

4th Western Pacific Congress on Chemotherapy and Infectious Diseases Workshop Consensus

Guidelines on Issues of Clinical and Public Health Importance

WORKSHOP 1

MULTI-DRUG RESISTANT TUBERCULOSIS

Chairperson : Dr. Tadao Shimao (Japan)
Rapporteur : Dr. Jaime Montoya (Phil)
Members : Dr. Reiko Nakamura (Japan)
Dr. Leonid Heifets (USA)
Dr. John Stanford (UK)

Objective :

At the completion of this workshop, the participants will be knowledgeable about the extent of the problem of multi-drug resistant TB (MDR-TB) in the Western Pacific Region and the current management of MDR-TB including newer modes of therapy.

Problem formulation:

The prevalence of drug resistance in tuberculosis particularly in previously untreated cases is still relatively low in most countries of the Western Pacific region. Multi-drug resistant tuberculosis, however, remains a potential problem based on local country reports from India, Thailand, Vietnam and Philippines.

The emergence of drug resistance may be due to the poor implementation of the national tuberculosis control programs resulting in either inadequate regimen of chemotherapy or poor adherence of patients to tuberculosis treatment. This will ultimately result in a worsening of the drug resistance problem.

There may also be inadequate strategies for diagnosis and treatment accessible to a great majority of tuberculosis cases. This problem of drug resistance is further compounded by the emergence of HIV infection in most developing countries.

Consensus

1. To address the problem of growing drug resis-

tance, there is a need to develop new diagnostic techniques which are more rapid such as Polymerase Chain Reaction and nucleic acid probes. However, because of the cost of such techniques, there is a greater need to improve on existing methods of diagnosis. A combination of the old conventional tests, such as mycobacterial smears and cultures, and newer tests or modifications of existing tests may be helpful. Bacteriologic detection of tuberculosis within 2 weeks, using liquid media such as BACTEC or 7H9 with standard solid media, may be very helpful. BACTEC may also be used in combination with nucleic acid probes to shorten the time for diagnosis. Newer methods of susceptibility testing, such as luciferase test and HPLC, still require standardization aside from the fact that it requires a pure culture. Difluorescein acetate (DFA) and ethidium bromide (EB) staining are also being evaluated for drug susceptibility testing. All these potential areas of research should be done in the context of making diagnostic facilities more available to the great majority of TB patients, particularly treatment failures. This would require the establishment of a good diagnostic referral system for surveillance of drug resistance which will decide the national regimen for tuberculosis.

2. Therapeutic options for drug resistance should also be developed. In the area of chemotherapy, short course chemotherapy with 3 or 4 drugs may be crucial in the prevention of drug resistance. The addition of at least 2 new drugs to which the organism is proven to be sensitive, should be considered as early as the third month of treatment if specimen cultures remain positive.

Other therapeutic options may be chest surgery or medical collapse therapy as necessary or when chemotherapy fails. If the organism is resistant to all available drugs, it is recommended to continue isoniazid alone expecting attenuated virulence of highly resistant

TB bacilli. New agents that may be used, such as immunotherapy with *Mycobacterium vaccae*, may be considered as another therapeutic option.

The over-all success of these options will depend on the concerted efforts of government and the private sector which include the pharmaceutical industry, research groups and other non-governmental organizations committed to tuberculosis control programs.

WORKSHOP 2

RATIONAL USE OF ANTIMICROBIALS IN PEDIATRIC DIARRHEA

Co-chairpersons : Dr. James Tulloch
Prof. Somsak Lolekha

Rapporteur : Dr. Norma Abejar

Members : Dr. Celia Carlos
Dr. Mohammed Abdus Salam
Dr. Michael Tan

Objective:

At the end of the workshop, the participants will be knowledgeable about the current WHO recommendations on antimicrobial use in pediatric diarrheas in developing countries.

