

# **SHUNT TECHNOLOGY: CHALLENGES AND EMERGING DIRECTIONS**

Sponsored by  
United States Food and Drug Administration  
Center for Devices and Radiological Health  
at  
National Naval Medical Center  
Bethesda, Maryland  
Friday, January 8, 1999

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## **INTRODUCTION**

FDA's first STAMP (Systematic Technology Assessment of Medical Products) conference was held at the National Naval Medical Center (NNMC), Bethesda, Maryland, January 8, 1999. The one-day international conference brought together over 140 attendees from various groups, including neurosurgical, nursing, patient advocacy, government and industry. The meeting addressed -- *Cerebrospinal Shunt Technology: Challenges and Emerging Directions* -- and was introduced by Dr. Bruce Burlington, Director, Center for Devices and Radiological Health (CDRH). Dr. Burlington explained the STAMP effort as similar to one in 1997, evolving from the concerns of another medical device -- the pulmonary artery catheter (PA catheter). This early effort involved both FDA and the National Heart Lung and Blood Institute and focused on the utilization, technology, and training associated with the use of the pulmonary artery catheter (PA catheter). Similarly, this STAMP effort deals with cerebrospinal fluid shunt systems and meets the STAMP mission criteria.

The STAMP mission reviews families of closely related medical devices having broad use and most often, several years of marketing experience, as well as, a significant potential for adverse events. In the process of device selection for STAMP, certain device aspects are raised including, product characteristics, evidence of performance and effectiveness, adverse event experience, and manufacturing and supply issues. The expected outcome is

to interact with stakeholders in a public forum (medical community, patient groups, others) as well as to develop recommendations on steps to improve patient outcome.

In 1976 FDA's Neurological Devices Classification Panel recommended Regulatory Class II for CSF shunts, which require premarket clearance for marketing. Classification was based upon the belief that standards could be written to assure the safety and effectiveness of marketed shunts, and that clinical experience had proven shunts to be reasonably safe and effective. Today, marketing requirements for shunts with significant design change require bench testing (ASTM Standard F4794) as well as clinical data to show that the modification does not impact the safety and effectiveness of the device. Furthermore, biocompatibility data and labeling are carefully reviewed.

Over the past five years, between 114 and 160 adverse event reports for CSF valves were submitted by manufacturers through the FDA Medical Device Reporting System. The reports involved the following valve technologies: proximal slit, distal slit, diaphragm, ball-in-cone, gravitational (hydrostatic) ball-in-cone, siphon-preventing diaphragm, and auto-regulated (flow-limitation) diaphragm and needle.

While CSF shunts have been used to manage and treat hydrocephalus for over 40-years, clinical experience and adverse event reporting indicate continuing problems, despite advances in technology. Over 60% of shunt patients manifest some type of shunt complication over their lifetime such as shunt obstruction, over-drainage, infection, device migration, disconnection and fracture. This conference aims to examine the issues and explore different approaches to improving patient outcome.

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## **SESSION I**

**Title:** Shunt Technology Perspectives

**Objective:** To recognize alternative perspectives of shunt technology from selected stakeholders.

**Moderator:**

*JANINE M. MORRIS, Mechanical Engineer  
Center for Devices and Radiological Health  
Food and Drug Administration*

**Speakers:**

*EMILY S. FUDGE  
Executive Director  
Hydrocephalus Association  
[“Patient and Family Perspectives and Needs”](#)*

*SUSAN MCGEE, CNP  
Pediatric Special Focus Group Facilitator  
American Association of Neuroscience Nurses  
[“Shunt Technology – A Nursing Perspective”](#)*

*MARVIN L. SUSSMAN, Ph.D.  
Industry Consultant  
[“Shunt Technology: Challenges and Emerging Directions – A Manufacturing Perspective”](#)*

*HAROLD REKATE, MD  
Neurosurgeon  
Barrows Neurological Institute  
[“BioPhysics of the CSF Pathways: What Can and What Should a Shunt Do?”](#)*

## **SESSION II**

**Title:** Hydrocephalus and Assessment of Shunt Function

**Objective:** To develop an increased understanding of the relationship between the pathophysiology of hydrocephalus and shunt performance.

**Moderator:**

JEAN RINALDI, Biomedical Engineer  
Center for Devices and Radiological Health  
Food and Drug Administration

## **SESSION IIA**

**Title:** Pathophysiology of Hydrocephalus

**Speakers:**

ANTHONY MARMAROU, Ph.D.  
Professor and Vice Chairman  
Division of Neurosurgery  
Medical College of Virginia  
["Fundamentals of Intracranial Pressure"](#)

CONRAD E. JOHANSON, Ph.D.  
Professor and Director of Cerebrospinal Fluid Laboratory  
Department of Clinical Neurosciences  
Brown University Medical School  
["Growth Factor Induction of Normal Pressure Hydrocephalus"](#)

MARK G. LUCIANO, MD, Ph.D.  
Head, Section of Pediatric Neurosurgery  
Department of Neurosurgery  
The Cleveland Clinic Foundation  
["Animal & Clinical Testing of Systems for Adult Onset Chronic Hydrocephalus"](#)

## **SESSION IIB**

**Title:** Assessment of Shunt Function

**Speakers:**

MICHAEL A. WILLIAMS, MD  
Assistant Professor and Medical Director  
Clinical Neurocirculatory Laboratory  
Johns Hopkins Medical Institutions  
["In Vivo Assessment of Shunt Function and Failure"](#)

AZAR P. DAGHER, MD  
Diagnostic Radiology Department  
National Institutes of Health

["Radiological Tools Used in the Evaluation of Shunt Malfunction"](#)

PROFESSOR JOHN PICKARD, MChir, FRCS, FmedSci  
MAREK CZOSNYKA, PhD, DSC, and ZOFIA CZOSNYKA  
University of Cambridge  
Cambridge England  
["UK Shunt Evaluation Laboratory"](#)

## ***SESSION III***

**Title:** Challenges of Infection and New Perspectives

**Objective:** To identify potential approaches to mitigate or prevent shunt-centered infections

**Moderator:**

ROGER BAYSTON, MMedSci, FRCPATH  
Biomaterials-Related Infection Group  
University Division of Microbiology  
University of Nottingham England

**Speakers:**

ROGER BAYSTON, MMedSci, FRCPATH  
Biomaterials-Related Infection Group  
University Division of Microbiology  
University of Nottingham England  
["Incidence and Aetiology of Shunt-Associated Infections"](#)

WILLIAM R. JARVIS, MD  
Chief, Investigation and Prevention Branch  
National Center for Infectious Diseases  
Centers for Disease Control and Prevention  
["Vancomycin Use in Pediatric Neurosurgery Patients--Can We Improve Compliance with Vancomycin Recommendations?"](#)

ROBERT J. SHERERTZ, MD  
Chief, Section on Infectious Diseases  
Department of Medicine  
Wake Forest University School of Medicine  
["Pathogenesis and Prevention of Foreign Body Infections"](#)

## **SESSION IV**

**Title:** Clinical Outcomes and Methods of Surveillance

**Objective:** To describe selected strategies to improve clinical outcomes and the performance of CSF shunts.

**Moderator:**

*JANINE M. MORRIS, Mechanical Engineer  
Center for Devices and Radiological Health  
Food and Drug Administration*

**Speakers:**

*PROFESSOR. JOHN PICKARD, MChir, FRCS, FMedSci  
HUGH RICHARDS, PhD, HELEN SEELEY and MERYL MADAKBAS  
University of Cambridge  
Cambridge England  
["Experience with Setting up and Maintaining the UK Shunt Registry"](#)*

*ROBERT E. HARBAUGH, MD, FACS  
Chairman, AANS/CNS Outcomes Committee  
American Association of Neurological Surgeons and Congress of Neurological Surgeons  
Dartmouth-Hitchcock Medical Center  
["On-Line Neurosurgical Outcomes Studies"](#).*

*JOHN R. W. KESTLE, MD, M.Sc., FRCSC  
Division of Pediatric Neurosurgery  
University of Utah  
Primary Children's Medical Center  
["Issues in Data Collection and Outcome Analysis"](#)*

## **PANEL DISCUSSION**

**Title:** Future Directions – Prioritizing Our Efforts

**Objective:** To achieve a shared vision on how to advance shunt technology in the management and treatment of hydrocephalus and establish priorities for future action.

