Dissertation on

A STUDY ON VENTRICULOPERITONEAL SHUNT INFECTIONS

Dissertation Submitted in partial fulfillment of

M.D. DEGREE EXAMINATION

BRANCH IV – MICROBIOLOGY

MADRAS MEDICAL COLLEGE, CHENNAI.

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

SEPTEMBER 2006

CERTIFICATE

This is to certify that the Dissertation "**A STUDY ON VENTRICULOPERITONEAL SHUNT INFECTIONS"** presented herein by **Dr. R. VIDHYA RANI** is an original work done in the Institute of Microbiology, Madras Medical College and Government General Hospital, Chennai for the award of Degree of M.D. (Branch IV) Microbiology under my guidance and supervision during the academic period of 2003-2006.

Prof. Dr. Kalavathy Ponniraivan,
B.Sc, M.D.,
DEAN,
Madras Medical College & Hospital,
Chennai.

Prof. Dr. A.Lalitha M.D., D.C.P.,
Director and Professor
Institute of Microbiology,
Madras Medical College & Hospital,
Chennai.

ACKNOWLEDGEMENT

I wish to express my sincere thanks to our Dean **Dr. Kalavathy Ponniraivan,** B.Sc., M.D., Madras Medical College, Chennai for having allowed me to conduct the study.

I owe special thanks to our Director **Dr. A. Lalitha,** M.D., D.C.P., Institute of Microbiology, Madras Medical College, for her constant support, invaluable suggestions and encouragement throughout my study.

I am immensely grateful to our former Director **Dr. T.S. Vijayalakshmi,** M.D., Institute of Microbiology, Madras Medical College for her guidance and encouragement throughout my study.

I wish to express my thanks to our Vice-Principal **Dr. S. Geethalakshmi**, M.D., Professor, Institute of Microbiology, Madras Medical College for her constant support.

I owe a deep sense of gratitude to **Dr. G. Sasirekha**, M.D., D.G.O., for her unflinching interest, valuable advice, excellent guidance and encouragement throughout my study.

I wish to thank **Dr. G. Sumathi,** M.D., **Dr. A. Shameen Banu**, M.D., **Dr. Kalavathi Victor**, M.D., D.C.P., Professors of Microbiology, Madras Medical College for their guidance and encouragement.

I owe special thanks to **Dr. S. Mohan Sampathkumar**, M.S., M.Ch., Professor and Head of Department of Neurosurgery, Institute of Neurology, Madras Medical College for permitting me to carry out this study in his department.

I am deeply indebted to **Dr. Sujatha Vardarajan**, M.D., Assistant Professor of Microbiology, Madras Medical College for her invaluable suggestions excellent guidance and encouragement throughout the study.

I would like to thank **Dr. Sheela Doris**, M.D., **Dr. K. Radhika**, M.D., D.A., D.N.B., **Dr. M. Indumathy**, M.D., D.G.O., **Dr. K. Kaveri,** M.D., D.Ch., **Dr. T. Latha**, M.Sc., Ph.D., **Dr. R. Selvi**, M.D., **Dr. T. Girija Devi**, M.D., PGDHM., Assistant Professors of Microbiology, Madras Medical College for their support and encouragement.

I would also like to thank my colleagues and technical staffs for their continued co-operation to carry out the work successfully.

I would like to thank **Dr. P. Ranganathan**, Post-graduate of Neurosurgery, Madras Medical College for helping me in collecting the samples.

I would like to thank my family for being a constant source of encouragement.

Last but not the least, I would like to express my sincere gratitude to **Lord Almighty**.

TABLE OF CONTENTS

ABBREVIATIONS

ATCC	-	American type culture collection
BAP	-	Blood agar plate
CAP	-	Chocolate agar plate
CDC	-	Centres for Disease Control
CNST	-	Coagulase-negative *Staphylococci*
CSF	-	Cerebrospinal fluid
ESBLs	-	Extended-spectrum beta-lactamases
EVD	-	External ventricular drainage
MAC	-	MacConkey agar plate
MIC	-	Minimum inhibitory concentration
MRSA	-	Methicillin resistant *Staphylococcus aureus*
MRSE	-	Methicillin resistant *Staphylococcus epidermidis*
NA	-	Nutrient agar plate
NCCLS	-	National committee for clinical laboratory standards
O/F	-	Oxidative - Fermentative
RCM	-	Robertson cooked meat broth
SEM	-	Scanning electron micrographs

INTRODUCTION

Neurosurgeon Dr. James Drake writes “Perhaps no neurosurgical complication is as distressing as a CSF shunt infection”.

The placement and revision of ventriculoperitoneal shunt remains a mainstay in the surgical treatment of hydrocephalus. Ventriculoperitoneal shunting is by far the most popular technique for cerebrospinal fluid (CSF) diversion. It is relatively simple, suitable for patients of all ages with hydrocephalus from any cause like myelomeningocele, aqueductal stenosis, preceding meningitis, preceding subarachnoid haemorrhage, CNS tumour, postopertive adhesion, head trauma, other congenital malformations and other acquired etiology. Ventricular shunts have obviously changed the prognosis for individuals with hydrocephalus, and most attain fairly normal intelligence.

In patients who never had a VP shunt inserted before, a shunt can usually be inserted usually in less than an hour. It is important to try to do the procedure as quickly as possible to minimize the risk of infection.

Infection is unfortunately a relatively frequent complication of shunt placement, which contributes significantly to excess morbidity and mortality. Shunt infections put the patient at increased risk of intellectual impairment, development of loculated CSF compartments, and even death. In several large studies since 1971, the case incidence of shunt infection has ranged from 8-40% and the operative incidence has ranged from 2.8-14%.[10]

Four mechanisms may be postulated by which shunts become infected:

a) colonization at the time of surgery being the most frequent cause

b) retrograde infection from the distal end,

c) wound or skin breakdown

d) hematogenous seeding which is a possible occurrence but not a frequent one.

Most infections present in early postoperative period which suggests that the perioperative contamination from the patient's skin may be an etiologic mechanism. Of all the factors that have been reported to predict an increased risk of shunt infection (time of surgery, etiology of hydrocephalus, use of prophylactic antibiotics, number of revisions, site of shunt placement, type of revision, age of patient, surgeon), only poor skin condition and age of the patient are clear predisposing factors.

The presentation of shunt infection can be quite variable. The signs and symptoms of shunt infection are fever, seizures, symptoms related to shunt malfunction such as headache, vomiting, change in mental status, wound infections and cellulitis along the shunt.

The most frequently isolated microorganisms are of *Staphylococcus* species including *Staphylococcus epidermidis* and *Staphylococcus aureus.* Furthermore increases in polymicrobial, Gram-negative bacilli infections (*Escherichia coli, Klebsiella* species*, and Pseudomonas* species) are observed now-a-days. The remainder are due to *Streptococcus* species*, Enterococcus* species*, anaerobes* and yeasts.

DEFINITION OF SHUNT INFECTION

Shunt infection can be defined as isolation of the organism from the ventricular fluid or shunt hardware along with clinical signs and symptoms

suggestive of shunt infection or malfunction like fever, peritonitis, meningitis, signs of infection along the shunt tract, or nonspecific signs and symptoms of headache, vomiting, change in mental status, or seizures.

A combination of clinical suspicion and laboratory testing, primary analysis of the CSF aid in the identification of shunt infection. Positive culture results from either the CSF or shunt apparatus provide a reasonable working diagnosis for shunt infection.

The value of prophylactic antibiotic administration in the prevention of shunt infection remains unproved.

Like prevention of shunt infection, treatment of shunt infection is equally challenging. Four treatments of shunt infection have evolved:

1. Medical (antibiotic) treatment,
2. Shunt removal with delayed replacement,
3. Shunt removal with immediate replacement,
4. Externalization of the shunt or installation of external ventricular ventricular drainage (EVD) along with antibiotics, which is the most effective treatment.

AIM OF THE STUDY

- To find out the infection rate associated with ventriculoperitoneal shunts.
- To study the association between the underlying conditions that necessitate shunt and the development shunt infection.
- To evaluate the risk factors associated with shunt infection.
- To isolate and identify the causative pathogens.
- To evaluate the usefulness of CSF Gram staining, cell count and biochemical parameters to identify infections at an early stage.
- To determine the antimicrobial susceptibility pattern of the isolates so as to use appropriate antibiotics.
- To study the therapeutic outcomes.

REVIEW OF LITERATURE

The use of ventriculoperitoneal shunts to treat hydrocephalus in both children and adults has made hydrocephalus one of the most treatable neurological conditions. Shunting is the commonest surgical procedure in a paediatric neurosurgical practice. There are a few conditions treated by neurosurgeons that are at once so gratifying and so frustrating as hydrocephalus. Likewise, there are few operations performed by neurosurgeons that are at once so simple and so unforgiving as cerebrospinal fluid (CSF) shunt insertion.

HISTORICAL BACKGROUND

The existence of CSF was known to the author of Edwin Smith papyrus in the 18th century B.C., and hydrocephalus was recognized by Hippocrates. Magendie gave a name to CSF in 1825.In 1875,Key and Retzius worked out its circulatory pathways.[46] Modern notions of the secretion and absorption of CSF were developed by Weed in the first part of this century, while Dandy and Blackfan deserve credit for defining the concepts of the pathophysiology of hydrocephalus that led to the first successful treatments.[68]

Review of the medical measures that have been employed in the treatment of hydrocephalus places the evolution of modern surgical practices in a favourable perspective. Before the era of scientific medicine, hydrocephalus was treated by the usual armamentarium of uncritically selected and totally ineffective measures: venesection, cupping, leeching purgatives, diuretics, and so on.[19]

From our vantage point at the end of the twentieth century, it is clear that many surgeons who attacked the problem of hydrocephalus at the beginning of the

century had the right idea: CSF must be diverted to a body cavity where it can be absorbed at low pressure. Apparently the first CSF shunt was a “nail” of glass wool communicating the lateral ventricle with the subgaleal space.[19] Tubes fabricated from platinum, gold, silver, glass, and rubber as well as linen threads, coiled silver wires, and strips of omentum were used by various surgeons as drains into subgaleal, subdural, and subarachnoid spaces. Diversion of CSF directly into the peritoneum was attempted as early as 1898 and there were early attempts to utilize the pleural space and vascular tree as receptacles for CSF as well.[46]

Also in 1908, the first ventriculoperitoneal shunt was inserted by Kaush, who used a rubber tube to connect the lateral ventricle with the peritoneal surface. The 1950s marked the introduction of extracranial ventricular shunting, first to the vascular system and subsequently to the peritoneal cavity. The widespread use of ventricular shunting was made possible following the introduction of unidirectional valve systems and biologically inert silicone elastomer tubing. The initial ball valve used by Nulsen and Spitz was primitive and ineffective. A better “slit” valve was developed by Holter in the mid-1950s. Holter’s slit valve became one of the most widely used shunt valves throughout the world. Working at about the same time as Holter but unaware of his work, Pudenz of Padenza, California, developed an effective unidirectional valve that was tested rigorously in an animal model and implanted successfully in patients.[68]

Before ventriculoperitoneal shunting had achieved widespread use, there were reports of techniques to shunt CSF from the cerebral ventricles or subarachnoid space to almost every body cavity. The distal shunt catheter has been placed in body cavities such as the subgaleal space, salivary duct, mastoid process, orbit, stomach, intestine, thoracic duct, gallbladder, kidney, ureter, and even the fallopian tube. The high complication rate for ventriculovascular shunts and their requirement for

frequent revision led ultimately to the development of the ventriculoperitoneal shunt, which remains the surgical standard for the treatment of hydrocephalus today.[68]

HYDROCEPHALUS

Hydrocephalus is a clinical state in which disruption in normal CSF dynamics occurs. The disruption may be in production, absorption, or mechanical obstruction to the flow of CSF and is usually associated with an increase of ventricular size. The changes in CSF dynamics may be caused by congenital brain malformations or by many disease processes occurring with in the ventricle, the brain parenchyma, or the subarachnoid spaces.