Consensus

1. The workshop agreed that antimicrobial use in diarrhea in children should follow the WHO Guidelines. These state that antimicrobials should not be used in the routine treatment of pediatric diarrhea. Exceptions are cases of severe cholera and diarrhea with visible blood in the stools should be presumptively treated as shigellosis. In both cases, antibiotics of demonstrated efficacy against locally prevailing strains of the organisms concerned should be prescribed. Safety of use in children, simplicity of the dosage regimen and cost should be taken into account when choosing between antibiotics.

2. Anti-parasitic drugs should only be used for:

2.1 amoebiasis: after antibiotic treatment of bloody diarrhea for *Shigella* has failed or trophozoites of *E. histolytica* containing red blood cells are seen in the feces.

2.2 giardiasis: when diarrhea has lasted at least 14 days and cysts or trophozoites of *Giardia lamblia* are seen in the feces or small bowel fluid.

3. Because of the increasing rates of resistance to commonly used antibiotics, it is important to establish monitoring of such resistance using reliable laboratories

and methods.

4. New antibiotic must be evaluated in appropriately designed and well conducted studies to ensure their efficacy and safety in children.

WORKSHOP 3

POLICIES AND STRATEGIES FOR PROMOTING APPROPRIATE ANTIBIOTIC USE

Co-chairpersons : Dr. Ken Harvey
Dr. Angeles Tan-Alora

Rapporteur : Dr. Rodrigo Romulo

Members : Dr. Estrella Paje-Villar
Dr. Bill Kean
Dr. Degnan Ross

Objective:

At the end of the workshop, the participants will be knowledgeable about innovative strategies and policy initiatives for promoting appropriate use of antibiotics.

Problem formulation

The clinically and economically inappropriate use of antibiotics (and other drugs) is a major international problem which receives comparatively little attention. There is both overuse and underuse. The consequences include preventable mortality and morbidity from treatment failure and unnecessary adverse effects of drugs, increased selection pressure on antibiotic-resistant microorganisms and waste of scarce health care resources. While these problems affect all countries, they are most acute in developing countries that can least afford them.

Contributing factors can be divided into the following categories:

Patient/Consumer

These include their demand for a "pill for every pain"; their expectation that every consultation ends with a prescription; and their perception that a "good" doctor writes a "long" prescription; that more is better; their lack of knowledge, especially concerning the risk/benefit concept of medicine.

Health providers

These include their lack of problem solving and communication skills; their lack of knowledge and failure to keep up-to-date; their reliance on habit rather than reasoning; their resistance to limited drug lists, prescribing restrictions, antibiotic audits, etc.; their unhealthy dependence on the pharmaceutical industry.

Pharmaceutical manufacturers

These include pressure on industry to make profit which conflicts with promoting rational drug use; extensive promotion which creates unhealthy drug prescribing/consumption habits.

Social and economic milieu

These include practices such as the use of a prescription to end a consultation; cultural expectations in some societies encourage polypharmacy (more is better); perceptions that injections are a more "powerful" form of medicine; common observation that rules and regulations are systematically ignored (e.g. prescription-only antibiotics are freely available over-the-counter); ineffectual communication due to the hierarchical relationships and power imbalance between physician and patient; powerful opinion leaders promulgate ill-founded views reinforced by peer and institutional norms; perverse economic incentives often conflict with rational drug use, such as in those countries where physicians (&/or hospitals) get their fees from prescribing and dispensing drugs not for consultations; the low percentage of GDP spent on health by developing countries compared to developed countries (most spent in the private sector rather than the public sector).

Infrastructure

The lack of laboratory and other diagnostic facilities; high workloads that limit the time spent with patients especially in the public sector; the lack of access to health facilities and drug outlets, especially for rural population; the limited public resources for health departments to enforce regulations or provide independent information and education.

Access to information

There is a marked imbalance between scanty, independent, unbiased, and relevant information about the treatment of choice (including non-drug options) compared to voluminous drug specific promotional material; there is a poor distribution and uptake of the independent information that does exist.

In short, the problem of inappropriate use of antibiotics (and other drugs) is complex, multi-factorial and involves numerous stakeholders (government, industry, health providers and consumers). There is no simple solution. The first step is to get all stakeholders to acknowledge that a major problem exists and that cooperation is essential if national and global solutions are to be achieved.