**Moderator:**

LARRY KESSLER, Sc.D.  
Director, Office for Surveillance and Biometrics  
Center for Devices and Radiological Health  
Food and Drug Administration

**Panel:**

HAROLD REKATE, MD  
Neurosurgeon  
Barrows Neurological Institute

JOHN R. W. KESTLE, MD  
Division of Pediatric Neurosurgery  
University of Utah  
Primary Children's Medical Center

ROGER BAYSTON, MMedSci  
Biomaterials-Related Infection Group  
University Division of Microbiology  
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GREG A. TOCCO  
Hydrocephalus Foundation (HyFl)  
Boston, Massachusetts

KIMBER RICHTER, MD  
Deputy Director  
Office of Device Evaluation  
Center for Devices and Radiological  
Health  
Food and Drug Administration

MICHAEL D. WALKER, MD  
Director  
Division of Stroke, Trauma, and  
Neurological Degenerative Disorders  
National Institute of Neurological  
Disorders and Stroke  
National Institutes of Health

**Summary:**

The discussion began with suggestions on improving patient protection. One idea was to issue patient cards containing basic information on the type of shunt implanted as well as the size of patient's ventricles. These cards could be used in case of emergency. Additional comments included the potential benefit of on-line data collection in reducing the burden on neurosurgeons, providing framework for longitudinal follow-up, and reducing chances of missed forms. Standard definitions would increase the understanding between individual neurosurgeons as well as sequential enrollment of all cases by participating neurosurgeons and hospitals would be needed in order to rigorously assess the effectiveness of care.

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# **SESSION I**

## **Shunt Technology Perspectives**

### **Patient and Family Perspectives and Needs**

Emily Fudge, Executive Director  
The Hydrocephalus Association  
San Francisco, California

The first generation of infants and children treated for hydrocephalus is now reaching adulthood. While many are living normal and productive lives, they have been beset with a myriad of problems and complications – learning disabilities, developmental and social skill delays, neurological impairment, visual problems, and all too frequently, shunt malfunction.

The Hydrocephalus Association (HA) founded in 1983, provides support, education, and advocacy resources to individuals with hydrocephalus and their families. Also it functions as a source of educational materials for distribution by health care providers. There were 900 dues-paying members in 1998. In addition to individuals and parents of infants and children with hydrocephalus, health professionals and organizations with complementary goals maintain membership.

In preparation for the conference a twelve-item survey of 675 HA members was initiated. The sample represented members with a diagnosis of hydrocephalus. Completed surveys were returned by 239 males and 175 females, i.e., 414 respondents (61%).

### **DIAGNOSIS / CAUSE OF HYDROCEPHALUS**

40.3%	CONGENITAL (AQUEDUCTAL STENOSIS, SPINA BIFIDA, ARACHNOID CYSTS, DANDY-WALKER, CHIARI MALFORMATIONS...)
27.3%	Acquired ( Intraventricular Hemorrhage, Meningitis, Trauma, Tumor...)
11.6%	Normal Pressure Hydrocephalus
17.6%	Unknown
3.1%	Other

### **CURRENT AGE of RESPONDENTS with SHUNTS**

3.6%	LESS THAN YEAR OLD
31.4%	1 to 5yrs
25.6%	6 to 12yrs
12.6%	13 to 20yrs



7.2%	21 to 35yrs
6.0%	36 to 50yrs
13.5%	51yrs or older with 85yrs being the oldest

**AGE at which FIRST SHUNTED**

65.5%	LESS THAN YEAR OLD
5.1%	1 to 2 yrs
6.8%	2 to 5yrs
2.7%	6 to 12yrs
1.4%	13 to 20yrs
2.7%	21 to 35yrs
4.8%	36 to 50yrs
11.1%	51yrs or older

**KNOWLEDGE of SHUNT TYPE**

233	YES
<b>169</b>	<b>No</b>

**IDENTIFICATION CARD on PERSON**

97	YES
<b>303</b>	<b>No</b>

**NUMBER of REVISIONS**

32.6%	NONE
49.6%	1 to 5
9.7%	6 to 10
3.5%	11 to 15
2.2%	6 to 20
2.7%	> 20

**REASONS for REVISIONS**

154	OBSTRUCTION (DISTAL AND/OR PROXIMAL)
71	Malfunction (Mechanical or Unknown)
63	Infection
61	Pressure related
47	Broken or disconnected catheter
29	Lengthen the catheter
24	Place a 2 <sup>nd</sup> shunt
14	Hemorrhage; hematoma
7	Distal catheter migration
39	Others

**RECD NEUROPSYCHOLOGICAL/  
DEVELOPMENTAL TESTING**

238	YES
239	No

**SIDE EFFECTS EXPERIENCED**

<b>198</b>	<b>YES</b>
190	No

EXAMPLES

131	HEADACHE
81	Balance and Coordination problems
38	General Pain
24	Dizziness
8	Visual disturbance
8	Learning
6	Seizures
4	Confusion
2	Short term Memory problems
29	Other

**PERCEIVED DISADVANTAGES  
With SHUNT TECHNOLOGY**

137	MALFUNCTION, REVISION, OBSTRUCTION, BREAKS
51	Technology, No interest/money, Moving too slowly
35	Difficulty Assessing shunt function
33	Infection
27	Need for Specialized Care and Knowledge/Interested Doctors
26	Invasive techniques needed to diagnose malfunction and replace shunt
22	Lifestyle Restrictions
19	Pressure related problems
13	Brain Injury
54	Other

**PERCEIVED ADVANTAGES With SHUNT TECHNOLOGY**

133	ALLOWS A NORMAL LIFE
115	Saved Life
63	Treats Hydrocephalus
53	Good Technology; New Technology possible
37	Design is simple; Shunt is invisible and reliable

16	Surgery is a simple operation
21	Other

In summary it was found that individuals with hydrocephalus and their families are grateful for the extension of life that shunt technology has provided. However, they believe additional measures need to be explored to improve quality of life. These include attention to the high revision rate resulting from the complications of infection, and mechanical failure. Increased support for development of new technologies is eagerly awaited.

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## Shunt Technology – A Nursing Perspective

Susan McGee, RN, MSN, CNP  
Pediatric Special Focus Group Facilitator  
American Association of Neuroscience Nurses (AANN)

The AANN is composed of 4000 members with chapters in the United States and Canada. Activities include an annual scientific meeting, journal, newsletter, and clinical guidelines publications. Drawing on her experience as an AANN Pediatric Focus Group Facilitator, Ms. McGee discussed ongoing problems for caregivers related to discrepancies between patients' subjective symptom reports and objective diagnostic tool findings as well as inability to identify implanted hardware. Patients' problems include headache, pain control, and intervention-associated infections. Furthermore, the potential for shunt malfunction and the transition to adult care, involving new health care providers, are frequent sources of patient anxiety.