The causes of hydrocephalus are many:

In utero causes of hydrocephalus include aqueductal stenosis, spina bifida (Chiari malformation, myelomeningocele), and Dandy-Walker malformation. Encephaloceles, holoprosencephaly, intracranial hemorrhage or cerebral infarction, porencephalic cyst, vein of Galen aneurysms, congenital tumours (teratomas, ependymomas, and astrocytomas), infection, agenesis of the corpus callosum, and septo- optic dysplasia.

Major non-CNS associations include trisomy 13 and 18, achondroplasia, pulmonary and renal hypoplasia, transposition of the great vessels, endocardial cushion defects, hydronephrosis, esophageal atresia, omphalocele, and intestinal malrotation. Post hemorrhagic hydrocephalus is common in premature neonates.

Causes of childhood hydrocephalus include mainly congenital aqueductal stenosis and primary CNS tumours like astrocytomas, medulloblastomas, gangliogliomas, craniopharyngiomas, and ependymomas. Other causes include

bacterial meningitis, trauma, and other congenital abnormalities.

Acquired hydrocephalus in adults has many causes. Tumour related hydrocephalus is most common with posterior fossa tumours, suprasellar tumours, and third ventricle and pineal region tumours. Vascular causes include Galen vein arteriovenous malformations, giant midline aneurysms, and subarachnoid hemorrhages.

In a representative series of 107 children, the causes for hydrocephalus were myelomeningocele (54%), idiopathic (13%), posthemorrhagic (13%), postmeningitic (10%), aqueductal stenosis (7.5%), hydranencephaly (0.1%) and congenital toxoplasmosis (0.1%).[1]

DIAGNOSIS AND CLINICAL FEATURES

The identification of hydrocephalus begins with the clinical suspicion based on history and physical examination. In infants the signs include enlarging head size, split cranial sutures, sunset appearance, inability to gaze upward, papillary abnormalities, convergence abnormalities, and nystagmus, and scalp vein enlargement, nuchal rigidity. In children with chronic hydrocephalus, the complaints are more likely to relate to poor school performance and a decreased energy level.[1]

Imaging techniques often determine the etiology and the extent of hydrocephalus. Computerized tomography (CT) is the commonest imaging procedure used to detect hydrocephalus. Ventricular size can be identified with CT, as can causative intracranial lesions. Magnetic resonance imaging (MRI) has added to the accuracy of diagnosis in hydrocephalus, identifying sites of obstruction as well as small lesions not seen on CT.

VENTRICULOPERITONEAL SHUNT PROCEDURE

Two body cavities must be entered during the procedure, the ventricle and the peritoneum. The ventricular catheter is usually placed in the anterior horn of the lateral ventricle, as close to the foramen of Monro as possible. The site of entry of the distal peritoneal catheter into the peritoneal cavity is as high on the abdomen as possible (shortest distance possible from ventricle to peritoneum), subxiphoid or subcostal usually just over the liver are the most commonly used approaches for exposure of the peritoneum during VP shunt insertion.

The ventricular catheter, valve and peritoneal tubing are all foreign bodies that can harbor bacteria introduced by contamination at the time of surgery or by seeding of organisms introduced into the bloodstream by a variety of surgical and non-surgical mechanisms unrelated to the VP shunt insertion procedure.

A subcutaneous tunnel is made from the scalp to the abdominal incision by use of a blunt salmon passer. The tunnel is created by pushing a hollow metal tube down through the soft tissues under the skin above the fascia of the neck and chest muscles. The distal catheter is passed through the subcutaneous tunnel. A special instrument set has been recently designed to assemble shunts with “no-touch” technique.

The dura is then opened with a crucial incision. Using the landmarks mentioned earlier, the ventricle is cannulated with the proximal catheter on a stylet. The stylet is withdrawn as soon as the ventricle is entered, and the catheter is pushed in about 1cm more than the distance of the parietal burr hole from the coronal suture.

The CSF specimen is obtained from the distal catheter, and good flow is confirmed. At this stage, the posterior rectus sheath is opened, the peritoneum is identified, and the distal catheter is placed intraperitoneally under direct vision.

About 90-120 cm of tubing is left in the abdomen, which may be sufficient for life in some patients. The anterior rectus sheath is closed with absorbable suture, and subcuticular abdominal sutures are placed for good cosmesis. The scalp wound is closed with absorbable galeal sutures and running nylon on the skin.

SHUNT REVISION

Revision (reoperation for removal or adjustment of one or all components of VP shunt system) is one of the most common procedures done by neurosurgeons.

Recovery: The abdominal and scalp incisions heal within seven days. Patients can return to work with in two weeks of shunt insertion.

INDICATIONS AND CONTRAINDICATIONS FOR CSF SHUNT INSERTION

Generally hydrocephalus should be treated if it is progressive, even if it is asymptomatic, and it should be treated if it is symptomatic, even if the symptoms are subtle or atypical.

Indications of shunt treatment can be brought into focus by examining the contraindications which include: Ventriculitis, other inadequately treated infections, acute intraventricular haemorrhage, hydrocephalus due to treatable obstructive lesions futility on the basis of extreme brain pathology (i.e., hydranencephaly), asymptomatic, nonprogressive hydrocephalus and ventriculomegaly without elevated intracranial pressure.

SHUNT COMPLICATIONS

Following ventricular shunting a wide variety of complications occur, which

include: i) Infections, and wound complications, ii) Proximal and distal shunt obstruction leading to shunt malfunction, iii) Seizures, iv) Extra cerebral fluid collections, v) Subdural hematomas, vi) Spontaneous pnemocephalus, vii) The overdrainage syndrome, viii) Ascites, ix) Bowel perforation, x) The slit ventricular syndrome.

EPIDEMIOLOGY

Infection is unfortunately a relatively frequent complication of shunt placement, with most authorities quoting a figure of approximately 7 to 10 percent per procedure, which contribute significantly to excess morbidity and mortality.[74]

While the North American infection rate averages nearly 8-10%, published infection rates for VP shunt infection below 1% have been reported.[69] Postoperative infections of CSF shunt infections occur in 5-27% of cases in most neurosurgical units throughout the world.[51, 85]

In a review 612 procedures performed on 306 patients, infection occurred following 46 of the procedures with an infection rate of 7.5 per procedure involving 39 patients. The infection rate per child was 12.7%.[24]

From 1986 to 1989 273 ventriculoperitoneal shunts were performed, out of which twenty eight infectious episodes (8%) occurred in 25 patients during a median follow-up time of 20 months.[49]

An infection rate of 4% occurred in a study done in Department of neurosurgery, Indianapolis from 1980-1983 involving about 505 operations.[82]

PATHOGENESIS

Four mechanisms[10] have been postulated by which shunts become infected.

a) colonization at the time of surgery,
b) retrograde infection from the distal end,
c) wound or skin breakdown
d) hematogenous seeding which is a possible occurrence but not a frequent one.

Colonisation at the time of surgery is probably the most frequent cause of shunt infections. This is suggested in particular by the timing of most shunt infections and by the organisms isolated from these infections. At operation, direct exposure and handling of the shunt can allow bacterial contamination.

Most shunt infections occur with in 2 months of shunt insertion. 80% will present with in three months and 90% within six months.[33]

Clustering of approximately 70% of infections within 2 months postoperative period suggests that colonisation during shunt placement is an important initiating event.[31]

Most often the infection results from colonization of the shunt device by normally nonpathogenic normal skin flora at the time of surgery.[6, 82]

Retrograde infection includes infection of the distal end by transluminal passage of bacteria without perforation, delayed perforation of the bowel by the distal catheter. It is the most likely mechanism involving infection of the externalized devices. Organisms may track from the exit site alongside the device or, in case of devices that drain CSF, gain entry into fluid column and ascend into CNS.

Breakdown of the surgical wounds or the skin overlying the shunt hardware allows direct access of microbes to the shunt. This may be surgically acquired, when

the incision fails to heal for intrinsic causes like malnutrition, improper closure or because an impaired patient picks at or scratches open the wound. Direct extension from adjacent infected tissues like tracheostomy wounds, an intravenous access site, severe skin infections like acne, boils, cellulitis.[53]

In a prospective study by Duhaime *et al.*[21] on distribution of bacteria in the operating room environment and its relation to ventricular shunt infections, bacteria most often associated with shunt infections are airborne in the operating room, rather than originating from the patient's skin, and are distributed in the highest concentration near the surgical team.

The mere presence of a foreign body can markedly increase the pathogenic potential of an organism of otherwise low virulence.[30,54] The foreign material can directly interfere with natural host defense mechanisms, such as chemotaxis, phagocytosis, or the inflammatory process.[88,98]

MECHANISM OF SHUNT COLONISATION

- Attachment of bacteria to the shunt is the initial step in colonization and infection.
- Implanted shunt is almost immediately coated with glycoproteinaceous film, which is derived from serum and extracellular matrix proteins.[34]
- This provides potential receptor sites for bacterial or tissue adhesion.
- If tissue cells are the first to adhere to and integerate within the shunt surface, then the surface resists bacterial colonisation.
- Bacterial adhesion and multiplication produces a biofilm on the surface of the shunt which will eventually produce a clinical shunt infection. This biofilm

reduces the penetration of antibiotics and prevents elimination of bacteria, with antibiotic treatment alone. *S. epidermidis* produces an extracellular glycocalyx slime (composed mainly of a mixture of polysaccharides and proteins) and therefore bind well to a shunt and may account for their likelihood in presenting with true shunt infection.[10]

Bacterial adherence to cerebrospinal fluid (CSF) shunts was analyzed *in vivo* and *in vitro*. Scanning electron micrographs (SEM's) of catheters removed from pediatric patients with shunts infected by *Staphylococcus aureus* or *Klebsiella pneumoniae* revealed numerous bacterial cells and microcolonies, leukocytes, and erythrocytes attached to the CSF catheters' inner walls, as well as the existence of surface irregularities, such as fissures, rugosities, and holes. Permeability analyses and SEM's demonstrated that catheters develop physical alterations over the period of implantation. Different bacterial strains presented a different in vitro adherence to CSF shunts, suggesting that this attachment may be affected by specific properties of the outer structures of each strain.[37]