Consensus

1. The desired goal is clinically appropriate, cost-effective and equitable use of antibiotics (and other drugs) in order to slow the development of antibiotic-resistance and improve health outcome (quality use). To attain this, the recommended strategies are:

1.1 Policy framework

There is a need for the formulation and acceptance of a comprehensive national drug policy involving all stakeholders which attempts to balance the following potentially conflicting objectives: the timely introduction of high quality, safe and efficacious products; equity of access, at least to a limited list of essential drugs; a profitable, research-oriented pharmaceutical industry quality drug use.

1.2 Tools

These include authoritative and regularly up-dated independent sources of information such as drug formularies, antibiotic guidelines for the management of common conditions, drug bulletins and/or newsletters; ethical codes of conduct concerning pharmaceutical promotion and health workers' interaction with the pharmaceutical industry; data (from audits, surveys, research) about drug prescribing and consumption practices, attitudes, beliefs, promotional techniques, adverse drug reactions, antibiotic-resistant organisms, etc.; information, education and communication campaigns (IEC) involving all stakeholders, targeting common problems, based on a clear understanding of prevailing drug prescribing and consumption habits, knowledge, attitudes, beliefs and cultural practices. A key principle is to work off with target groups in order to achieve involvement, problem ownership and commitment to change. In addition, person-to-person interaction (e.g. small group problem solving and "academic" detailing) has been shown to be much more powerful than didactic lectures.

Administrative incentives and sanctions to encourage appropriate behaviour include awards for appropriate prescribing, limited lists of drugs appropriate to the level of health care, limiting authority to prescribe certain drugs to specialized units, supplying reserve antibiotics only after consultation and approval from an infectious disease expert, automatic stop orders for prophylactic antibiotics and limiting the range of antibiotics for which sensitivity tests are routinely reported.

The regulatory underpinning of the above together with adequate financial and human resources

for implementation (from government, industry, academe, health professionals, NGOs and the mass media) are essential.

1.3 Process

The above tools should be employed using a cyclical quality assurance process: establishing standards of practice, auditing actual practice against these standards and, where discrepancies exist, reflection and remedial action, such as IEC campaigns, the application of incentive and sanctions, and the progressive refinement of standards of practice.

The application of the above tools should be at the international, national, district, institutional, community and individual level via national, district and hospital drug committees, industry and professional organizations, NGOs, consumer groups and committed individuals.

2. Since quality use of antibiotics (and other drugs) is a crucial objective of national drug policy, and is of particular relevance to the Western Pacific Region, we propose that the Western Pacific Society of Chemotherapy formally endorse quality use of antibiotics (QUA) as an objective of the Society and as such, the Society establishes an international QUA taskforce consisting of experts from all stakeholder groups to formulate and implement a multi-country action plan based on the principles outlined above and that this taskforce reports back to 5th WPCCID in Singapore in December 1996.

WORKSHOP 4

MANAGING CANCER WITH LIMITED RESOURCES

Co-chairpersons : Dr. Ian T. Magrath
 Dr. Nazli Gad-el Mawla
Rapporteur : Dr. Julius A. Lecciones
Members : Prof. Lin Hai Peng
 Dr. V. Shanta

Objective:

At the completion of this workshop, the participants will have a heightened awareness of the advances in cancer management, the constraints in the developing world, and strategies to optimize care despite limitations. The opportunities and obstacles for collaboration between researchers and care-givers in advanced and developing countries will be evaluated.

Problem formulation

Cancer is a problem of increasing importance in

developing countries. Because of a higher population burden, while cancer incidence is comparatively lower than in advanced countries, the actual number of cancer cases is greater. While the prevalent types of cancer in developing countries are preventable and curable, a significant number of patients present in the late stages and these patients have a higher degree of treatment rejection and default. The reasons for this phenomenon are multifactorial and are socio-cultural and economic in character.

The resources and facilities available for cancer management and research are limited and have to compete in priority of fund allocation. They are likewise unevenly distributed, generally inaccessible and have underdeveloped manpower.

These frequently lead to inefficient use of even the limited resources available.