As a pediatric nurse practitioner, Ms. McGee is responsible for the nursing management of inpatients and outpatients with hydrocephalus treated with ventricular shunting devices. This includes: teaching patients and families about hydrocephalus and treatment options, recognizing and reporting symptoms of shunt malfunction, caring for patients during acute malfunction episodes, and assisting with patient and family lifestyle management issues. At the Cincinnati Children's Hospital Medical Center, over the first year of initial shunt implantation, 14% malfunction, and 3% infection rates were reported. Of third ventriculostomies 80% were an initial procedure with a 67% success rate. A 75% success rate was reported in 20% of previously shunted patients converted to a third ventriculostomy. Success is defined as a minimum of one year post-surgery without recurrent symptoms of hydrocephalus.

From a nursing perspective it was proposed that the following shunt-related issues continue to be addressed:

- Outcomes improvement for premature infants
- Malfunction assessment
- Reality of "stiff ventricles," overshunting, and post-shunting synostosis
- Reliability of intracranial pressure (ICP) monitoring
- Headache/pain reduction
- Safety of external ventricular drains
- Criteria for selection of third ventriculostomy candidates
- Transition to adult care
- Real life/time testing of hardware

## Shunt Technology: Challenges and Emerging Directions – A Manufacturing Perspective

Marvin L. Sussman, PhD  
Industry Consultant  
Miami, Florida

Dr. Sussman spent 20 years in the corporate neurological shunt industry. He served as co-chair of the American Society for Testing and Materials (ASTM) Shunt Standards Committee that developed the Standard Practice for Evaluating and Specifying Implantable Assemblies for Neurosurgical Application (F647-94) and worked on the development of the International Organization for Standardization (ISO) Shunt Standard (ISO/TC 150/SC-7197).

According to Dr. Sussman valve designs consist of five types: silicone slit, hybrid silicone, ball-in-cone, hybrid silicone/ruby and programmable ball-in-cone. Self-adjusting flow control, programmable differential pressure valves, and coating for friction-reducing lubricity are examples of recent advances in neurological shunt technology that may not be addressed by current standards. Biomaterials currently used include:

- Silicone elastomer – catheters, valve housings/mechanisms, suture clamps, guides, siphon devices, etc.
- Polypropylene/Polysulfone/Nylon/Polyethersulfone – valve housings/seats, needle stops, connectors, reservoirs, etc.
- Ruby/Sapphire – valve pins, balls, seats
- Titanium/Stainless Steel – valve housings, needle stops
- Tantalum – radiopaque markers
- Barium – radiopacifier (homogenous or stripe)

Self-healing properties and the ability to elongate with patient growth, may be characteristic of future biomaterials. Silicone elastomers are the primary materials used for neurological shunts at present. In 1998, the American Medical Association published a position paper in response to concerns raised by issues identified with silicone breast implants in which it was stated that, “data do not suggest a specific immune response to silicone elastomer in shunts. It is recommended that research and development continue on materials, as well as designs and procedures for shunts. Also that monitoring of adverse reactions to devices take place so that appropriate research can be conducted.

Methodologies to assess shunt component radiopacity; flexibility; security of assembly; tensile properties; unidirectional flow; and leakage are manufacturer-

specific and therefore not readily comparable between manufacturers. In-vitro assessment of factors that may affect the performance of certain shunts or shunt components, such as tissue encapsulation of siphon devices, and effects of sleeping on the valve/siphon device and position of the device relative to the Foramen of Monro, are not addressed in ASTM standard F647-94.

As illustrated in the following 1990 table, another issue not resolved in industry’s approach to the specification of shunt operating characteristics, under dynamic and steady-state conditions, is agreement regarding standardized definitions of the various differential pressure ranges.

**DP Shunt Specifications (Ca. 1990)**

	<b>Cordis</b>	<b>J&amp;J/Codman Accu-Flo</b>	<b>Denver</b>	<b>Codman Holter</b>	<b>P-S Flow-Control</b>	<b>Radionics</b>
<b>Nominal Range</b>	mm H <sub>2</sub> O Operating Pressure 5 ml/hr	mm H <sub>2</sub> O Closing Pressure 5/50 ml/hr	Flow Rate (cc/hr) @ 100 mm H <sub>2</sub> O	mm H <sub>2</sub> O Operating Pressure 8.6 ml/hr	mm H <sub>2</sub> O Operating Pressure 5/50 ml/hr	mm H <sub>2</sub> O Operating Pressure 5/40 ml/hr
<b>Very/Extra/ Low Low</b>	15-40 Blue			0-10	5/40	
<b>Low</b>	40-80 White	2/75	6-17	11-40	10/70	35
<b>Medium</b>	80-120 Yellow	45/140	18-59	41-75	60/130	75/100
<b>High</b>	120-170 Brown	100/220	60-120	76-110	120/200	175/175
<b>Very High</b>	170-230 Green					
<b>Nominal Ranges</b>	5	3	3	5	3	3
<b>1998 Manufacturer</b>	<b>NMT</b>	<b>J&amp;J Codman</b>	<b>J&amp;J Codman</b>	<b>J&amp;J Codman</b>	<b>Medtronic P-S</b>	<b>Radionics</b>

Reference: The Shunt Book (Drake and Sainte-Rose; 1995 pp. 75-92)

In addition, there is little consensus regarding the definition of terms: differential pressure valve, flow-control valve, and physiological valve. Indeed, the neurosurgeon is often the “final manufacturer-assembler” of a neurological shunt using components from a variety of manufacturers. This leads to attempts to “test” shunt assemblies in the operating room and complicates labeling efforts. No standardized tests or outcomes have been approved for this practice which also invites increased risk of infection.

In many instances, shunt components are not identifiable once implanted. There is a need to give patients generic device identification cards on which all the

shunt assembly components are specified. Improvement in physician and patient instruction materials using a variety of approaches, such as, handouts, manufacturer and FDA web sites, and support groups, are suggested by Dr. Sussman.

It was also noted that the approximately 100 annual neurological shunt adverse event reports may reflect under-reporting. A need for guidance on what shunt-related events should be reported was proposed, as was repetition of the CDRH/WEAC 1990 study, *Conformance Assessment to Voluntary Standards*, using the 1994 ASTM standard F647, and extension of the Drake & Kestle study (1998 – 2 year results), *Pediatric Cerebrospinal Fluid Shunt Design*.

In summary, it was recommended that from an industry perspective, the following actions were proposed:

- Information dissemination
- Shunt comparison efforts
- Development of new technologies and biomaterials
- Protection of biomaterials supply access

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## BioPhysics of the CSF Pathways: What Can and What Should a Shunt Do?

Harold L. Rekate  
Chief, Pediatric Neurosurgery  
Barrow Neurological Institute  
Phoenix, Arizona

Dr. Rekate has been an attending neurosurgeon for twenty years. He is primarily involved in the clinical care of pediatric patients with hydrocephalus, but also treats adults with complex sequelae of hydrocephalus. His extensive research experience in CSF physiology includes a comparison of computer simulation of a mathematical model of cerebrospinal fluid (CSF) flow to physiology experiments in animal models of hydrocephalus. In addition, Dr. Rekate is the author of sixty publications, and holds several administration positions in professional neurosurgical groups.

In his presentation, Dr. Rekate stated that from 50% to 90% of the CSF is produced within the cerebral ventricles by both choroid plexuses. The remainder is produced as a by-product of cerebral metabolism in the cerebral and spinal cord whitematter. CSF flows from the ventricles through a series of conduits to the subarachnoid space and eventually is absorbed into the dural venous sinuses – primarily the superior sagittal sinus (SSS).

Intracranial pressure (ICP) in the normal, non-hydrocephalic condition is primarily a function of cerebral vein pressure.

