointestinal wall and enter blood and lymph vessels and then transmigrate through the body within a few hours postmortem. In the

presence of glucidic substrates, such as glucose or ribose, bacteria can produce ethanol (8). Since glucose is the primary substrate of postmortem ethanol production, tissues (liver, skeletal muscles, lungs, and myocardium) with high glucose storage capacity are the greatest source of ethanol production. Urine is a poor medium for microbial ethanol production unless the deceased was diabetic.

Movement of body by various individuals (police, health care workers, family etc) can have a significant impact as a few hours after death blood starts to settle (hypostasis) in the lower part of an organ or the body. Hypostasis occurs by sedimentation of blood and plasma to the lower part of the corpse. Postmortem blood sediments and clots unevenly. This is brought about by blood clotting followed by lysis. Clots trap red blood cells so sampling this can influence the concentration of drugs that are bound to the erythrocytes and therefore unevenly distributed between red cells and plasma e.g. tacrolumus. Movement of blood within the vessels also occurs shortly after death and can be part of the explanation of PMR.

Sampling sites: It is important in postmortem analysis to compare concentrations in blood from several sites, even when reference values are available. Blood must be taken at the central (cardiac) and peripheral sites. Cardiac blood samples are collected from right and left chambers separately. Femoral blood is less affected by time delay as compared to central blood and is the specimen of choice (9). Other tissues such as liver, lungs, skeletal muscle and vitreous humor have been used for drug analysis. Of these, vitreous humor that is isolated is less susceptible to PMR. It contains no micro-organisms or glucose and is protected from putrefaction. It is therefore the sample of choice to differentiate exogenous ethanol from endogenous ethanol production from putrefaction. Premortem blood ethanol concentration can be estimated from vitreous humour, unfortunately, concentrations of other drugs may not be accurately estimated from vitreous humor. Animal studies have shown that vitreous humor concentrations of cocaine and other drugs were significantly higher when collected 8 hours after death (10). Flanagan and co-workers provide guidelines for sample collection, labeling, transport and storage for specimen taken during postmortem examination (11).

Cook and co-workers reviewed coroners' cases from October 1990 to July 1997 and found six cases where both ante-mortem and postmortem blood levels were

available (12). They compared ratios of ante-mortem levels with postmortem levels from central (cardiac-blood) to peripheral (femoral blood). They found that the drugs that have a high PMR also have a high postmortem to antemortem ratio. They caution on interpreting antemortem drug concentrations and amount ingested from postmortem measurements.

Recently Reis (2007) and co-workers reviewed 95% of the autopsies performed in Sweden where femoral blood was available. For 15 different antidepressants they provide both therapeutic and postmortem blood levels. Having reviewed a total of 8591 cases they state "*We would like to point out that, because no exact cut-off limits for fatal levels can be defined, common sense, a thorough review of all medico-legal findings, and circumstances cannot be replaced by a blood drug concentration*"(13).

Recommended reviews for further information

Pelissier-Alicot AL, Gaulier JM, Champsaur P, Marquet P. Mechanisms underlying postmortem redistribution of drugs: a review. J Anal Toxicol 2003; 27(8):533-544.

Yarema MC, Becker CE. Key concepts in postmortem drug redistribution. Clin Toxicol 2005; 43(4):235-241.

Drummer,O.H.; Gerostamoulos,J. Postmortem drug analysis: analytical and toxicological aspects. Ther Drug Monit. 24(2):199-209, 2002