Consensus

The priority and focus of programs shall be on the following:

1. Cancer prevention and early detection through education, cancer awareness programs and cost-effective diagnostic strategies.

2. Cancer treatment shall be supported through:

2.1 Enhancement of therapeutic facilities as in the development of regional cancer centers thereby encouraging decentralization.

2.2 Human resource development and manpower training emphasizing team approach to cancer care and the recognition of oncology as a distinct specialty.

2.3 Integration of clinical care and research disciplines in cancer management and training programs.

2.4 Encouragement of collaboration and inter-institutional cooperative projects.

2.5 Development of indigenous capability for the manufacture of appropriate equipment, drugs and other products needed in cancer care and since we cannot treat all cancer, we focus for the moment on early-stage and curable cancers.

3. Community financial resources and support shall be developed by forming cancer societies to develop funding for cancer research and to mobilize support for advocacy, particularly among well-educated parents or families.

4. Financing/insurance schemes for patients should be explored and developed.

5. Collaborative research programs shall be encouraged within the country and with other countries in accordance with the following pre-requisites:

5.1 Training programs must integrate both clinical and research disciplines.

5.2 The organization of collaborative groups within the country must be encouraged even before international collaboration.

5.3 Research programs must be oriented to problems of local importance.

5.4 Research programs must be mutually beneficial to both international and local collaborators. Moreover, they should include transfer of technology and/or training of local personnel so that researchers in developing countries can develop their own capability and potential.

WORKSHOP 5

ANTIMICROBIALS IN THE MANAGEMENT OF PNEUMONIA IN CHILDREN: PRIMARY HEALTH CARE APPROACH

Co-chairpersons : Prof. Ian Riley
Dr. Prasong Tuchinda
Rapporteur : Dr. Salvacion Gatchalian
Members : Dr. James Tulloch
Dr. Marilla Lucero
Dr. Nils Daulaire

Objectives:

At the completion of this workshop, the participants will be knowledgeable about the important etiology of pneumonia in childhood, the management-oriented classification of acute respiratory infections in children, the impact of the ARI case management on pneumonia mortality in field trials.

Consensus

The workshop:

ENDORSES the WHO Guidelines for case management of children with ARI which is the timely administration of antibiotics for children with tachypnea and chest indrawing which are simple clinical criteria for diagnosing pneumonia.

SUPPORTS the continuing education of physicians and pediatricians in the rational treatment of ARI.

DEPLORES the widespread use of antimicrobials and other inappropriate drugs as remedies for minor respiratory infections, i.e. "coughs and colds".

ADVOCATES cooperation and collaboration between ARI Control Programs and organizations promoting the rational use of drugs.

RECOMMENDS the training of community health workers in prescribing and dispensing antimicrobials of pneumonia in areas where access to health services is limited

RECOMMENDS the promotion and development of research that will lead to more specific diagnosis of pneumonia at the community level and in small hospitals and health centers and define the relationship between *in vitro* drug resistance and clinical outcome.

ADVOCATES the search for new cost-effective antimicrobials for the treatment of community-acquired pneumonia in children.

RECOGNIZES the need for valid data on drug resistance of *Streptococcus pneumoniae* and *Haemophilus influenzae*.

RECOMMENDS intensive support for selected laboratories in developing countries in conjunction with programs of quality control.

WORKSHOP 6

DRUG-RESISTANT MALARIA: IMPLICATIONS ON CHEMOTHERAPY AND TREATMENT

Co-chairpersons : Prof. Walther H. Wernsdorfer
Dr. Nelia Salazar
Rapporteur : Dr. Jennifer Chua
Members : Dr. Nicholas White
Dr. A. Benakis
Dr. Juntra Karbwang
Dr. Robert Steffen

Objectives:

At the end of the workshop, the participants will be knowledgeable of the problem of Multi-Drug Resistant Malaria and its global impact. They will be familiarized with the therapeutic options available and the diagnostic criteria and management.

Problem formulation

Malaria continues to be one of the most important communicable diseases, responsible for significant mortality and widespread suffering.