The attachment of microbial pathogens to CSF shunts seems to contribute to the persistence of bacterial cells within a catheter and the onset of recurrent shunt infection. This study demonstrated that some bacteria can remain attached within shunts *in vitro* despite a CSF flow at rates up to 200 times higher than those normally demonstrated *in vivo*. Furthermore, surface irregularities found throughout this study may help to anchor and hide bacterial microcolonies. Based on these findings, it seems advisable to remove an infected shunt and to replace it with a new one after proper antimicrobial therapy, in order to prevent recurrent infections.[37]

There is recent evidence to suggest that the adherence capacity of *Klebsiella pneumoniae* strains to CSF shunts and other smooth surfaces is genetically

correlated with the presence of some deoxyribonucleic acid (DNA) extra chromosomal elements. Abdominal complications and associated shunt infections suggested two potential modes of development: (1) descent of contaminated CSF from an infected shunt into the abdomen and the bacteria were predominantly Gram-positive, cutaneous microorganisms and (2) ascent of bacteria into the shunt from an abdominal source and the bacteria were mixed, Gram-negative intestinal microorganism.[77]

The most frequently isolated microorganisms are of *Staphylococcus* species including Staphylococcus *epidermidis* and *Staphylococcus aureus*. Furthermore increases in polymicrobial, Gram-negative bacilli infections (*Escherichia coli, Klebsiella* species, *and Pseudomonas* species) are observed now-a-days. The remainder are due to *Streptococcus* species*, Enterococcus* species*,* anaerobes, yeast.[9, 10, 51, 73, and 87]

Organisms responsible for shunt infections in children have been consistent over time and from series to series. *Staphylococcus epidermidis* is the commonest, and more than 40 percent of the positive cultures with *Staphylococcus aureus* are approximately 20 percent. Gram-negative organisms are the next commonest group, with *Escherichia sp., Klebsiella sp., and Pseudomonas sp.* being the organisms specified. Various other Gram-positive organisms, such as *Corynebacterium, Streptococcus faecalis, Micrococcus, H. influenzae, and Propionibacterium* also appear. Multiple organisms were presenting 30.5% of shunt infections in Odio and colleagues' series but in only 10% in Schoenbaum and colleagues' series. The source of organisms remains unclear; only 20% in one series were identical to skin organisms in those patients, suggesting that perioperative contamination from skin may not be the only etiologic mechanism.[1]

In a review of 35 CSF shunt infections in 32 patients , causative organisms included *Staphylococcus epidermidis* in twenty one, *Staphylococcus aureus* in seven, Gram-negative aerobic bacilli in seven, *diphtheroids* in five, *Streptococcus* species in four and *anaerobes* in three.[28]

In a review on Gram-negative bacilli (GNB) shunt infections treated at Children's Memorial Hospital from January 1986 to January 1990*, Escherichia* was isolated in 52% of cases, *Klebsiella pneumonia* from 22% and mixed GNB from 13% of cases.[86]

Morbidity and mortality rate are high in Gram-negative infections.[24, 81]

Clinical significance of slime production in ventriculoperitoneal shunt infections caused by Coagulase- negative *staphylococci*

Coagulase-negative *Staphylococci* (CNST) are the most-common cause of ventriculoperitoneal shunt infections. Some of these strains produce a slime-like substance. In a review of 19 episodes of ventriculoperitoneal shunt infections due to CNST in 17 patients, eleven episodes of infection were caused by slime-producing CNST and eight by non-slime-producing CNST. Shunt obstruction and abdominal pain occurred more frequently when infectious episodes were due to slime-producing CNST than to non-slime-producing CNST. Despite appropriate antimicrobial therapy, the mean duration of fever was longer and the failure to eradicate the infecting organisms was more frequent when the infectious episodes were due to slime-producing CNST than to non-slime-producing CNST.[20]

RISK FACTORS

The various risk factors of shunt infection as described by Stephen J. Haines[87] are

1. Young age[33, 72, 74]
2. Infection, disruption or poor condition of patient.[25]
3. concomitant systemic infection at time of shunting[15]
4. Postoperative wound dehiscence[61, 74]
5. Prolonged operating time[27]
6. Cause of hydrocephalus (Myelomeningocele > others) [40, 48, 56]
7. Limited surgeon experience with cerebrospinal shunts[89]
8. Shunt revision (versus initial shunt) [92]
9. Shunt surgery done late in day[33, 74]
10. Increased number of people in operating room[38]
11. Ventricular catheter revision[74]

Meirovitch *et al*.[58] had quoted in their work on CSF shunt infections in children that age younger than 3 years, previously infected shunt ,surgery to revise the infected shunt, patients with multiple revision, underlying myelomeningocele and meningitis have a greater risk of infection than others.

Shunt infections may also be related to transient bacteremias, lowered immunologic competence of that particular patient and other poorly understood factors.[46]

Statistically significant relationships were found between shunt infection and the following factors:

1. Age infection was as 2.6 times more frequent before 6 months than after 1 year of age.
2. poor condition of the skin.
3. type of operation: the rate of infection was 8.4% in primary shunt insertions, 5% in shunt revisions, and 17.5% in reinsertions following shunt removal for infection.[74]
4. end of shunt requiring revision: an infection rate of 7.7% followed revision of the ventricular catheter alone, and 2.6% followed revision of the other end alone and[74]
5. postoperative wound dehiscence or scalp necrosis.[74]

Young age (less than 6 months) seems to represent the main risk factor, and this is related both to the immunologic deficiency and to the particular features of residential bacterial flora in this group. Increased risk of Gram-negative infections also exists in this population.[18]

In a study, done in division of Neurosurgery in University of Toronto, Canada, the authors prospectively analyzed perioperative risk factors for CSF shunt infection in a cohort of children. Between 1996 and 1999, 299 eligible patients underwent CSF shunt operations (insertions and revisions) that were observed by a research nurse at a tertiary care pediatric hospital. Several perioperative variables were recorded. All cases were followed postoperatively for 6 months to note any development of CSF shunt infection. Thirty-one patients (10.4%) experienced shunt infection. Three perioperative variables were significantly associated with an increased risk of shunt infection: 1) the presence of a postoperative CSF leak;

2) patient prematurity (< 40 weeks' gestation at the time of shunt surgery), and 3) the number of times the shunt system was inadvertently exposed to breached surgical gloves.[50]

A trend showing a higher risk for shunt infections operation time was noticed in a study with an infection rate of 13.6% for an operation lasting more than 90 minutes and 5.2% for procedures of less than 30 minutes duration.[49]

CLINICL FEATURES

Clinical manifestations of shunt infections are often non specific and fever is the only consistent finding. Therefore a high index of suspicion and low threshold for diagnostic evaluation are indicated.[31] In many cases usual physical findings of meningitis may be absent with low grade temperature, shunt malfunction, wound infection as the only finding.

Shunt malfunction is being the least recognized symptom of shunt infection and studies show that shunt malfunction may be more specific to infection than heretofore believed. The symptoms of shunt malfunction are the same as seen with the initial hydrocephalus, with additional shunt specific findings such as fluid around the shunt, abdominal pain, or distention and symptoms referable to infection may be seen. In addition 23-65% percent shunt infections present as shunt malfunction.[93]

Shunt infection is suspected when there is unexplained fever in a shunted patient. Fever is present in 50% of shunt infections. There may be concomitant signs of shunt malfunction if obstruction occurs secondary to occlusion of a ventricular catheter or valve with infected material or to the development of peritoneal loculations. Non specific symptoms of raised intracranial pressure include headache,

nausea, vomiting, altered intellectual performance, seizures, ataxia and altered level of consciousness.[52]

In a retrospective review of 68 shunt infections in 61 children in Cardinal Glennon, Children's Hospital, USA[94] the presenting symptoms included fever (26%), abdominal pain (19%), wound changes (22%), and indicators of shunt malfunction (33%).

SIGNS

Bulging anterior fontanelle, raised blood pressure, bradycardia, paralysis of upward gaze, meningismus occurs in 15-25%. Wound may have cellulitis or dehiscence. There may be local signs of infection such as redness along the shunt tract or tender subcutaneous collections along or adjacent to the tubing. Peritoneal signs include abdominal tenderness with or without guarding, encystment of catheter with a palpable abdominal mass, or decreased absorption with ascites. Bacteremia is unusual unless the distal end is placed in venous space.[52]

DIAGNOSIS

Shunt infections are not uncommon and they are highly variable in presentation. Therefore, an important attitude in dealing with shunts is to have a high degree of suspicion for infection. In all cases, the correlation of the clinical situation, symptoms, laboratory findings, and cultures must be made to diagnose a shunt infection.

There are several diagnostic tests that may be obtained in an attempt to define a shunt infection. Blood counts, abdominal ultrasounds, and computerized tomographic (CT) scans of the head and abdomen are non-specific that would indirectly indicate infection.

BLOOD

i) Complete Blood Count- Where as one-third of patients with shunt infections exhibit a WBC count greater than 20,000 up to one-quarter will have no elevation in the count.[28, 80]

ii) Culture: When VP shunts are infected blood cultures are almost always negative, presumably due to lack of direct access of organisms to the blood stream.[50]

CT SCANS

Computerised tomography (CT) scans of head or abdomen show evidence of shunt dysfunction, an indirect indication of some infections.

X-ray shunt series may detect breaks or links in shunt tubing.

ULTRASOUND

Ultrasound abdomen can identify CSF loculations.

CSF ANALYSIS

CSF is sent for
- i) Biochemical analysis (glucose and protein, Pandy's test for globulin)
- ii) Cell counts - Total and differential counts
- iii) Gram stain
- iv) Culture.

A high WBC count in the CSF is highly correlated with the presence of infection but infection may still be present in spite of normal counts.[64, 80]

CSF protein and glucose often normal.[50]

Gram stain may reveal organisms but a negative Gram stain similarly does not exclude an infection with any degree of certainity.[95]

Once the suspicion of shunt infection is raised, the diagnosis must be made by sampling the CSF or the shunt apparatus**.**

Direct culturing of the shunt or any fluid in contact with it is the most accurate diagnostic test for infection.[28, 30, 64, 66]

The definitive diagnosis is made by recovery of the organisms in culture.

WOUND CULTURE: In 18-23% of shunt infections associated with wound infections, the diagnosis is made easy.

IMMULOCGIC EVALUATIONS

Evaluation of antibody titres to *S. epidermidis*, raised C-reactive protein levels and depressed complement levels can be used to confirm the diagnosis of shunt infection.[5]

MANAGEMENT

PREVENTION OF CSF SHUNT INFECTIONS

Given the significant cost, morbidity, and the occasional mortality associated with these infections and their treatment, effective treatment would be highly beneficial.

Alterations in the hardware, changes in operating techniques, as well as prophylactic use of antibiotics have been suggested.

Incorporation of antibiotics into the polymers used in shunt hardware has been attempted.[4, 6] The goal is for a relatively slow release of antibiotics from the compound during early postoperative period, thus preventing the establishment of infection.

Attention to operative techniques used during shunt surgery can also result in a decline in the rate of infection, either by reducing the potential for inoculating organisms or by reducing the size of the inoculum. Methods of skin preparation that reduce the total number of bacteria and that maintain that reduction (i.e., long acting iodinated compounds) would accomplish this.[6,47] Exclusion of skin from the operative field may have the same effect.