Drummer,O.H. Post-mortem toxicology. Forensic Sci Int. 165(2-3):199-203, 2007

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Figure 1

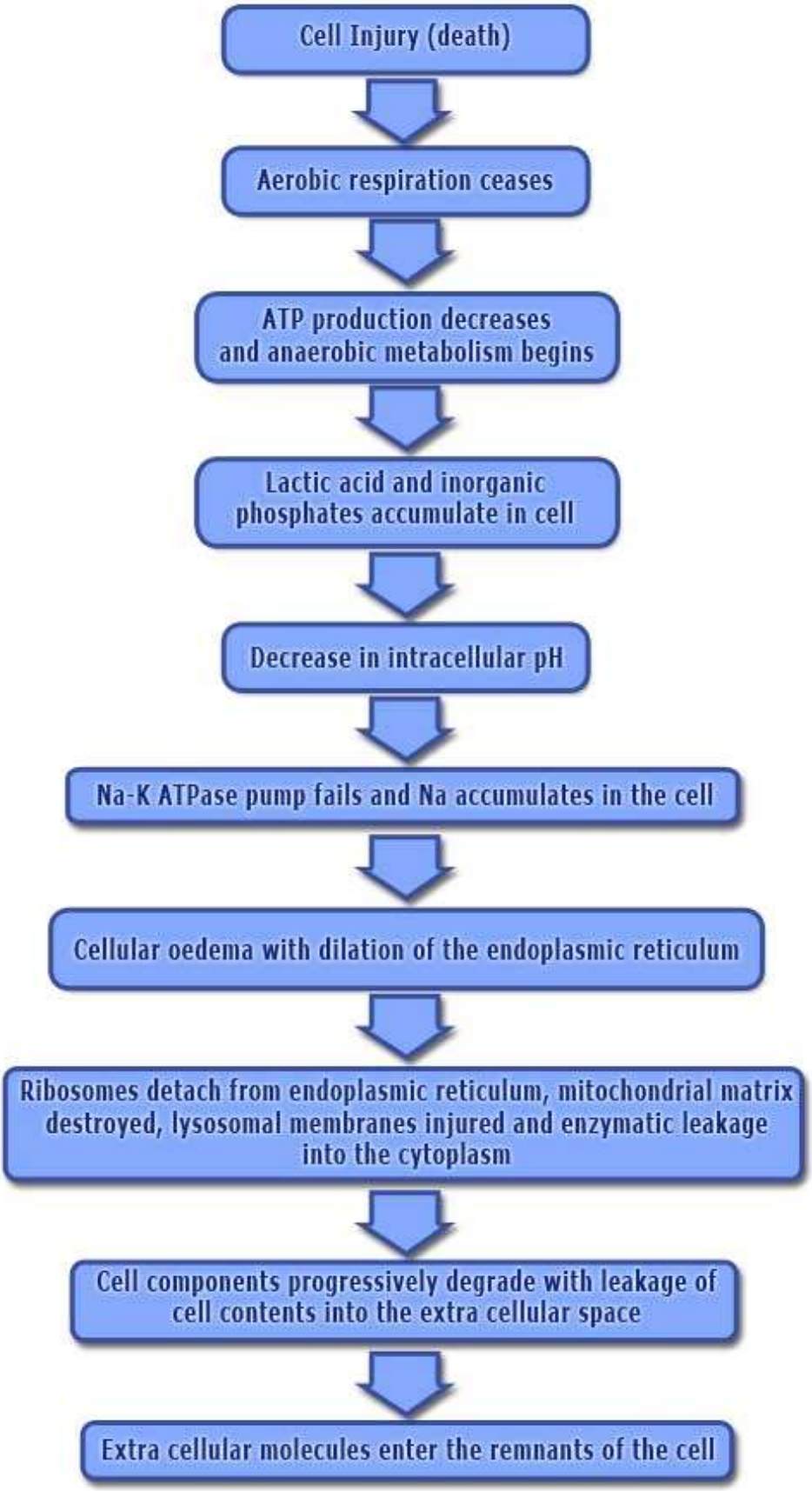
Cell Injury (death)
Aerobic respiration ceases
ATP production decreases and anaerobic metabolism begins
Lactic acid and inorganic phosphates accumulate in cell
Decrease in intracellular pH
Na-K ATPase pump fails and Na accumulates in the cell
Cellular oedema with dilation of the endoplasmic reticulum
Ribosomes detach from endoplasmic reticulum, mitochondrial matrix destroyed, lysosomal membranes injured and enzymatic leakage into the cytoplasm
Cell components progressively degrade with leakage of cell contents into the extra cellular space
Extra cellular molecules enter the remnants of the cell

Table 1: Factors to consider when interpreting post-mortem results

Putrefaction
Time of sampling since death
Site of sampling
Diffusion from various organs
Body position
Drug Characteristics
lipophilicity
pKa (pH)
volume of distribution

Table 2: Some selected examples of drugs with their volume of distribution (15)

Drug	Volume of Distribution (L/kg)
Acetaminophen	0.8 – 1.0
Amitriptyline	6 – 10
Amphetamine	3.2 – 5.6
Cocaine	1.6 – 2.7
Digoxin	5.1 – 7.4
Diphendydramine	3 – 14
Ethanol	0.43 – 0.59
Imipramine	20 – 40
Methadone	4 – 5
Morphine	2 – 5
Warfarin	0.1 – 0.2

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