- Sagittal sinus pressure (SSP) is 3-5mm Hg above right atrial pressure in recumbency
- Cortical veins have valve mechanisms that create about a 5 mm Hg differential between ICP and SSP. This pressure is transmitted to the brain parenchyma and is the primary determinant of brain turgor.
- Jugular veins are collapsible and close when their pressure falls below atmospheric pressure.

A CSF shunt is composed of a ventricular catheter, a reservoir that allows pressure measurement, a valve, and a distal catheter. Maintenance of normal intracranial pressure is relatively simple in the recumbent position, but that does not mean intracranial dynamics are normal.

- CSF flow in the normal situation is pulsatile with large volumes of CSF flowing back and forth across the aqueduct of Sylvius.
- Net flow of 0.3cc/min = 20cc/hour – a pint a day.



- With each pulsation, the CSF that flows through the shunt is irrevocably lost.
- Relatively large volumes of CSF are lost with cough and straining and essentially all available CSF is lost at the time of assuming the erect position.
- For much of the day there is often no flow through the device.

In the erect position, the height of the inflow (ventricular catheter) is much higher than the height of the outflow (peritoneal catheter). In a normally functioning differential pressure valve with an opening or closing pressure of 90-120 mm H<sub>2</sub>O (7-9 mm Hg) recumbent ICP at steady state also would be about 90-120 mm H<sub>2</sub>O. In the erect position, ICP is predicted to be, and has been measured to be, minus 20 to minus 30 mm Hg. Chronically shunted patients have significantly lower overall volumes of intracranial CSF, both in the ventricles and in the cortical subarachnoid spaces, resulting in markedly thickened skulls in patients who have been shunted in infancy, and enlarged paranasal sinuses that develop earlier than in age-matched controls. This leads to chronically decreased CNS buffering capacity for changes in ICP and leads to the question of whether there is a role for, or a possibility of, producing a shunt which incorporates a component which stores and can reinfuse stored CSF.

A natural shunt consists of a ventriculo-sagittal sinus where the arachnoid villi functions as a medium differential pressure valve that handles 20cc of CSF per hour without a siphon effect. There are four good re-creations of nature, however. A ventriculo-sagittal sinus shunt with a high differential pressure valve, the distance between the inlet and outflow does not change with changes in position and no siphoning occurs, but there is danger of occlusion and/or infection of the superior sagittal sinus, of which there is only one. In contrast, there are two transverse sinuses into which ventricular CSF can be shunted. Another option is a ventriculo-jugular shunt that functions against the direction of flow, and finally, ventricular-atrial or ventricular-peritoneal shunts that require a siphon-controlling mechanism if the patient is more than 2 ½ feet tall. There are several devices that have been developed to retard the overdrainage caused by siphoning.

- Anti-siphon device
- Siphon control device
- Siphon limiting device
- Delta valve
- Orbis sigma valve
- Horizontal-vertical valve
- Programmable valve – although even the highest valve pressure will not prevent very low ICP

Most patients do quite well regardless of the shunt selected, but some require specific types of shunts. The most important factor seems to be the concept of brain turgor. Specific condition/treatment pairs that have been identified include:

- Posthemorrhagic hydrocephalus of the premature newborn/Pressure differential valve of ball-in-cup or diaphragm design, because of the forgiveness of high protein and cellular debris.
- High brain turgor patients (achondroplasia, Crouzons, others)/Highest pressure valve tolerated. May even need valves in series.
- Low brain turgor patients (Normo Pressure Hydrocephalus)/Low pressure valve with a mechanism that prevents or retards siphoning.

Reflecting the perspective of a neurosurgeon, Dr. Rekate outlined the following problem areas as needing continued attention:

- Prevention of infection
- Maintenance of CSF pressure buffering capacity
- Development of valve programmability with a broader pressure range
- Development of more effective and reliable siphon prevention/retardation, and
- Exploration of alternatives to silastic

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## ***SESSION II***

### **Hydrocephalus and Assessment of Shunt Function**

#### **Fundamentals of Intracranial Pressure**

Anthony Marmarou, Ph.D.  
Professor and Vice Chairman  
Division of Neurosurgery  
Medical College of Virginia

Dr. Anthony Marmarou from the Medical College of Virginia began this session with an overview of the basics of intracranial pressure (ICP). An understanding of the fundamentals of ICP and its role in hydrocephalus and subsequent neurologic effects are important in understanding the use of shunts and other technologies in the treatment of ICP abnormalities. It is well-known that cerebrospinal fluid (CSF) production is based upon weight and that the bulk of CSF absorption takes place at the arachnoid villi. The arachnoid villi are the primary components to the resistance of flow of CSF.

The fundamental basis of intracranial pressure volume dynamics is affected by cerebrospinal fluid (CSF) diversion. Intracranial pressure (ICP) is defined as the pressure, which must be exerted on a needle placed in the cerebrospinal fluid space, sufficient to prevent the escape of fluid. According to Dr. Marmarou, a direct ventriculostomy gives the most accurate measure of ICP. The pressure is above atmospheric and contains both respiratory and cardiac pulsatile components. These components can be observed using different time scales when recording the ICP. As fluid enters the intracranial cavity, pressure will rise according to the pressure volume relationship, which defines the "compliance" of the intracranial contents. At equilibrium, the combination of all the compartmental volumes, blood, brain, and CSF, are constant. An increase in one compartment must be compensated by a decrease by another compartment capable of volume change. This occurs at the expense of pressure rise, which in part is governed by the transient pressure volume curve and by the resistance to outflow in the steady state. The pressure-to-volume relationship is not linear but exponential, and thus, derivation of the general equation describing intracranial pressure dynamics results in a first-order non-linear differential equation. This equation can be solved and a general solution obtained allowing the prediction of ICP change for any volume input. The relationship between ICP and volume can be described by the pressure-volume index (PVI). Infants have a lower PVI than adults, indicating a higher cranial compliance and subsequently greater ICP change resulting from a smaller volume change. In addition, in injury, a longer duration of elevated ICP results in a lower survival rate.

## Growth Factor Induction of Normal Pressure Hydrocephalus

Conrad E. Johanson, Ph.D.

Professor and Director of Cerebrospinal Fluid Laboratory

Department of Clinical Neurosciences

Brown University Medical School

Dr. Conrad Johanson from Brown University in Rhode Island, presented his research involving growth factor effects on the choroid plexus and how these growth factors as (peptides) may influence hydrocephalus. It is important to understand how these biochemicals interact in the central nervous system to further our knowledge of the etiologies of hydrocephalus.

Growth factor upregulation in CNS can alter brain fluid dynamics.

Hydrocephalus was induced in adult Sprague-Dawley rats by infusing basic fibroblast growth factor (FGF-2) at 1ug/d into a lateral ventricle for 2, 3, 5 or 10-12 d. Ventricular enlargement, without elevated cerebrospinal fluid (CSF) pressure, progressively increased from 2 to 10 d. At 10-12 d there was a 29% reduced CSF formation rate from 2.51 to 1.78 ul/min ( $P < 0.01$ ), and a concurrent 101% increased resistance to CSF absorption, i.e., 0.84 to 1.69 mmHg.min- $\mu\text{l}^{-1}$ . Choroid plexus, the main site of CSF formation, had an increased number of dark epithelial cells and a decrease in CSF formation, while the arachnoid villi region, a major absorption site for CSF, displayed enhanced fibrosis and collagen deposition thus inhibiting CSF absorption. A long-term pharmacologic goal has been to regulate CSF secretion. Diuretics have achieved a limited success. If control of drainage at the arachnoid villi can be accomplished using growth factors or other agents, perhaps an increase in outflow will reduce the need for CSF shunts. This is important since shunting may remove beneficial metabolites from the CSF that are crucial for brain function.