The results from the large number of studies on prophylactic use of antibiotics are less clear.

Some studies reveal a three-to-five-fold reduction in infection with the use of prophylactic antibiotics.[11, 35, 96]

Others have interpreted from their results that there is no benefit from antibiotic prophylaxis.[38, 79]

Meta analysis has been applied to the various studies of prophylactic antibiotic usage in shunt surgery.

It appears that prophylactic antibiotic use does reduce the risk of infection in shunt surgery. The greatest risk reduction occurs in those groups with a relatively high baseline rate of infection, perhaps>12%. A much smaller benefit is still likely at low rates of infection (5%).[39]

TREATMENT OF CSF SHUNT INFECTIONS

Three main goals in the treatment of any CNS prosthetic device infection are: a) minimizing the mortality and morbidity of the infection and its treatment; b) maintaining a functioning device if it is still needed; c) resolving the infection.

The different treatment modalities of shunt infection are:

1) Medical (antibiotic) treatment alone.
2) Shunt removal with immediate replacement.
3) Shunt removal with delayed replacement.

Externalization of the shunt (or installation of external ventricular drainage (EVD) with antibiotic therapy.

Medical Therapy Alone

Early in the experience of paediatric neurosurgeons, a CSF shunt infection was treated only with antibiotics, such as those for any systemic infection. The combination of poor antibiotic penetration, development of secondary bacterial resistance and bacterial colonization of the shunt material can result in high failure rate, followed by relapse. Such treatment is usually reserved for circumstances in which the clinician is unsure of the diagnosis and in which the shunt is still functioning.

Drugs very effective are vancomycin, nafficillin, rifampin, oxacillin, linezolid in case Gram positive organisms where as aminoglycosides, cephalosporins, polymixin B, meropemam are found effective against Gram-negative organisms.[29, 36, 45]

In case of fungal infections any of the antifungals like amphotericin B, 5-flurocytosine, miconazole and fluconazole can be used.[10]

Shunt Removal with Immediate Replacement

Combining the removal of presumably colonized shunt hardware with immediate shunt placement might be expected to cause an improvement in the rate of successful treatment. This would remove the densely adherent bacteria that are otherwise protected from the antibiotic by their glycocalyx or slime. It would also allow the continued control of the hydrocephalus. Infact, when parenteral antibiotics are combined with this approach, roughly 75% of the infection can be cured.[10,89]

The failure and reinfection rates still remain quite significant with this technique. In addition there is possibility that the replaced hardware may become colonized by the bacteria under treatment[48]

Shunt removal with delayed placement

When possible, the treatment of CSF shunt infections is complete removal, aggressive treatment with antibiotics, and placement of a new shunt after the CSF is completely negative on cultures for microorganisms. Delayed replacement does seem to improve the cure rate but it may also be associated with increased morbidity and mortality.[28, 93]

External Ventricular Drainage with antibiotic therapy

The final category of treatment is the procedure most commonly used in cases of shunt infection and appears to be the most effective treatment.[43,67, 80] It consisted of placing a sterile EVD system and removing the infected shunt, treating the patient with systemic (with or without intraventricular) antibiotics, and then removing the EVD and placing a new shunt. This method of treatment is probably the soundest in terms of removing the infected foreign body while continuing to treat the hydrocephalus and avoids the complications that might ensue with only shunt removal.[44, 45]

The most significant risk with external shunts is that of secondary infection.[10]

CSF SHUNTS – RESULTS

The simplest outcomes to analyze are patient survival and shunt survival.

Mortality rates from shunt infection have been reported as high as 35%, but rates from recent years are much lower.[46]

MATERIALS AND METHODS

This is a cross sectional study done involving 428 patients which included 404 patients who underwent primary ventriculoperitoneal shunt insertions during the study period and also 24 old cases of shunt insertion who underwent revision. During the study period 120 cases of malfunction occurred.

Place of study

Institute of Microbiology, and Department of Neurosurgery, Madras Medical College.

Period of study

MAY 2004 - OCTOBER 2005.

Study Group

120 patients both male and female of age group ranging from 0-60 were chosen. Patients with hydrocephalus of various etiology who had already undergone shunt surgery now presenting with signs and symptoms suggestive of shunt infection such as fever, seizures, headache, disturbed consciousness, vomiting, abdominal signs and other signs of shunt malfunction now undergoing shunt removal or shunt revision without removal of the shunt were studied.

Two groups were studied:

GROUP 1: This included 96 patients with shunt malfunction for whom shunt insertions were done during the study period. i.e. from 404 cases.

GROUP 2: This included 24 patients with shunt malfunction for whom shunt insertions and revisions were already done before the study period.

Data regarding patients were collected as per mentioned in the proforma.

COLLECTION AND TRANSPORT OF SPECIMENS

The samples collected were

1. CSF
2. CSF Shunt (Catheter) tip.
3. Blood.
4. Wound swab in cases of associated wound infection.
5. Swabs from the nose, ear, and skin around umbilicus.
6. Swabs from the environment- in the neurosurgery operation theatre as well as from the neurosurgical ward.

CSF AND CSF SHUNT TIP

1. CSF was obtained during surgery or by means of lumbar puncture or from the reservoir site like the external ventricular drainage, following sterile precautions.

2. CSF Shunt tip was obtained during surgery.

CSF and CSF shunt tip were collected in a sterile screw-capped containers.

Three separate tubes of CSF fluid were collected-

i) Tube 1 for cell counts - Total and differential counts.

ii) Tube 2 for Gram stain and culture.

iii) Tube 3 for biochemical analysis like protein, glucose and Pandy's test for globulin.

CSF was hand-delivered immediately to the laboratory. Specimens was not be refrigerated. If not rapidly processed, CSF was incubated at 37ºC or left at room temperature.

BLOOD[17]

Patient blood was obtained by aseptic venipuncture. In case of adults, about 10-20 ml was collected. In case of infants and children only 1-5 ml was collected. Blood was directly inoculated into Brain - Heart Infusion broth, in a ratio of about 1:5 to dilute any inherent antibiotics or other antibacterial substances.

WOUND SWABS

Two swabs with adequate material, taken from the depth of the wound, were collected-one for Gram staining and the other for the culture.

PROCESSING OF CSF AND CSF SHUNT TIP

This included microbiological, biochemical testing and cell count.

1. CELL COUNTING [17]

The leucocytes in the CSF were counted by microscopical observation of well mixed, uncentrifuged fluid in a slide counting chamber. The relative number of polymorphs and lymphocytes were noted and the number of erythrocytes in specimen contaminated with blood.

COUNTING CHAMBER

The cell count was performed in a modified Fuchs-Rosenthal slide chamber, with a film depth of 0.2 mm between the counting surface of the slide and the overlying cover-slip.

Normal CSF contains only 0-5 leucocytes/mm^3 mainly lymphocytes.

In purulent meningitis there are usually 100-3000 leucocytes/mm^3.

DIFFERENTIAL LEUCOCYTE COUNT

This was done using methylene blue staining.

BIOCHEMICAL ANALYSIS [62]

Biochemical tests included measurement of glucose, protein, and globulin. The supernatant fluid from centrifuged CSF or uncentrifuged CSF if the sample was clear was used.

Measurement of glucose

Specimens were transported to the laboratory without delay for further analysis. Total glucose in CSF was measured using a colorimetric technique.

Normal CSF glucose: This is about half to two thirds that found in blood i.e. 2.5-4.0 mmol/l (45-72mg %).

Measurement of CSF total protein and globulin

Total protein in CSF was measured using a colorimetric technique.

Total CSF protein is normally 0.15-0.40 g/l (15-40mg%).

Pandy's test done that detected CSF globulin which may be increased in all forms of meningitis.

MICROBIOLOGICAL ANALYSIS

MACROSCOPIC EXAMINATION

The specimen was examined with the naked eye and the following data noted: (1) whether clear, turbid, cloudy, or purulent or blood stained.

CSF samples were centrifuged at 1500 g for atleast 15 minutes.

A purulent fluid was not centrifuged.

DIRECT GRAM STAIN [7]

In CSF cells and bacteria may be scanty. A thick film was made within an area of about 10mm diameter, so that the area to be searched was clearly defined with a glass marking pencil. The smear was fixed with 95% methanol for one minute. Methanol fixation would preserve the morphology of bacteria as well as the host cells. The smear was then air dried and stained. The presence of host cells, morphologies, Gram reactions and relative amounts of bacterial cells was identified by the Direct Gram stain (Appendix xi).

CULTURE

Immediately after centrifugation of the CSF and the removal of some of the deposit for Gram film, the remainder of the deposit is seeded on to the culture media. Shunt tip was also used for culturing on to the media by rolling the shunt tip on the surface of the media and transferring to a liquid medium using sterile forceps.

PROCESSING AND FURTHER IDENTIFICATION OF AEROBIC BACTERIA [7,62]

For recovery of non fastidious organisms, the sample was plated on to Mac Conkey agar, nutrient agar, and was incubated at 37º c overnight for 24-48 hrs. For recovery of fastidious organisms, the sample was plated on to chocolate agar plate/ blood agar pate and incubated at 37ºC in 5%-10% carbon dioxide in a candle jar for atleast 72 hours.

The plates were examined for the growth at 24 hours. If growth was observed, colony morphology and Gram stain morphology were studied. If no growth was observed, the plates were further incubated for the next 48 hours.

The colonies were then further processed and identified by means of Gram staining, motility, and various biochemical reactions like catalase, oxidase, indole, citrate, urease, slide and tube coagulase, triple sugar iron agar test, phenylalanine deaminase test, modified Hugh and Leifson O/F test, mannitol motility, nitrate reduction, methyl red, Voges-Proskauer, bile esculin agar test, fermentation of sugars like glucose, sucrose, lactose, maltose, mannitol, mannose, ribose by standard microbiological techniques as recommended by NCCLS guidelines.

PROCESSING AND FURTHER IDENTIFICATION OF ANAEROBIC BACTERIA [7,62]

The sample was immediately inoculated into semisolid brain-heart infusion broth, and Robertson cooked meat broth enriched with vitamin k_1 (1 μg/ml) and haemin (5 μg/ml). The broths are overlayed with liquid paraffin and paraffin wax for providing anaerobic condition.

The broths were observed for the appearance of growth, gas production, and odour. The sample was inoculated on the CDC Anaerobic Blood Agar supplemented with vitamin k_1 (1 μg/ml) and haemin (5 μg/ml), Brain heart infusion agar supplemented with 0.5% yeast extract and Bile esculin agar (20%), from the broths at the bench and immediately incubated in anaerobic jar. Simultaneously plating was done in one aerobic blood agar which was incubated aerobically.

Incubation was done in McIntosh Fildes jar with the inlet and outlet closed and in 37ºC for 48 hours. Gas pack was used as the reducing agent with palladium as the catalyst. A test tube containing a few milliliters of methylene blue-sodium bicarbonate-glucose mixture was placed in the jars as the indicator.

The plates were then removed and observed for the colony characteristics, hemolysis and pigmentation. Gram stained smears of colonies from the plates were examined. Then subculturing simultaneously each colony type into an anaerobic plate as well as into an aerobic plate for aerotolerance tests were done to differentiate obligate anaerobes from facultative anaerobes.