Drug resistance of malaria parasites, especially of *P. falciparum*, has become a formidable obstacle to the management and control of malaria in large parts of

the world's malarious regions.

Multi-drug resistance of *P. falciparum* has important implications for the clinical and out-patient management of malaria and necessitates the continuous updating of measures for personal protection against malaria by drug prophylaxis and measures reducing vector contact.

Consensus

The workshop concludes that prophylaxis, early diagnosis and early, effective treatment are the most appropriate means for achieving the most elementary objective of malaria control, namely, the elimination of mortality and the reduction of suffering from malaria. In this context, it will be important to maintain the efficacy of the available antimalarial drugs for as long as possible as the prospects for new medications beyond the artemisinin line are quite limited.

Development of radically curative treatment schedules in accordance with sound clinical pharmacological principles, continuous qualitative and quantitative monitoring of drug response, post-treatment follow-up of patients, measures for the control of malaria transmission, development and application of

Table 1. Treatment of Uncomplicated *P. falciparum* Malaria.

Status of Area	Drug Regimen
Chloroquine-sensitive	Chloroquine (CHL) D0 10 mg/kg then D0 + 8h + D1-D2 5 mg/kg.
Chloroquine-resistant	Pyrimethamine (P) plus Sulfadoxine (S) or Sulfalene 1.25 mg P/kg + 25 mg S/kg = 3 tablets adult dose.
Chloroquine and S/P resistant	Mefloquine (Mef) D0 15 mg/kg, then D0 + 8h & 24 h 10 mg/kg or Quinine (QN) 10 mg/kg q 8 h for 7 days plus doxycycline 3 mg/kg daily for 7 days.
Multi-drug resistant (CHL, S/P, QN, Mef)	Artesunate** or Artemether** oral D0-D2 3-4 mg/kg plus Mefloquine (Mef) D1 15 mg/kg & D2 10 mg/kg

* Not in pregnant women & children < 8 yrs.

** Not in pregnant women during first trimester. (A single dose artemether regimen is currently being evaluated).

NB: There are no areas with chloroquine-sensitive *P. falciparum* in the Western Pacific. Resistance to S/P exists in most Western Pacific areas except parts of the Philippines, Malaysia and Laos.

Multi-drug resistance is so far limited to Cambodia, the Mekong delta in Vietnam and in the SEA Region to eastern and western Thailand and eastern border areas of Myanmar.

specific therapeutic management for treating migrants, and the implementation of epidemiological early warning systems are essential elements in the containment of multidrug resistance.

The current practice of antimalarial treatment and chemoprophylaxis is summarized in Tables 1-4. In the development of new drugs and drug formulations, due attention should be given to elucidating pharmacokinetic parameters and pharmacodynamic features so as

Table 2. Treatment of Severe and Complicated *P. falciparum* Malaria.

Status of Area	Drug Regimen
Chloroquine-sensitive	Chloroquine I.V. D0 10 mg/kg, D0 + 12 h 5 mg/kg D1 & D2 5 mg/kg
CHL &/or SP-resistant	Quinine HCl* I.V. (4 h drip) D0 20 mg/kg then 10 mg/kg q 8 h; shift to P.O. once oral medication is tolerated
Multi-drug resistant (CHL, S/P, QN, Mef)	Artesunate I.V.** D0 2.4 mg/kg, then D0 + 8h D1-D4 1.2 mg/kg or Artemether I.M.** D0 3.2 mg/kg then D1-D4 1.6 mg/kg

* To be complemented by Doxycycline 3 mg/kg daily for 7 days as soon as oral medication becomes possible

NB: doxycycline not for pregnant women & children < 8 yrs.

** Not for pregnant women during first trimester.

The treatment with artesunate or artemether should be complemented by oral mefloquine (Dx 15 mg/kg; Dx + 1 10 mg/kg) where the patient tolerates oral medication again.

Table 3. Treatment of *P. vivax* Malaria.

Status of Area	Drug Regimen
Chloroquine-sensitive	chloroquine D0-D1 10 mg/kg D2 5 mg/kg Primaquine* 0.25 mg/kg daily for 14 days or 0.75 mg/kg once a wk for 6 weeks**
Chloroquine-resistant	Mefloquine D0 15 mg/kg, then D1 10 mg/kg plus Primaquine* as above

* Primaquine should only be given if the patient returns to a malaria-free area or an area with low transmission.