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## Animal and Clinical Studies in Adult-Onset Chronic Hydrocephalus

Mark G. Luciano, MD, PhD  
Head, Section of Pediatric Neurosurgery  
Department of Neurosurgery  
The Cleveland Clinic Foundation

Dr. Mark Luciano from the Cleveland Clinic Foundation in Ohio brought his perspective on the usefulness of various animal models in hydrocephalus research. The advantages and disadvantages of various in vivo models were discussed. It is important to consider the three interrelated aspects of the brain and central nervous system when developing research methodologies. First, the brain can be treated as a purely mechanical system with associated pressures, flows, compliance, and resistance. Next, the brain can be affected by its surrounding biochemistry, expanded in the previous presentation by Dr. Johanson. Lastly, the overall neurological function of the brain can be considered.

Although hydrocephalus continues to take a significant neurological toll on a wide spectrum of neurosurgical patients, it remains incompletely understood and inadequately treated. Several different animal models have been used to explore a variety of basic pathophysiology questions. The variety of animal models reflect the heterogeneity of the disease and each animal model has limitations in application. One animal model has fetal hydrocephalus induced by ligation of the placental vessels or catheterization of the Aqueduct of Sylvius. This can cause undesired confounding effects on the development of the brain. Another type consists of genetic models occurring congenitally in dogs, pigs, horses, and oxen. Unfortunately, the basic pathophysiology underlying genetic models is poorly understood. Lastly, surgical induction of hydrocephalus has been tried using balloons, silicone oil, and kaolin. Hydrocephalus induced in this manner is affected by the amount of inflammation from the inducing agent. An animal model is described that is appropriate for the study of onset chronic hydrocephalus. This model uses cyanoacrylate to obstruct the fourth ventricle allowing the severity and time course of the disease to be repeatable with no ventricular deformation or tissue inflammation. This model can be used to study both basic pathophysiology and new clinically relevant hardware and procedures.

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## *In Vivo Assessment of Shunt Function and Failure*

Michael A. Williams, M.D.  
Assistant Professor and Medical Director  
Johns Hopkins Medical Institutions  
Baltimore, Maryland

Dr. Michael Williams from the Johns Hopkins Medical Institutions in Maryland opened this session with his work involving the assessment of shunt problems while in clinical use. According to Dr. Williams, shunt malfunctions in adults are common but severely under-recognized. This is critical because the assessment of shunt function is the determining factor for shunt revision, a highly invasive procedure with potential for complications. If shunts could be paired with intracranial pressure monitoring technology, an objective evaluation of shunt performance could be used clinical.

The treatment of hydrocephalus is predicated on a functioning shunt. Shunts can malfunction in at least 3 ways: 1) complete obstruction of the valve or catheters that results in symptomatic hydrocephalus, 2) valve mismatch, malfunction, or partial catheter obstruction that leads to under-drainage and higher than desired intracranial pressure (ICP) associated with symptomatic hydrocephalus, and 3) valve mismatch or malfunction that leads to over-drainage (siphoning) and ICP that is lower than desired and associated with postural headaches.

In vivo assessment of shunt function was reported for 52 adult patients whose first shunt for normal pressure hydrocephalus (NPH) was between July 1, 1989 and October 1, 1995 and were followed for a minimum of 1 year. Two methods of shunt assessment were used: 1) radionuclide shunt patency study, and 2) computer recorded overnight continuous ICP monitoring via a needle inserted in the shunt reservoir. Poor clinical outcome occurred in 2/3 of patients after shunt surgery for NPH. Up to 1/3 of adults shunt malfunctions were caused by obstruction of the peritoneal catheter, identified by radionuclide shunt patency study. A smaller proportion were caused by a mismatch between the valve function and the desired ICP, identified by ICP monitoring. In vivo ICP monitoring via the shunt also demonstrates that siphoning occurs, that it can be corrected by using a shunt system with an anti-siphon device, and that siphoning can also occur when an anti-siphon device is in place. Clinical recovery occurred in 75% of patients who had shunt revision surgery.

In vivo ICP monitoring is an invasive procedure requiring hospitalization and access to ICP monitoring technology. There is a need to monitor shunt regulation of ICP in most patients. JHU is currently evaluating a telemetered

ICP (TICP) sensor in a Phase I human study in 5 patients. Drift is a major problem.

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## Radiological Tools Used in the Evaluation of Shunt Malfunction

Azar P. Dagher, MD  
Diagnostic Radiology Department  
National Institutes of Health

Dr. Azar Dagher from the National Institutes of Health in Maryland brought a completely different aspect to the conference: radiologic imaging techniques. Dr. Dagher gave an overview of the types of imaging techniques used clinically, including standard cross-sectional techniques, scintigraphy, and magnetic resonance imaging (MRI). Any of these imaging modalities can be used to assess volume changes in the ventricular brain spaces. Imaging can be used to describe particular feature changes in hydrocephalus. These features are: commensurate temporal horn dilatation, dilatation of the anterior and posterior recesses of the third ventricle, widening of the ventricular angle, a narrowing of the mammillopontine distance, widening of the frontal horns and effaced sulci. There are additional changes evident with a malfunctioning shunt: increased ventricular size, abnormal MRI cerebrospinal fluid (CSF) flow analysis, evidence of infection, subdural hematomas, calvarial thickening, premature craniosynostosis, and interstitial leakage.

Regional normalized volumetrics, used in the Diagnostic Radiology Department in the NIH, Clinical Center is presented as a semi-automated, sensitive and accurate method for the detection of subtle changes in ventricular size. Images obtained by either MRI or computed tomography can be processed using the regional volumetric method. An example is described showing how the image processing tool preserved CSF volume as intensity-based maps. Also, the system provides a semi-automated method to detect regional change in CSF volume over time, making it possible to quantify types of hydrocephalus.

Dr. Dagher examined the day-to-day variations in the ventricular size for normal patients. This could provide a baseline for hydrocephalic patients' ventricular size and thus, the quantitation of shunt malfunction. In addition, Dr. Dagher performed a ventricular CSF study of aging. There are significant ventricular changes and atrophy associated in populations greater than 70 years of age.

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## Shunt Evaluation Laboratory

Professor John Pickard, MChir, FRCS, FMedSci.  
Marek Czosnyka, PhD, DSC, and Zofia Czosnyka  
University of Cambridge  
Cambridge, United Kingdom

Dr. John Pickard from the University of Cambridge in the United Kingdom explained the need to evaluate various types of shunts using in vitro testing techniques in order to understand the relationship between the patient, the shunt, the surgeon, and the management team. This is particularly important considering shunts are used from youth (infancy) all the way through old age. Dr. Pickard also noted that testing involved the use of current shunt standards, and warned that these standards are the lowest common denominator. That is, the standards are primarily designed for industry, not for the clinic, and that the standards are generally governed by liability concerns rather than overall usefulness.

A computer-supported shunt testing laboratory, based on the new ISO standard, was described. Various aspects of pressure-flow shunt performance were characterized, such as: ability to drain CSF and its variability with time, susceptibility to reflux, hysteresis, temperature, external pressure, presence of pulsation in differential pressure, particles in the perfusion fluid, siphoning, etc.

Sixteen different valve models used in the U.K, have been tested:

- Medtronic PS Medical: Delta Valve, Flow Control and Lumbo-Peritoneal Shunt
- Heyer-Schulte Neuro-Care: In-line, Low Profile and Pudenz Flushing Valve
- Codman: Codman-Medos Programmable, Hakim Precision Valve, Accu-Flo, Holter Valve and Uni-Shunt
- Sophysa: Sophy Programmable Valve
- Radionics: Contour-Flex Valve

The majority of tested valves had a non-physiologically low hydrodynamic resistance (with the exception of Orbis-Sigma, PS Lumbo-Peritoneal and Heyer-Schulte In-Line). This may result in overdrainage related to both posture and during nocturnal cerebral vasogenic waves.