PROCESSING AND IDENTIFICATION OF FUNGUS [42]

DIRECT MICROSCOPIC EXAMINATION USING WET MOUNT:

A drop from centrifuged CSF sample was put on the slide and covered with a coverslip and viewed under high power objective for any fungal elements like hyphae, pseudo hyphae and yeast cells.

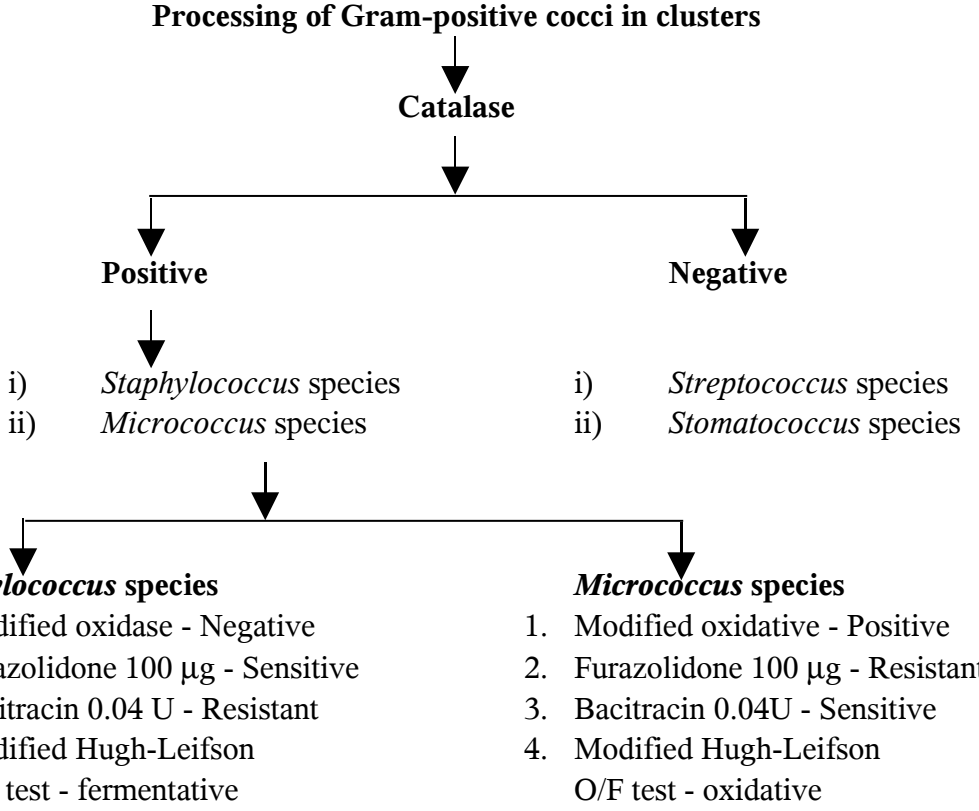
For CSF fungal cultures, two drops well mixed sediment was inoculated into Sabouraud dextrose agar and was incubated in air at 30ºC for 4 weeks. The colonies were further identified by Gram staining and Germ tube test (Appendix xii).

PROCESSING OF BLOOD [17]

Brain-heart infusion broth was used as the primary culture medium for blood and subcultures were made into BAP, MAC and NA plates after 48 hours or on signs of growth like turbidity, lysis, pellicle & clot formation. The plates were then examined for the growth. The colonies were then identified by Gram stain and various biochemical reactions and tested for its susceptibility to various antimicrobial agents.

PROCESSING OF SWABS [17]

For swabs collected from the wound as well as the environment, Direct Gram stain is performed and cultured on to the MacConkey agar, Blood agar and nutrient agar plates. The organisms were isolated and identified and tested for its antimicrobial susceptibility.



IDENTIFICATION OF CLINICALLY SIGNIFICANT *STAPHYLOCOCCAL* SPECIES AND SUBSPECIES[23]

This is done based on the following tests.

Organisms	Slide coagulase	Tube coagulase	Urease	Nitrate reduction	Polymixin B 300U	Bacitracin 10 U	D-mannitol	D-mannose	Fructose	Sucrose	Maltose	Lactose	D-trehalose	Ribose
S aureus	+	+	V	+	R	S	+	+	+	+	+	+	+	+
S.epidermidis	-	-	+	+	R	S	-	+[sl]	+	+	+	V	-	V
S.haemolyticus	-	-	-	+	S	R	V	-	V	+	+	V	+	V
S.hominis	-	-	+	V	S	S	-	-	+	+[sl]	+	V	V	-
S.capitis subsp. *capitis*	-	-	-	V	S	S	+	+	+	+[sl]	-	-	-	-
S.capitis subsp. *urealyticus.*	-	-	+	+	NA	NA	+	+	+	+	+	V[sl]	-	-
S. lugdunensis	+	-	V	+	S/R	S/R	-	+	+	+	+	+	+	-
S. warneri	-	-	+	V	S	S	V	V	+	+	+[sl]	V	+	V
S. saprophyticus	-	-	+	-	S	S/R	V	-	+	+	+	V	+	-
S. simulas	-	-	+	+	S	S	+	V	+	+	+[sl]	+	V	V

+ – ≥ 90% strains positive, - – ≥ 90% strains negative, +[sl] - ≥ 90% strains positive, reaction slow, V - 11-89% of strains positive

DEMONSTRATION OF SLIME PRODUCTION BY *STAPHYLOCOCCUS EPIDERMIDIS* BY THE TUBE TEST METHOD [23]

The test organism was inoculated in tryptic soy broth contained in a standard glass culture tube and incubated overnight at 35ºC in ambient air. After 18-24 hour incubation, the broth is gently poured off, and the tube was examined for the presence of a film lining the inner surface of the tube which was indicative of adherent growth. The absence of a film or the mere presence of a ring at the liquid-air interface was interpreted as negative. The contents of the tubes were removed and the tube was stained with safranin to demonstrate the adherent growth. (Christensen *et al* [16], Ishak *et al* [41])

PHAGE TYPING FOR *STAPHYLOCOCCUS AUREUS*

Phage typing was done for the all *Staphylococcus aureus* isolates at Moulana Azad Medical College, New Delhi.

DETECTION OF ANTIMICROBIAL SUSCEPTIBILITY PATTERNS

Antimicrobial susceptibility pattern was done in Mueller- Hinton Agar plate by Kirby-Bauer Disc diffusion method as recommended by NCCLS (Appendix xiii).

Test inoculum- 0.5 McFarland lawn culture.

Incubation-37 ºC for 16-18 hrs.

Control strains:

Staph aureus-ATCC 25923

E. coli-ATCC-25922

Pseudomonas aeroginosa-ATCC 27853.

The antibiotics used for Gram-positive cocci were

Penicillin (10 U), ampicillin (10 µg), oxacillin (1 µg), co-trimaxozole (25 µg), chloramphenicol (30 µg), gentamycin (10 µg), ofloxacin (5 µg), amikacin (30 µg), cefotaxime (30 µg) and vancomycin (30 µg).

The antibiotics used for Gram negative bacilli were ampicillin (10 mg), co-trimaxozole (25 µg), chloramphenicol (30 µg), gentamycin (10 µg), ofloxacin (5 µg), amikacin (30 µg), ceftazidime (30 µg), cefaperazone (75 µg), cefaperazone-sulbactam (75 µg / 30 µg) and imipenam (10µg).

The diameters of the zones of inhibition were interpreted according to NCCLS standards for each organism.

DETECTION OF BETA-LACTAMASE PRODUCTION[59]

All the Gram-positive cocci were tested for β-lactamase production by iodometric method. It is based on the principle that penicilloic acid produced by the hydrolysis of Benzylpenicillin by beta-lactamases reduces iodine and reverse the formation of the blue colour when the later complexes with starch.

IODOMETRIC METHOD

REQUIREMENTS

i) 1% soluble starch solution prepared by dissolving the starch at100^{o}C

ii) Iodine reagent consisting of 2.03g iodine and 5.32 g potassium iodide in 100 ml distilled water.

PROCEDURE

From an overnight incubation culture of the test organism, a heavy suspension was made (containing 10^9 colony-forming units/ml) in 100mm sodium phosphate buffer at pH 7.3 containing penicillin at 6 g/litre. A negative control was put up without the organisms. An organism known to produce beta-lactamase was put as a positive control. The test and the control organisms were inoculated into the wells of a microtitre plate. After incubation for 1 hr at 37°C, two drops of freshly prepared 1% soluble starch solution were added to each well. A drop of iodine reagent was then added. If blue colour was lost within 10 minutes, the presence of beta-lactamase was inferred. If, however, the blue colour persisted, the culture was considered to be beta-lactamase negative.

DETECTION OF EXTENDED-SPECTRUM BETA-LACTAMASES (ESBLs)

12 isolates showing a zone of inhibition<22 mm for ceftazidime were tested for ESBL production as per NCCLS criteria. Two methods were adapted for detection of ESBLs using standard control strains.

1. COMBINED DISC METHOD [32]

A combined disc method using cefaperazone (75µg) and cefaperazone-sulbactam (75µg/30µg) performed for phenotypic confirmation of ESBL production, as recommended by the latest guidelines of NCCLS. Organism was considered as ESBL producer if there was a more than 5 mm increase in zone diameter of cefaperazone-sulbactam disc and that of cefaperazone disc alone.

2. DOUBLE DISC SYNERGY TEST [59]

In this test a lawn of the test strain on Mueller-Hinton agar plate was exposed to discs of ceftazidime (30μg) and augmentin (20 μg amoxycillin/10 μg clavulanic acid) arranged in pairs. The discs are arranged so that the distance between them was approximately twice the radius of the inhibition zone produced by the ceftazidime tested on its own. After overnight incubation, the test strain was an ESBL producer if the inhibition zone around the ceftazidime disc was extended on the side nearest the augmentin disc.

SCREENING FOR Amp-C and ESBL PRODUCING ISOLATESUSING MODIFIED DOUBLE DISC SYNERGY TEST [84]

12 isolates with zone of inhibition <22mm for ceftazidime were tested. A 0.5 McFarland of test isolate was swabbed on Mueller-Hinton agar plates and disc of ceftazidime (30 μg) was placed adjacent to clavulanic acid (10 μg) and cefoxitin (30 μg) was placed at a distance of 20mm from each other. After incubation, an enhanced zone of inhibition between ceftazidime and clavulanic acid were interpreted as presumptive evidence for the presence of ESBL. Three isolates that showed reduced susceptibility to ceftazidime and cefoxitin were considered as screen positive and selected for detection of AmpC β-lactamase.

CONFIRMATORY TEST FOR AmpC β-LACTAMASES

AmpC DISC TEST [84]

A lawn culture of *E. coli* ATCC 25922 was prepared on Mueller-Hinton Agar plate. Sterile discs (6mm) were moistened with sterile saline and inoculated with several colonies of test organism. The inoculated disc was then placed beside a cefoxitin disc almost touching on the inoculated plate. The plates were incubated

overnight at 35ºC. A positive test appeared as flattening or indentation of the cefoxitin inhibition zone in the vicinity of the test disc. A negative test had an undistorted zone.