Caveat: Not for pregnant women & children < 5 years and for person with G6PD deficiency.

** Schedule for patients with mild variants of G6PD deficiency.

NB: Chloroquine-resistant vivax malaria may occur in Papua New Guinea, West Irian, Indonesia, Solomon Islands and Vanuatu.

Table 4. Chemoprophylaxis of Malaria.

Status of Area	Drug Regimen
Chloroquine-sensitive	Chloroquine 5 mg/kg once a week (1st dose repeated on 2nd day)
Chloroquine-resistant	Mefloquine* 3.5-4.0 mg/kg once a week
Multidrug resistant (CHL, Mef, S/P)	Doxycycline** 1.5 mg/kg daily

* Not for pregnant women during 1st trimester.

** Only in case of considerable risk of infection.

Not for pregnant women & children < 8 years.

NB: Chemoprophylaxis should start 7 days before entering malarious area and be continued until 4 weeks after leaving malarious area.

In addition to chemoprophylaxis, it is recommended to use ancillary protective measures minimizing exposure to mosquito bites.

to optimize therapeutic and chemoprophylactic dose regimens. Clinical trials should pertain to the target populations.

The group also considered the cost aspects of alternative treatment, especially in the clinical and out-patient management of multi-drug resistant malaria. With regard to the production of artemisinin and its derivatives, it would be reasonable to encourage some of the malaria endemic countries of the Western Pacific Region to undertake or improve such production, using cost-effective methods and adhering to GNP standards.

WORKSHOP 7

MANAGING HIV/AIDS WITH LIMITED RESOURCES

Co-chairpersons	Dr. Ofelia T. Monzon Dr. Wilina Lim
Rapporteur	: Dr. Corazon Manaloto
Members	: Dr. Prasert Thongcharoen Dr. Kate Clezy Dr. Praphan Phanuphak Dr. John Dwyer

Objectives:

The participants will be made aware of the different issues that need to be considered in some AIDS-related strategies. The issues associated with establishing priorities in resource allocation for AIDS control strategies and how to maximally utilize available support for both, management and prevention of HIV disease will be tackled by the participants and panelists.

Consensus

1. HIV Antibody Testing

1.1 Testing for HIV infection is mandatory for donated blood, blood products, organs/tissues for transplant, donated semen and breast milk.

1.2 Anonymous HIV testing should initially be carried out to determine prevalence of HIV infection among various population groups.

1.3 Depending on the prevalence, HIV testing should be offered to individuals attending STD clinics, commercial sex workers, IVDUs, and patients in TB and antenatal clinics. Testing should be done in a manner which ensures confidentiality and non-discrimination.

1.4 Pre- and post-test counseling should be an integral part of HIV testing.

1.5 Compulsory HIV testing in general is not recommended.

1.6 HIV testing for the diagnosis of HIV infection in patients with AIDS indicator disease should be performed after informed consent is obtained and adequate pre-test counseling is given.

2. Anti-Retroviral Therapy in HIV Diseases

2.1 Cheaper primary and secondary prophylaxis of opportunistic infections has to be sought and implemented.

2.2 Depending on available resources, guidelines should be established to prioritize the use of antiretrovirals and their distribution.

2.3 Efforts should be made to secure the lowest priced, effective antiretroviral agents.

2.4 If resources permit, antiretroviral treatment is recommended for the following:

- a) to reduce perinatal HIV transmission
- b) to delay progression of symptomatic HIV disease

2.5 Pharmaceutical companies, government and non-government organizations should be asked to support scientifically and ethically valid trials of safe and promising antiretrovirals in developing countries.

2.6 Training in HIV medicine should be encouraged and promoted at all levels of health care.

2.7 Screening laboratories should be encouraged to use inexpensive simple tests which do not require sophisticated equipment. Initially reactive samples should be confirmed.