A long distal catheter increases the resistance of these valves by 100-200%. A few shunts (Delta, LowProfile and Pudenz-Flushing with Anti-Siphon Devices) offer a reasonable resistance to negative outlet pressure, and hence potentially prevent complications related to overdrainage.

Drainage through valves without siphon-preventing mechanism is very sensitive to body posture. This may result in grossly negative intracranial pressure after implantation. In most of the silicone-diaphragm valves, closing pressure varied and reached pressures lower than that specified by the manufacturer (exception: Heyer-Schulte Pudenz Flushing Valve). Pulsatile flow will also shift opening and closing pressures, creating pressure waves. The OSV is an example. Valves with siphon-preventing device may be blocked by raised subcutaneous pressure. All programmable valves are susceptible to overdrainage in the upright body position. Programmed settings may be changed by external magnetic fields. Most shunts are very sensitive to the presence of small particles in the drained fluid. The behavior of a valve revealed during such testing is of immediate relevance to the surgeon and may not be adequately described in the manufacturer's product information.

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## ***SESSION III***

### **Challenges of Infection and New Perspectives**

#### **Incidence and Aetiology of Shunt – Associated Infections**

Roger Bayston, MMedSci, FRCPath  
University of Nottingham  
Nottingham England

Dr. Roger Bayston from the University of Nottingham began the session reviewing the basics of shunt infection. He described the current thinking as to why and how shunt infections occur and what is necessary for treatment. Dr. Bayston indicated that the uniqueness of shunt infection may be tied to shunt design, i.e., shunt is a tubular device with multiple components and, in most cases, includes a reflux valve which may affect the symptomatology of shunt infections. The site of many, but not all infections, is within the cerebral ventricles; however, many practitioners that tap the ventricles find normal clear acellular CSF. This is the situation when infection is confined distal to the shunt valve in the peritoneal catheter where the presenting symptom of shunt infection in the peritoneal catheter is catheter obstruction. True shunt infections, as opposed to post-surgical wound infections, occur within the lumen of the device catheter. Remembering that these devices are tubular, it has been found that the infection is confined to the lumen in the early stages, which will progress to the outside by the effects of reflux up the catheter track. The presenting features of the most commonly used shunt in the U.S., ventricular peritoneal (VP) shunt, manifests infections that are found to be different from the ventricular atrial (VA) infections. VP infections usually occur within 6 months of surgery; begin in the lumen; progress distally and emerge below, causing obstruction through the development of adhesions, as well as, inflammatory response. Sometimes the result is the formation of a cyst due to the wrapping of the peritoneal catheter by the greater omentum. This scenario usually presents itself as a recurrence of hydrocephalus due to obstruction of the distal catheter. It is not easily diagnosed as an infection without removing the distal catheter. In some cases, erythema may be found around the catheter track, which is a good indicator of infection.

Often, the incidence of shunt infections is reported in the literature as 10% of shunt operations. However, upon careful examination the incidence is profoundly disproportionate between patients older than and less than 6 months. That is, most adults, and children older than 6 months, have been found to have a 3-6% incidence of shunt infection, whereas those less than 6 months old demonstrate a rate of 15% or greater incidence. The theories as to

why infants less than 6 months old have such a high incidence of shunt infection include: immunological immaturity; limitations of the small infant size; nutritional factors; and bacterial factors. Dr. Bayston dismissed all of these factors except bacterial factors as legitimate reasons of their high incidence. Most nutritional factors may have some basis for some infections but not the type under discussion for shunts. The immunological immaturity of infants is not global, but specific where several parts of the complex immune system have not been found to play a role in the prevention or protection of shunt infections. According to Dr. Bayston, bacterial factors seem to present the only currently known basis for the high incidence of shunt infections in infants less than 6 months. From a study to assess the bacterial factors associated with the high infection incidence in these infants, it was found that they were often born prematurely and survived periventricular haemorrhage leading to the onset of hydrocephalus requiring a shunt. From birth, infants are exposed to hospital acquired skin flora not of the mother. Infants with a shunt infection were found to have three interesting facts:

- high skin bacterial densities;
- correlation with the number of bacteria found at the incision; and,
- higher incidence of highly adherent bacteria.

According to Dr. Bayston, the belief that these infections are caused from bacteria in the bloodstream that then attach themselves to the shunt is unfounded. The majority of shunt infections occur from bacteria on the patient's skin. This was supported by data where 100 wound impressions were taken and 58 were found positive with bacteria. 32 of the samples were found with organisms from the patient, with colonies up to 55. The remaining 26 samples were from other unknown sources with fewer colonies, that is, 1-7. Of those patients having an infection, 12/14 of the infections were caused by strains from incision at surgery and the same as those on the patient's skin. No patients with post-operative bacteraemia developed a shunt infection. It is believed that bacteria enter the shunt during surgery either by direct transfer via instruments, gloves, shunt catheter, or via skin edges, irrigation fluid, blood or CSF. Staphylococcus epidermidis is the target micro-organism causing 70 to 85 percent of shunt infections. The problems associated with treatment of S. epidermidis shunt infections involve the fact that the bacteria are often multi-resistant with biofilm formation that enhances resistance and is often out of reach of therapeutic medication. Biofilm is instrumental in causing the problems associated with treating shunt infections. The level of antibiotic necessary to kill bacteria is more than 1000 times higher than for non-biofilm type infections. Because of pharmacological constraints and the blood brain barrier, antibiotic treatment fails. Even when antibiotic treatment is given intraventricularly, it is still necessary to remove the shunt to eradicate the infection because of the effects of bacterial adherence.

In concluding, Dr. Bayston emphasized that in the development of any strategy for prevention of shunt infections, it is necessary to have knowledge of the following factors:

- Source of bacteria
- Time of entry
- Nature of infection and pathogenesis
- Other risk factors

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## The Role of Standard Medical Treatment for Infection in the Emergence of Antimicrobial Resistance

William R. Jarvis, M.D.  
Hospital Infections Program  
Centers for Disease Control and Prevention (CDC)

One of the strategies in the prevention of infection is the use of antimicrobials. The wide spread use of antimicrobials has led to antimicrobial resistance. To bring attention to this problem, Dr. Jarvis described the following:

- epidemiology of antimicrobial resistance;
- Vancomycin use in adult and pediatric patients;
- Vancomycin use in pediatric neurosurgery patients; and,
- CDC recommendations for appropriate use of antimicrobials.

Vancomycin is critical in the armamentarium for treatment of patients with infection; frequently neurosurgeons are using it prophylactically. Multidrug resistance has become an increasing worldwide problem; the annual cost in the United State exceeds \$30 billion. Nearly half this cost is attributable to the treatment and care of inpatient nosocomial infections. The major risk factors associated with antimicrobial resistance are the misuse of antimicrobial agents and the non-compliance with infection control practices. From the National Nosocomial Infections Surveillance System (NNIS), Dr. Jarvis showed that from 1978 through 1997, there was a dramatic increase in resistant organisms, particularly to the primary drug used to treat these pathogens. When examining antibiotic use in hospitals, Dr. Jarvis described three categories of antibiotic treatment:

- Empiric therapy, where there is an unidentified infection;
- Definitive therapy, where there is a confirmed infection by an identified organism; and,
- Prophylaxis

Up to 41% of all antibiotic use has been found to be inappropriate. There is a wide variety of approaches for optimizing antibiotic use, for which Dr. Jarvis has provided a reference (Avorn et al., Rev Infect Dis, 1987, 9:S285-S296).