MINIMUM INHIBITORY CONCENTERATION(MIC) [59]

Minimum inhibitory concentration is the least amount of antimicrobial that will inhibit visible growth of an organism after overnight incubation

MIC was done for the drugs benzylpenicillin and ceftazidime by agar dilution method for penicillin resistant Gram-positive cocci and ceftazidime resistant Gram-negative bacilli respectively.

PROCEDURE

Media

19 ml of Mueller-Hinton agar is prepared in tubes, autoclaved and allowed to cool in a 50ºC water bath.

Antibiotic

i) Benzyl pencillin was dissolved in sterile water and then serial dilutions of the antibiotic from 0.25 mg/l to 128 mg/l were then made using Mueller-Hinton broth, at 10 times the final concentration of antibiotic required. One ml of the antibiotic solution is added to 9 ml of the medium. After adding the antibiotic the medium is mixed well, and poured into the Petri dish. A control plate containing the test medium without the antibiotic is prepared for each series of the dilution. After the plates have set, they were dried at 37ºC.

ii) In case of ceftazidime, the powder was dissolved in saturated $NaHCO_3$ and sterile water. Serial dilutions of the antibiotic were made from 2 mg/l to 256 mg/l similarly as mentioned above.

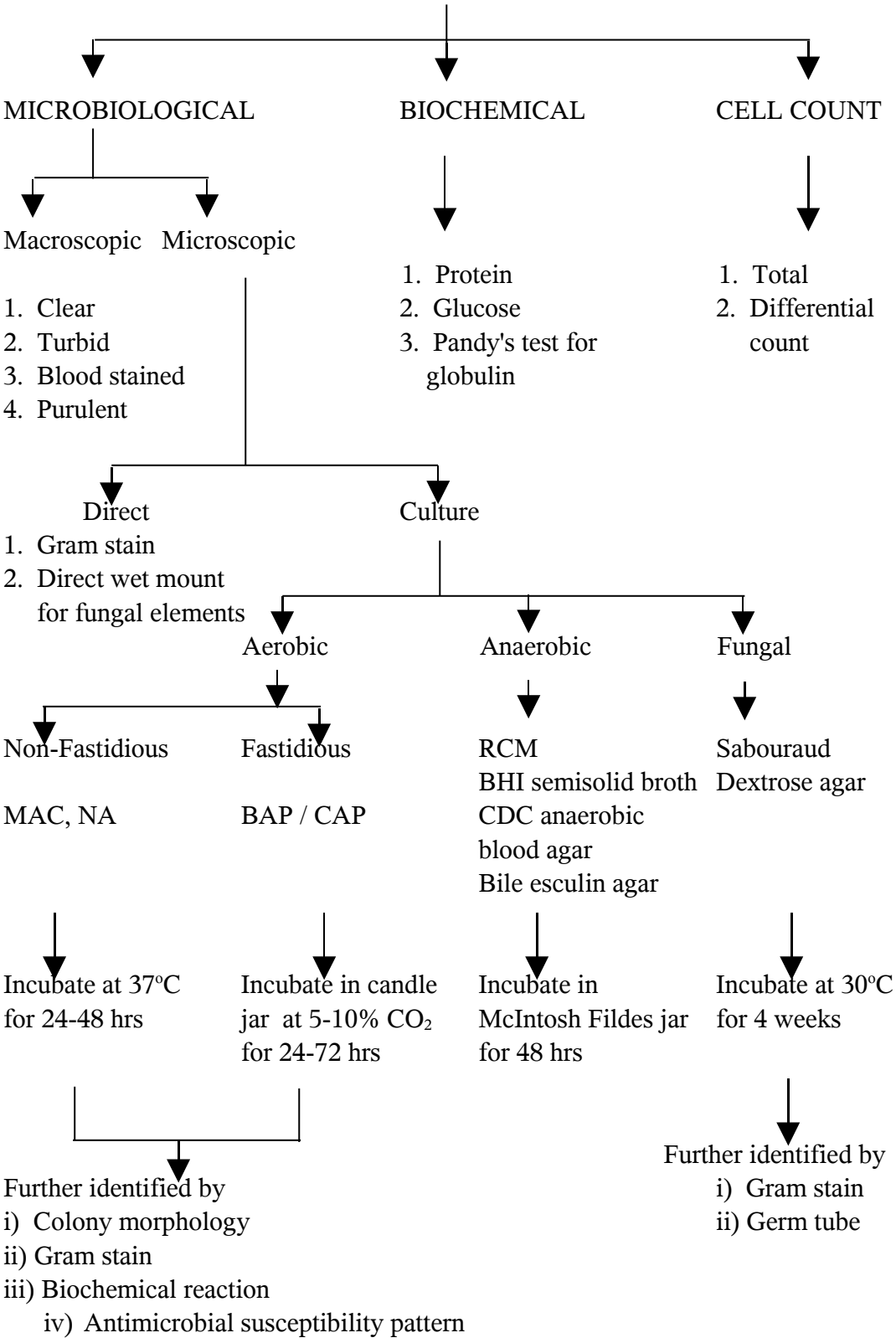
Test inoculum

The test strains were inoculated in peptone water and its turbidity adjusted to 0.5 McFarland standard to get a working inoculum of 10^7 cfu/ml. A micropipette was used to deliver 2 µl so that the final inoculum on the agar surface would be 10^4 cfu/ml.

Controls

Standard control strains were used in every batch of MIC tests.

PROCESSING OF CSF



OBSERVATION AND RESULTS

TABLE 1

SEX DISTRIBUTION

Sex	n = 428	Percentage
MALE	238	55.6%
FEMALE	190	44.4%

No significant predilection was observed between the sexes.

TABLE 2

AGE DISTRIBUTION

Age	n=428	Percentage
0-6 MONTHS	72	16.8
6-12 MONTHS	46	10.7
1-4 YEARS	45	10.5
5-8	31	7.2
9-12	26	6.1
13-16	28	6.5
17-20	39	9.1
21-24	23	5.4
24-28	25	5.8
29-32	26	6.1
33-36	19	4.4
37-40	14	3.3
41-44	11	2.6
45-48	7	1.6
49-52	6	1.4
53-56	5	1.2
57-60	5	1.2

Patients in the age group less than 16 were considered under the paediatric category-248(57.9%)

Patients in the age group more than 16 were considered under adult group-180 (42.1%)

TABLE 3

ETIOLOGY OF HYDROCEPHALUS NECESSIATING SHUNT

Reason for shunt	Children (n=248)	Adult (n=180)	Total (n=428)
Preceding meningitis	54 (21.8%)	51 (28.3%)	105 (24.5%)
CNS tumour	39 (15.7%)	90 (50%)	129 (30.1%)
Congenital malformations	135(54.4%)	-	135(31.5%)
1) Aqueductal stenosis	26 (10.5%)	-	26 (6.1%)
2) Dandy-walker syndrome	22 (10.5%)	-	22 (5.1%)
3) Myelomeningocele	14 (5.6%)	-	14 (3.3%)
Other congenital malformations	73 (29.4%)		73 (17.1%)
Idiopathic	15 (6%)	39 (21.7%)	54 (12.6%)
Subarachnoid haemorrhage	5 (2%)	-	5 (1.2%)

Space occupying lesions were observed in 50% of adults patients, where as in children congenital malformations were more common. Meningitis was observed as a precipitating factor in both categories.

TABLE 4

CLINICAL FEATURES OF PATIENTS

Clinical Features	Children (n=77)	Adult (n=43)	Total (n=120)
Fever	34	11	45(37.5%)
Seizures	29	9	38(31.7%)
Headache	42	24	66(55%)
Vomiting	53	26	79(65.8%)
Altered consciousness	31	21	52(18.3%)
Abdominal signs	12	10	22(18.3%)
Wound changes	7	9	16(13.3%)
Displaced shunt	9	7	16(13.3%)
CSF leak	8	4	12(10%)

Symptoms such as vomiting, headache, altered consciousness and fever were present in children and adults. Seizures were common in children.

TABLE 5

PATIENTS CATEGORY FOR THE STUDY

Study population	Total no	Cases selected	Culture positive cases
Primary VP shunt Insertions	404	96	36
Old cases with Multiple revisions (n=24)	24	24	5
TOTAL	**428**	**120**	**41**

404 patients were treated surgically for hydrocephalus during the study period of which 96 showed signs of shunt malfunction. 2 of them had dual episodes

of malfunction. Additional 24 patients who had undergone surgery previously and presented with malfunction were also included in the study. Out of 96 cases, 36 cases were proved culture positive with an infection rate of 8.9%. Two patients had recurrence of infection during the study period. In 24 cases with multiple revisions, the infection rate was 20.8% involving 5 patients.

TABLE 6

DURATION BETWEEN INSERTION OF SHUNT AND ONSET OF INFECTION IN PRIMARY SHUNT INSERTION CASES

Duration	Malfunction (n=96)	Infection (n=36)
0-1 MONTH	42 (43.8%)	23(63.9%)
1-2 MONTHS	23 (23.9%)	8 (22.2%)
2-3 MONTHS	18 (18.8%)	3(8.3%)
3-6 MONTHS	13 (13.3%)	2 (5.6%)

In 24 cases of malfunction, multiple revisions were done before the study period. All cases presented were more than six months duration.

About 63.9% infection presented with in one month, 86.1% presented with in 2 months and and 94.4% presented with in 3 months and the remaining presented with in 6 months. No case of infection was present beyond six months during the study period.

TABLE 7

AGE AS A RISK FACTOR

Age	n=428	No Infected	Percentage
0-6 MONTHS	72	13	18.1
6-12 MONTHS	46	5	8.7
1-4 YEARS	45	6	10.9
5-8	31	2	6.4
9-12	26	2	7.7
13-16	28	1	3.6
17-20	39	3	7.7
21-24	23	1	4.3
24-28	25	2	8
29-32	26	2	7.7
33-36	19	1	5.3
37-40	14	1	7.1
41-44	11	1	9.1
45-48	7	0	0
49-52	6	0	0
53-56	5	0	0
57-60	5	0	0

Age < 6 months was found to be a significant risk factor for shunt infection as 13 cases (18.1%) were within 6 months of age as compared to only < 11% in all other age groups.

TABLE 8

UNDERLYING CONDITION OF THE PATIENT AS A RISK FACTOR

Reason for shunt	Children (n=248)		Adult (n=180)		Total (n=428)	
	Total cases	Total Infected	Total cases	Total infected	Total Cases	Total infected
Preceding meningitis	54	11(20%)	51	3	105	14(13.3%)
CNS tumour	39	3(7%)	90	7	129	10(7.7%)
Congenital malformations			-			
1) Aqueductal stenosis	26	2(7.7%)	-		26	2(7.7%)
2) Dandy-walker syndrome	22	2(9.1%)	-	-	22	2(9.1%)
3) Myelomeningocele	14	3(21.4%)	-		14	3(21.4%)
Other congenital malformations	73	6(7.9%)	-		73	6(7.9%)
Idiopathic	15	1(6.7%)	39	1	54	2(3.7%)
Subarachnoid haemorrhage	5	1(20%)	-		5	1(20%)

Surgery for a postinfectious and post hemorrhagic hydrocephalus showed highest incidence of shunt infection in both adult and children. Among the congenital malformations infection rates were higher in patients with myelomeningocele.