2.8 HIV testing should be performed in laboratories that practice good quality control. Screening

laboratories should have access to a reference laboratory for confirmation of reactive samples. Training and quality assessment programs should be available.

2.9 Home testing is not recommended.

2.10 Testing using body fluids obtained through non-invasive procedures may be considered in laboratories experienced in this technique.

2.11 Prevention is still the major approach to the control of HIV infection. Educational strategies that provide practical information to avoid HIV infection should be implemented.

WORKSHOP 8

MANAGEMENT OF DENGUE HEMORRHAGIC FEVER

Co-chairpersons : DR. Suchitra Nimmanitya
Dr. Esperanza Rivera

Rapporteur : Dr. Cecilia Montalban

Members : Dr. Usa Thisyakorn
Dr. Sompon Tassniyom
Dr. Melchor Frias III

Objectives:

At the end of the workshop, the participants will be updated on the current etiologies and pathophysiology of Dengue Hemorrhagic Fever. They will be able to distinguish the controversies in treatment, and know when to use the appropriate measures.

Problem formulation

Dengue hemorrhagic fever (DHF), the most severe form of dengue virus infection, presents a unique natural history that differentiates it from the other viral hemorrhagic fevers.

DHF is characterized by 4 major manifestations of fever, hemorrhagic manifestations, hepatomegaly, and a tendency to develop shock, the dengue shock syndrome (DSS).

Two constant laboratory features are thrombocytopenia and hemoconcentration. The major pathophysiologic hallmarks in DHF/DSS are plasma leakage that leads to hypovolemic shock and abnormal hemostasis that may lead to severe, massive bleeding. Evidences of plasma leakage that clearly distinguish DHF from DF are: rising or high hematocrit, pleural effusion/ascites, hypoproteinemia/hypoalbuminemia.

Consensus

1. Management of DHF/DSS

1.1 No specific antiviral agent is recommended.

1.2 Supportive/Symptomatic treatment is effective and life-saving if given appropriately.

1.3 Prognosis depends on early diagnosis of DHF and early recognition of potential shock cases.

1.4 Early and effective replacement of lost plasma with electrolyte and colloidal solution results in favorable outcome. Plasma substitute is as good as plasma when there is massive leakage. It is the volume expander, not plasma factors that is needed during the period of leakage. Plasma factors or other blood elements are needed only in cases with massive bleeding and severe DIC.

1.5 Serial follow-up of platelets and hematocrit is helpful in the early recognition of plasma leakage; and if present, fluid replacement is indicated.

1.6 Platelet transfusion as prophylaxis is not recommended. Studies have shown that there is no difference in the duration of thrombocytopenia or increase in platelet counts whether platelet transfusion was administered or not. There was no difference in the bleeding episodes between the 2 groups either.

1.7 Steroids have no benefit. It has been documented by several studies that high dose corticosteroids have no benefit in the management of DHF/DSS.

1.8 The use of Vitamin K is of no benefit because bleeding in DHF is due to DIC, thrombocytopenia, and impaired platelet function. The administration of heparin in DHF with prolonged shock with DIC needs further studies. IV Immunoglobulin needs further investigation.

2. Treatment Regimen of DSS

2.1 Immediate replacement of plasma loss is recommended with isotonic salt solution at 10-20 ml./kg/hr; or if there is no BP or palpable pulse, it should be given as bolus. If there is no improvement after 1/2-1 hour, give colloid if the hematocrit is still high or is rising.

If the hematocrit drops, but there is no clinical improvement, concealed internal hemorrhage must be suspected.

2.2 Replacement of further plasma loss should continue another 24-48 hours until stable. Judicious administration of fluid is mandatory to avoid volume overload. The rate of IV replacement should be adjusted

according to the vital signs, hematocrit levels, and urine output.

2.3 Correction of acid-base and electrolyte imbalance (metabolic acidosis, hyponatremia).

2.4 Blood Transfusion: Fresh whole blood

is given if there is severe, massive bleeding or prolonged refractory shock, with decreased hematocrit even with adequate fluid/colloid replacement. Platelet transfusion is given if DIC is present, with evidence of bleeding.