Dr. Jarvis presented NNIS data on the percentage of Methicillin-resistant Staphylococcus aureus (MRSA) infections in hospitals from 1975 through 1996. The data show that there was not a particular problem in the late 70s or early 80s, but by the mid-80s there was a dramatic increase in the prevalence of MRSA infections. There have been no data on the proportion of patients with

methicillin resistant S. aureus colonization; failure to recognize this population and to use appropriate infection control measures, especially handwashing before and after contact with such patients, has contributed to the establishment of MRSA endemicity in the United States. This increase in MRSA led to the widespread use of Vancomycin. Vancomycin, a glycopeptide, is one of our medicine miracles and the only agent uniformly effective against MRSA. Out of concern for the increased use of Vancomycin and knowledge that resistance was to emerge, in 1995 the Hospital Infections Program, CDC with its Hospital Infection Control Practices Advisory Committee (HICPAC) issued Vancomycin-use recommendations. From 1996 through 1997 it was shown that as much as 50 to 60% of Vancomycin use was not consistent with the CDC/HICPAC recommendations. A number of hospital based studies in 1998 have shown that Vancomycin use can be improved.

A concern of widespread Vancomycin use is the emergence of Vancomycin-resistant enterococcus (VRE). An organism not identified in this country until 1989; however, over the past 5 to 10 years there has been a dramatic increase. Today, VRE account for 15-16% of the enterococcal infections reported at NNIS hospitals.

Dr. Jarvis described a retrospective epidemiological pharmacy review of Vancomycin usage data collected from 1981-91 at a university hospital. It reviewed all patients receiving intravenous Vancomycin. The most significant finding was a 200 fold increase in Vancomycin use, primarily in oncology service. Upon review, the overall use indicated approximately 1/3 was for empiric therapy, 1/3 was for definitive therapy and 1/3 for prophylaxis. Upon closer examination over 60% of Vancomycin use was found to be inappropriate primarily due to inappropriate monitoring. Risk factor review for receipt of Vancomycin revealed that patients with a medical device had a 14 times greater risk of receiving Vancomycin than patients without a medical device. A multivariate analysis controlling risk factors indicated a significant risk of receiving Vancomycin with intravenous and Hickman catheters, as well as devices such as CSF shunts.

Until recently, S. aureus was always susceptible to Vancomycin. In July, 1997 the first documented case of Vancomycin (or glycopeptide) Intermediate Resistant S. aureus was reported in Japan. Dr. Jarvis described this case, as well as two other case studies documented in the U.S. shortly after the Japanese occurrence.

In a 1993-97 study from a children's hospital surgical services, it was found that 75% of patients receiving Vancomycin were from either Cardiovascular or Neurosurgery. Since nearly 18% of all Vancomycin use at the hospital were in pediatric neurosurgery patients a closer examination of these patients was

performed to determine why Vancomycin was used and if it was used appropriately:

Age:		0.2 – 17.8 years	median 8 years
Gender:		56.7% male	
Hospitalization:		1 – 12 days	median <b>2 days</b>
Procedures:	cranial	13.3%	4
	Spinal	6.7%	2
	<b>Shunt</b>	<b>76.7%</b>	23
	Primary	30.4%	7
	Revision	69.6%	16
Duration:	< 3 hrs	<b>82.8%</b>	
	3-6 hrs	13.8%	
	> 6 hrs	3.4%	

Surgical prophylaxis use was found in all patients except one where the number of doses ranged from 1-12, with a median of 2. It is alarming that in six cases, treatment was administered post-incision. Noting that organisms are presumed at the site of incision, to be effective it is necessary to have peak antibiotic prophylactic levels at the time of incision. Another fact is, a large proportion of the procedures (82.8%) were less than 3 hours in duration. It is recognized that antibiotic prophylaxis for a procedure of this duration would require only one dose.

In comparison with CDC/HICPAC recommendations it was found:

- Vancomycin use was inconsistent with CDC/HICPAC recommendations because of surgical prophylaxis in 28 patients;
- in six patients (21.4%), the initial dose was administered post-incision; and,
- prophylaxis was continued inappropriately in 26 patients (92.9%) where a total of 50 extra doses were administered in 28 patients.

The current CDC/HICPAC recommendations for appropriate Vancomycin use includes situations for:

- Treatment of serious infections due to beta-lactam resistant gram-positive microorganisms;
- Treatment of infections due to gram-positive microorganisms with serious allergy to beta-lactam antimicrobials;
- Treatment of serious or potentially life-threatening antibiotic-associated colitis (AAC) or AAC which fails to respond to metronidazole;



- Prophylaxis as recommended by the American Heart Association for endocarditis following certain procedures in patients at high risk for endocarditis; and,
- Prophylaxis for major surgical procedures involving implantation of prosthetic materials or devices, e.g., shunts, at institutions with a high rate of infection due to Methicillin-resistant S. aureus or S. epidermidis (maximum 2 doses).

Situations in which the use of Vancomycin should be discouraged include:

- Routine surgical prophylaxis;
- Empiric antimicrobial therapy for febrile neutropenia;
- Treatment for a single blood culture positive for coagulase-negative Staphylococcus; and,
- Continued empiric use for presumed infection in patients whose cultures are negative.

In summary, Dr. Jarvis restated the highlights of his talk:

- Over- and inappropriate antimicrobial-use is associated with the emergence of antimicrobial-resistant pathogens;
- Patients with “plastics,” including CSF shunts, are at risk of receiving Vancomycin;
- Pediatric neurosurgery patients were one of the top three groups to receive Vancomycin at a children’s hospital;
- At one children’s hospital, Vancomycin was inappropriately used as surgical prophylaxis or empiric therapy in all patients evaluated; and,
- Improved practice of Vancomycin use and other antimicrobials are needed in neurosurgery patients.

In conclusion, Dr. Jarvis stated that there is currently no published study in the English language that shows prophylactic use of antimicrobials is efficacious, nor is the use of Vancomycin more effective than other agents.

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## Pathogenesis and Prevention of Catheter-Related Infection

Robert J. Sherertz, MD  
Chief, Section on Infectious Diseases  
Department of Medicine  
Wake Forest University School of Medicine

Dr. Sherertz, an infectious disease physician with expertise in the pathogenesis and prevention of infection associated with vascular catheters, described some of the current work being done to prevent catheter-related infections.

Dr. Sherertz described skin as the major source of early infections for catheter-related infections. Whereas breaks in the line, resulting in contamination of the lumen, is the most common source of infections for long term catheters. Dr. Sherertz showed data on vascular catheters demonstrating the relationship of the number of organisms (*S. aureus*) and the likelihood of purulence associated with infection of a foreign body. In a rabbit model, it was shown that likelihood of associated purulence with inoculation up to 100,000 organisms occurs about 50% of the time when there is no foreign body. However, when a foreign body, e.g., catheter, is introduced, the likelihood of associated purulence is 100% at the same level of organisms.

Dr. Sherertz discussed the difference in the risk of infection between different biomaterials. According to Dr. Sherertz, silicone has a higher likelihood of purulent infection than materials polyurethane (PU), polyvinyl chloride (PVC), and Teflon. One theory is that there is less killing of bacteria by neutrophils on the surface of silicone as opposed to PU. Looking at chemotaxis, data Dr. Sherertz showed that neutrophils migrate differently, i.e., the data showed when using serum as a stimulus neutrophils move faster on silicone when compared to other materials, e.g., glass, polystyrene, and PU. In a rabbit model, catheters composed of different materials, e.g., silicone, PU, PVC, and Teflon, were implanted in the subcutaneous space and evaluated by an inflammatory index. The inflammatory index associated with the silicone catheter was greater than in the other materials. This was shown whether the specimens were inoculated with bacteria or not. According to Dr. Sherertz a possible mechanism for this difference is complement activation. Complement activation associated with silicone is 10 times greater than with other materials. Excessive complement activation during the time of insertion may produce a unique microenvironment next to the catheter that may lead to an increased likelihood of infection.