TABLE 9

SIGNIFICANCE OF CLINICAL FEATURES AS INDICATORS OF SHUNT INFECTION

CLINICAL FEATURES	TOTAL CASES (n=120)	PERCENTAGE IN INFECTED
Fever	45	60%
Seizures	38	52.6%
Headache	66	21.2%
Vomiting	79	27.8%
Altered consciousness	48	54.2%
Abdominal signs	22	31.8%
Wound changes	16	50%
Displaced shunt	16	50%
CSF leak	12	66.7%

Symptoms such as fever, seizures, altered consciousness, CSF leak, displaced shunt were associated with a high risk of infection. Headache, vomiting abdominal signs were less specific signs of infection.

TABLE 10

CSF CELL COUNT AND BIOCHEMICAL PARAMETERS AS PREDICTORS OF SHUNT INFECTION

I

Variable CSF WBC > 100 mm³	Infected cases (n=41)	Non infected cases (n=79)
Positive	26	3
Negative	15	76

Sensitivity- 63.4%, Specificity- 96.2%

II

Variable CSF Neutrophils>10%	Infected cases (n=41)	Non infected cases (n=79)
Positive	28	4
Negative	13	75

Sensitivity- 68.3%, Specificity- 94.9%

III

Variable CSF protein>50 mg/dl	Infected cases (n=41)	Non infected cases (n=79)
Positive	25	13
Negative	16	66

Sensitivity- 61%, Specificity- 83.5%

IV

Variable CSF glucose<40 mg/dl	Infected cases (n=41)	Non infected cases (n=79)
Positive	24	6
Negative	17	73

Sensitivity- 58.5%, Specificity- 92.4 %

Using Chi-square test the values of the infected group was found to be significantly different from the non infected group with $P<0.05$

Abnormal biochemical values can indicate the presence of infection but normal biochemical parameters cannot rule out the presence of infection. They are useful in starting empirical antibiotic therapy till culture results are awaited**.**

TABLE 11

GRAM STAINING AS A PREDICTOR OF SHUNT INFECTION

I

Total isolates=49	**Gram staining positive**	**Percentage**
Gram positive n=27	9	33.3%
Gram negative n=22	19	86.4%

II

Gram staining	**Infected cases (n=41)**	**Non infected cases (n=79)**
Positive	26	0
Negative	15	79

Sensitivity- 63.4%, Specificity- 100 %

The correlation of Gram staining and CSF biochemical analysis is very useful in choice of antibiotic for empirical antibiotic theraphy till culture results are available.

TABLE 12

PATHOGENS ISOLATED IN 41 CASES OF SHUNT INFECTION

Organisms	Total No = 50	Percentage
GRAM POSITIVE COCCI		
*Staphylococcus epidermidis**	16	32
*Staphylococcu aureus**	9	18
Micrococcus luteus	1	2
Enterococcus faecalis	1	2
GRAM NEGATIVE BACILLI		
*Escherichia coli**	5	10
Klebsiella pneumoniae	6	12
*Klebsiella oxytoca**	2	4
*Pseudomonas aeroginosa**	5	10
*Acinetobacter baumannii**	2	4
Citrobacter diversus	1	2
Morganella morganii	1	2
FUNGUS		
Candida albicans	1	2

Staphylococcus epidermidis was the commonest pathogen followed by *Staphylococcus aureus, Escherichia coli, Klebsiella species,* and *Pseudomonas aeroginosa.*

* In mixed infections the organisms isolated were
i) Morganella morganii with *Escherichia coli, ii) Staphylococcus aureus* with *S. epidermidis,* iii) *Staphylococcus aureus* with *Acinetobacter baumannii,* and iv) *Klebsiella oxytoca* with *Pseudomonas aeroginosa.*

TABLE 13

Recurrence	First episode	Second episode
PATIENT-1	*Klebsiella pneumoniae*	*Klebsialle pneumoniae + Pseudomonas aeroginosa + Candida albicans*
PATIENT-2	*Staphylococcus epidermidis*	*Staphylococcus epidermidis + Klebsiella pneumoniae*

TABLE 14

MONOMICROBIAL AND POLYMICROBIAL INFECTIONS

	Children (n=30)	Adult (n=11)	Total=41
MONOMICROBIAL	29	8	37 (90.2%)
POLYMICROBIAL	1	3	4 (9.8%)

Most of the infections were monomicrobial in nature.
Two cases of recurrent infection were polymicrobial in nature.

TABLE 15

ORGANISMS IN EARLY AND LATE INFECTION

Organisms	Early infection	Late infection
Staphylooccus epidermidis	16	0
Staphylococcus aureus	9	0
Micrococcus luteus	1	0
Enterococcus faecalis	1	0
Escherichia coli	3	2
Klebsiella pneumoniae	5	1
Klebsiella oxytoca	2	0
Pseudomonas aeroginosa	3	1
Acinetobacter baumannii	1	1
Citrobacter diversus	1	0
Morganella morganii	0	1
Candida albicans	1	0

Gram-positive cocci produced early infection. Infection due to Gram-negative bacilli resulted in early and late infection.

TABLE 16

SLIME PRODUCTION IN S.EPIDERMIDIS

S. epidermidis	**Slime positive**		**Slime negative**	
	NO	**%**	**NO**	**%**
16	10	(62.5)%	6	(37.5)%

62.5 % of the *S. epidermidis* strains were positive for slime production.

TABLE 17

BACTEREMIA IN INFECTED CASES

Total infected cases	**Positive**	**%**
41	2	4.9%

Bacteremia was detected in 4.9% of the infected cases and carried grave prognosis. *Klebsiella pneumoniae* was isolated in both the cases

TABLE 18

ANTIMICROBIAL SENSITIVITY PATTERN OF GRAM-POSITIVE COCCI

Organisms	**Penicillin (10 U)**	**Ampicillin (10 µg)**	**Oxacillin (1 µg)**	**Chloramphenicol (30 µg)**	**Ofloxacin (5 µg)**	**Co-trimoxozole (25 µg)**	**Cefotaxime (30 µg)**	**Gentamicin (10 µg)**	**Vancomycin (30 µg)**
S. epidermidis (16)	6 (37.5%)	10 (68.7%)	12 (75%)	12 (75%)	13 (81.3%)	10 (68.7%)	12 (75%)	12 (75%)	16 (100%)
S. aureus (9)	3 (33.3%)	6 (66.7%)	7 (77.8%)	7 (77.8%)	8 (88.9%)	7 (77.8%)	7 (77.8%)	7 (77.8%)	9 (100%)
Micrococcus luteus (1)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)
Enterococcus Faecalis	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)

TABLE 19

ANTIMICROBIAL SENSITIVITY PATTERN OF GRAM-NEGATIVE BACILLI

	Ampicillin (10 µg)	**Ofloxacin (5 µg)**	**Amikacin (30µg)**	**Chloramphenicol (30 µg)**	**Co-trimoxozole (25 µg)**	**Ceftazidime (30µg)**	**Cefaperazone (75µg)**	**Cefaperazone +Sulbactam (75/30µg)**	**Imipenam (10µg)**
E. coli (5)	3 (60%)	4 (80%)	4 (80%)	4 (80%)	3 (60%)	3 (60%)	3 (60%)	5 (100%)	5 (100%)
K. pneumoniae (6)	4 (66.7%)	5 (83.3%)	4 (66.7%)	5 (83.3%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	5 (83.3%)	6 (100%)
K. oxytoca (2)	1 (50%)	2 (100%)	2 (100%)	1 (50%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)
P. aeruginosa (5)	3 (60%)	4 (80%)	5 (100%)	4 (80%)	4 (80%)	4 (80%)	4 (80%)	5 (100%)	5 (100%)
Acinetobacter baumannii (2)	1 (50%)	2 (100%)	2 (100%)	1 (50%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)
Citrobacter diversus (1)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%
Morganella	1	1	1	1	1	1	1	1	1

morganii (1)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)

TABLE 20

BETA–LACTAMASES PRODUCTION IN GRAM-POSITIVE COCCI

Organisms	NO	%
S.epidermidis (16)	6	37.5%
S.aureus(9)	3	33.3%

β-lactamase production was detected in 37.5% of the isolates in *S. epidermidis* and 33.3% of the isolates in *S. aureus*

TABLE 21

EXTENDED-SPECTRUM β-LACTAMASES (ESBLs) PRODUCTION IN GRAM-NEGATIVE BACILLI

Organisms	NO	%
Escherichia coli (5)	2	40 %
Klebsiella pneumoniae(6)	2	33.3%
Pseudomonas aeroginosa(5)	1	20%

ESBLS were detected in *Escherichia coli* (40%), *Klebsiella pneumoniae* (33.3%), *and Pseudomonas aeroginosa* (20%)

One strain of *Klebsiella pneumoniae* was an AmpC producer.

TABLE 22

MIC OF BENZYL PENCILLIN FOR PENCILLIN RESISTANT GRAM-POSITIVE STRAINS

Organism	8 µg/dl	16 µg/dl	32 µg/dl	MIC $_{50}$
S.epidermidis(10)	6	2	2	8µg/dl
S.aureus(6)	1	1	4	32µg/dl

MIC break points of penicillin resistant Gram-positive strains were between 8-32 µg/dl with a MIC $_{50}$ of 8µg/dl for *S.epidermidis* and MIC$_{50}$ of 32µg/dl for *S.aureus*

TABLE 23

MIC OF CEFTAZIDIME FOR CEFTAZIDIME RESISTANT GRAM-NEGATIVE STRAINS

Organism	32 µg/dl	64 µg/dl	128 µg/dl	MIC_{50}
Escherichia coli (2)	1	0	1	128 µg/dl
Klebsiella pneumoniae (3)	0	1	2	128 µg/dl
Pseudomonas aeroginosa (1)	0	0	1	128 µg/dl

MIC of six ceftazidime resistant Gram-negative bacilli were between 32-128µg/dl with a MIC_{50} of 128 µg/dl

TABLE 24

OUTCOMES IN INFECTED PATIENTS

	Children(n=30)	Adult(n=11)	Total =41
Survived	29	9	38
Death	1	2	3

The overall mortality rate was 7.3% among the shunt infected patients.

DISCUSSION

Ventriculoperitoneal shunt placement is a relatively common neurological procedure performed for the treatment of hydrocephalus as well as associated conditions in which the natural flow of cerebrospinal fluid is obstructed. Shunts are quite susceptible to bacterial infection, which contribute to excess morbidity and mortality.

In our study males constituted 55.6% and females constituted 44.4%. No significant predilection was observed between the sexes (Table 1).

In our study 248 (57.9%) patients in age groups less than 16 were grouped under paediatric category. 180(42.1%) patients in the age group more than 16 were considered under adult category as per the criteria fixed by Kuo-Wei-Wang *et al.*[51] (Table 2).