Dr. Sherertz presented an overview of some current methods being investigated in the prevention of infections on the outer surface of catheters. He restated what was previously stated by other speakers that there is no good data to support the use of prophylactic antibiotics based on 3 randomized studies of

vascular catheters that demonstrate prophylaxis does not work. Another prevention method is that of anti-infective coatings, where at least 3 clinical trials have shown a definitive reduction in risk of bloodstream infection. It is unclear whether such anti-infective coatings will be appropriate for CSF shunts because of the unique environment of the brain resulting in unwanted effects, e.g., toxicity, inflammation, neural damage, etc.

The concept of anti-infective coatings has been investigated on animals, where it has been shown that the size of the zone of bacterial inhibition of implanted specimens in animals correlates with the size of the zone of inhibition on the surface of agar plates.

The use of intermittent or continuous flow of anti-infective solutions within the lumen of catheters has been investigated to try to minimize infections within the vascular catheter lumen. Such solutions include: Vancomycin, EDTA, Gentamycin/Chymotrypsin, chlorine dioxide, and Minocycline/EDTA.

In an *in vitro* study, *S. epidermidis* survival on various catheter surfaces was evaluated. Dr. Sherertz showed that a combination of Minocycline and EDTA demonstrated the greatest effect, where no organisms could be detected on the surface. The results presented were as follows:

Control (broth) – 10,000 organisms	control
Urokinase	no effect
Heparin	no effect
Vancomycin/Heparin	decreased by 1 to 2 log scale
Vancomycin	decreased by 1 to 2 log scale
EDTA	some effect
Minocycline	some effect
MEDTA specimen	large effect; equivalent to a sterile

Although the data show some promise in the prevention of catheter-related infections there is only minimal clinical data available for such preventive measures. Further work needs to be done to understand how best to use these new technologies to decrease the risk of catheter-related infections.

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## ***SESSION IV***

### **Clinical Outcomes And Methods Of Surveillance**

#### **Experience with Setting up and Maintaining the UK Shunt Registry**

Professor John Pickard, MChir, FRCS, FmedSci  
Hugh Richards, PhD, Helen Seeley and Meryl Madakbas  
University of Cambridge  
Cambridge, United Kingdom

Professor John Pickard from the University of Cambridge, United Kingdom, presented experience of the UK Shunt Registry in collecting the data on neurological shunts. The Registry was established in May 1995 following a successful pilot phase, and since that time has compiled data from 10,000 shunt operations performed on 7,400 patients, at 61 neurosurgical and pediatric units in the United Kingdom. The Registry was founded to collect neurological shunt data; to provide an accurate picture of the types of shunts used; establish risk stratification criteria; identify substandard shunt systems; and to facilitate audit of standards of care.

According to Professor Pickard, the data were collected on all shunt procedures, all shunt revisions; and third ventriculostomy interventions. The Registry data allowed for examination of the device used; operator's experience; operation length; types of complications; reasons for revisions; and antibiotic use. The overall annual revision rate was 25.8 %. The most frequent reasons for revisions were identified as: underdrainage, discontinuation, fracture, infection and overdrainage. The revision rate was calculated for operations involving valve insertion or replacement. The annual valve failure rate was found to be 16.2 %.

In conclusion, Professor Pickard proposed that the Medical Device Agency in the United Kingdom introduce the registry as a posmarket surveillance technique for neurological shunts.

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## On-Line Neurosurgical Outcomes Studies

Robert E. Harbaugh, MD, FACS

Chairman, AANS/CNS Outcomes Committee

American Association of Neurological Surgeons and Congress of Neurological Surgeons

Dartmouth-Hitchcock Medical Center

Dr. Robert E. Harbaugh, Chairman of the AANS/CNS Outcomes Committee presented collaborative efforts of the Outcomes Committee of the American Association of Neurological Surgeons (AANS), Congress of Neurological Surgeons (CNS) and the AANS Information Services Department and Outcome Sciences on the development of the system for conducting on-line outcomes studies in order to provide a rigorous evaluation of the effectiveness of care.

Potential advantages of on-line outcomes, as outlined by Dr. Harbaugh, include: an ease of data submission, storage, analysis, feedback, ease of neurosurgical recruitment; maintenance and accession of national and international databases; and decreased cost per patient.

Dr. Harbaugh presented Physicians' Outcomes Initiative and Networking Technology (POINT) system that was developed as an Internet based system for outcomes studies data collection, analysis and feedback accessible through the N://OC web site. The data collection forms can be downloaded directly from the web site and entered into the POINT database with a capacity of 800,000 hits per day and more than 1,000,000 patient records.

According to Dr. Harbaugh, the "modular" approach to neurological on-line outcomes studies was adopted in order to develop this technology in the most cost-effective way. Dr. Harbaugh presented different modules, such as registration, administrative and disease-specific data; functional health status; patient satisfaction and resource utilization. Modular approach to on-line outcomes will allow each subsequent study to build on previous data and is expected to reduce cost.

Dr. Harbaugh talked about Carotid Pilot Project to illustrate a study that was done entirely on-line, using the POINT system. Goals of this pilot project were to develop a national outcomes database at the N://OC web site. In order to do that, the initial modules needed to be refined to allow rapid and economical implementation of subsequent outcomes studies; allow neurosurgeons to easily become involved in outcomes studies; as well as to allow feedback of local practice outcomes and comparison to national standards.

According to Dr. Harbaugh, the modular approach to on-line outcomes studies will allow subsequent studies to be built on previous work. That would allow subsequent studies to be conducted on-line at low cost. Dr. Harbaugh informed the audience that a “Neurosurgical Report Card” is now available and a spine study should be available on-line soon.

Dr. Harbaugh concluded his presentation by pointing out that the availability of reliable outcomes data will be essential for documenting the effectiveness of surgical intervention and that outcomes data may best be done using an internet based approach. Therefore, Dr. Harbaugh suggested that this approach could be used to collect and evaluate data on shunt technology.

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## Issues in data collection and outcome analysis

John R.W. Kestle, M.D., MSC, FRCSC  
Division of Pediatric Neurosurgery  
University of Utah  
Primary Children' Medical Center  
Salt Lake City, Utah

Dr. John Kestle, from the University of Utah, Salt Lake City, presented examples from the two multicenter trials in pediatric hydrocephalus in order to illustrate data issues, outcome definitions, and analyses.

The importance of readable, understandable, and easy-to-use forms was highlighted. Additionally, using separate forms for each event and use of such forms in a pretest phase, clearly enhanced the quality of data collection. Methods of data collection were outlined as well as data accuracy assessment. According to Dr. Kestle, data accuracy depends on prospective acquisition; prospective review at data center; internal consistency and source verification. Data monitoring components were presented with emphasis on accrual; database safety (infection rate, surgical complications, and deaths) and rechecking sample size.

Dr. Kestle highlighted the importance of clear definition of primary outcome and applying the definition in a consistent unbiased way. Using neurological shunts as an example, Dr. Kestle presented a shunt failure as a primary outcome including categories of shunt obstruction, overdrainage, loculated compartments and shunt infection.

In conclusion, Dr. Kestle discussed methods of assessing the observer bias; presented examples of blinding; and analyzed the effects of learning curve and the center volume on shunt survival.

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