In this study the etiology of hydrocephalus that necessitated shunt among children were preceding meningitis (21.8%), CNS tumour (15.7%), congenital malformations like aqueductal stenosis (10.5%), Dandy-walker syndrome (8.9%), myelomeningocele (5.6%), idiopathic (6%) and subarachnoid haemorrhage (2%). Thus in children congenital malformations were common followed by meningitis. Among adults, space occupying lesions were common (50%) followed by preceding meningitis (28.3%) and idiopathic (21.7%) (Table 3).

In a study done by Latifa T.F *et al*.[52], on CSF shunt infections in children the indications of shunt were myelomeningocele (20%), aqueductal stenosis (18%), CNS tumour (13%),) preceding meningitis (6%), preceding SAH (3%), other congenital malformations (13%), other acquired etiology (11), idiopathic (18%).

In our study, the clinical features of the patients with shunt malfunctions due to both mechanical causes or infection were fever (37.5%), seizures (31.7%), headache (55%), vomiting (65.8%), altered consciousness (43.3%), abdominal signs (18.3%), wound changes (13.3%), displaced shunt (13.3%), and CSF leak (10%). Symptoms such as headache, vomiting, fever and altered consciousness were common in both categories. Seizures were commonly observed in children. Abdominal signs, wound changes and displaced shunts were common in few patients (Table 4).

Alexa *et al*.[1] have observed the symptoms of shunt malfunction are the same as seen with the initial hydrocephalus such as headache, vomiting and altered consciousness and in addition to these there were shunt specific findings, such as fluid around the shunt, i.e., CSF leak, abdominal pain or distension. Symptoms referable to infection such as fever, seizures may be seen. Our study findings were similar with this study.

The rate of cerebrospinal shunt infection varied considerably in different studies, ranging from 0.33% to 39 %.[8, 26, 55, 75]

In our study in about 404 patients, with primary shunt insertions, 96 malfunctions occurred (23.7%) of which 36 were infected after their primary shunt surgery resulting in an infection rate of 8.9 %. Two cases had recurrence of infection during the study period. In 24 cases with multiple revisions, the infection rate was 20.8%, involving 5 patients indicating higher infection rate compared to primary shunt surgery (Table 5). Our results correlated with the infection rate of many other studies.

Calderri *et al*.[12] the authors of department of neurosurgery from catholic University Medical School, Rome have analysed the incidence of early mechanical

and infective CSF complications in 170 patients with hydrocephalus in the first postoperative year. They found that about 45.9% of the patients presented with one shunt malfunction three quarters of which were due to mechanical causes and one quarter due to infection.

Recently, Borgbjerg and associates[60] studied 884 shunt patients who underwent placement of newshunt in Copenhagen from 1958-1989. The overall infection rate in their study was 7.4 % (5.7-9.3%).

Gardner P *et al.*[30] in his work on Infections of central nervous system shunts had quoted about 1 out of every 10 ventricular shunts for hydrocephalus will become infected.

George *et al.*[33] however, showed that the operative incidence of infection in a patient undergoing a third or greater revision was significantly greater compared to one underlying a first or second revision.

Among paediatric patients, the majority of shunt infections occurred relatively soon after the placement of shunt.[18]. In our study 63.9% of infections occurred with in one month, 86.1% in 2 months and 94.4% infections presented with in three months. All the cases of infection in primary shunt surgery presented within six months (Table 6).

This was similar to that reported by Choux *et al*[15] . In their study on reducing the incidence of shunt infection, they had roughly 66% of shunt infections diagnosed with in one month after surgery, and close to 80% manifested by 6 months.

In one larger series of paediatric patients with extended follow-up, Casey and Colleagues[13] reported that among children with shunted hydrocephalus who underwent a first shunt revision for infection, 92% of infections occurred with in 3

months of the initial shunt placement.

In an effort to reduce the rate of infection associated with the use of shunt devices, attempts were made to identify the risk factors. In general, the factor most frequently associated with an increased rate of shunt infection was the age of the patient. Neonates and very young children were at greater risk.[22]

In our study, in about 43 cases, 13 cases (18.1%) were with in six months of age, as compared to < 11% among all the other age groups (Table 7). In their cohort study, Casey and colleagues[13] reported that children aged 6 months or younger had a 19% rate of infection, versus a rate of 7 % among older children.

Young age (less than 6 months) seemed to represent the main risk factor, and this was related both to the immunologic deficiency and to the particular features of residential flora in this group.[18]

Pople *et al*.[12] in their study on etiological factors of CSF shunt infections in infants had shown an infection rate of 15.7% for infants younger than 6 months of age , as compared with only 5.6% for older children . This might be due to the age related changes in the skin and its resident bacterial flora with the density of aerobic cocci being higher in infancy.

Along with age, numerous other factors such as reason for shunt surgery, previous shunt history, number of early revisions have been examined for their role in shunt infection.[22]

In our study, surgeries for myelomeningocele (21.4%) postinfectious hydrocephalus (20%), posthaemorrhagic hydrocephalus (20%) showed the highest incidence of shunt infections in children. Among adults infection rates were higher in tumour patients (7.7%) followed by postinfective hydrocephalus (5.9%) (Table

8).

Dallacasa[18] and associates reported that half of the children in the post-infectious-posthaemorrhagic hydrocephalus group had at least one episode of shunt infection by the end of one year. Also children with myelomeningocele might be at greater risk for infection than with congenital hydrocephalus.[2]

According to various studies the clinical manifestations of shunt infections were variable. In trying to assess the significance of the various symptoms in patients with shunt infection symptoms such as CSF leak (66.7%), fever (60%), altered consciousness (54.2%), seizures (52.6%), displaced shunt (50%), were associated with a high risk of infection. Headache, vomiting, abdominal signs and wound changes were also observed (Table 9).

Many studies on CSF shunt infections had shown that fever may be present in as few as 14% to as many as 92% of shunt infection and about 65% of the patients had reported to have change in mental status.[10]

In our study abdominal signs were present in 22 patients, 31.25% of whom developed shunt infection (Table 9).

In the study done by Nelson *et al.*[65], abdominal complaints were present in 19-36% of the cases. Infections with wound dehiscence as well as drainage of the purulent material are obvious signs.

Odio *et al.*[67] showed in 18-36% of cases associated wound infection may be present. In our study, wound changes were observed ion 16 patients, 31.8% of which developed shunt infection.

The clinical characteristics of my study correlated with various other studies.

CSF examination is useful in the investigations of shunt infection. Our study showed CSF pleocytosis WBC> 100 mm³ (sensitivity-63.4%, specificity-96.2%), neutrophilia >10% (sensitivity -68.3%, specificity-94.9%), high protein level > 50 mg/dl (sensitivity-61%, specificity-83.5%), low glucose level<40mg/dl (sensitivity-58.5%, specificity-92.4%) (Table 10).

Our study was comparable with the study done by Cheng-Chou Lan *et al.*[14] on Early diagnosis of ventriculoperitoneal shunt infections and malfunctions, which showed CSF WBC >100 mm^3 (sensitivity-60%, specificity-96%), CSF neutrophils >10% (sensitivity-90%, specificity-85%), CSF protein >50 mg/dl (sensitivity-80%, specificity-84%), CSF glucose <40 mg/dl (sensitivity-60%, specificity-93%).

Abnormal biochemical values indicate the presence of infections but normal biochemical parameters cannot rule out the presence of infections. They are useful in starting empirical antibiotic therapy till culture results are obtained.

In our study Gram staining was useful in detecting Gram-negative infections as Gram staining was positive in 86.4% of cases. In case of Gram-positive infections Gram staining was positive only in 33.3% of cases. The overall sensitivity was 63.4% but specificity was 100% (Table 11).

Odio *et al.*[67] had showed Gram stain was positive only in 46% of the episodes and Gram-positive cocci were isolated in 75% of the patients.

Nelson *et al.*[65] had showed Gram stains were highly positive in *S. aureus* and Gram-negative infection (82 and 91%) but may be misleading in *S. epidermidis* in which Grams stains may be positive in as few as 4% of shunt infections.

This correlated with our observation where *S. epidermidis* was detected in only 3.7% of infection.

The correlation between Gram staining and CSF neutrophilia is very useful in choice of antibiotic for empirical theraphy.

Since shunt infections are life threatening early antibiotic therapy is essential. Gram staining and neutrophil counts can be of immense help in ensuring a good outcome.

In my study infecting pathogen was a single organism in 37 cases (90.2%) and mixed infections occurred in 4 cases (9.8%). Two patients had recurrence of infection i.e., more than one episode (Table 14).

Staphylococcus epidermidis (32%) was the commonest organism isolated followed by S*taphylococcus aureus* (18%), *Klebsiella pneumonia* (12%), *Escherichia coli* (10%), *Pseudomonas aeroginosa* (10%)*, Klebsiella oxytoca* (4%)*, Acinetobacter baumannii* (4%). The remaining organisms isolated were *Micrococcus luteus, Enterococcus faecalis, and Citrobacter diversus all* contributing to about 2%. *Morganella morganii* (2%) was isolated in a mixed infection along with *E. coli.* One *Candida albicans* was isolated in a recurrent infection (Tables 12 & 13).

Bruce A. Kauffman article[10] on Infections of cerebrospinal fluid shunt infections revealed the common etiological agents in shunt infections as follows: *staphylococcus epidermidis* is the most frequently isolated of the organisms being responsible for about 47-64% of the infections. *Staphylococcus* is the next common organism, occurring in 12-29% of infections. Gram-negative organisms, usually *Escherichia coli and Klebsiella* species, are responsible for the next most frequent group of infections having an incidence ranging from 6-20%. *Proteus* and *Pseudomonas* species are also frequently isolated. *Streptococcal* species are found in 8-10% of infections. A variety of much less common organisms make up the

remainder of the infections, including fungi and other commensal microbes. In approximately 10-15% mixed infections occur.

The above results correlated well with the results of the present study Meivoritch *et al*[58] accounted Coagulase negative *Staphylococci* for 28% and *Staphylococcus aureus* for 14% of the initial infectious episodes that occurred in 46 episodes involving 32 patients. Eight patients (25%) had more than one episode.

Sharpio S *et al*.[82] showed the infecting pathogens *as Staphylococcus epidermidis* (45%), *Staphylococcus aureus* (20%), *Micrococcus (*5%). Gram-negative bacilli (15%).

In our study, the organisms isolated in early infection were mostly Gram-positive cocci i.e. *Staphylococcus epidermidis* and *Staphylococcus aureus*; where as Gram-negative organisms were isolated from both categories and with significant isolation in late infection (Table 15).

In 16 episodes of infection caused by *Staphylococcus epidermidis* 10 (62.5%) episodes of infection were caused by slime producing *Staphylococcus epidermidis* and 6 (37.5%) by non slime producing *Staphylococcus epidermidis* (Table 16).

In a study by Diaz Mitomaf *et al*[20] on 19 episodes of shunt infection, 11 episodes were caused by slime producing coagulase negative *Staphylococci* (CNST) and 8 episodes by non slime producing CNST. He also showed failure to eradicate the infecting organisms by antimicrobial therapy that occurred more frequently with infections due to slime producing CNST.

Various studies had shown that slime producers account for 60-80% of the coagulase negative *Staphylococci* isolated from shunt infections.[20, 37, 97]

In our study the protocol was to replace the shunt whenever *Staphylococcus epidermidis* was isolated.

In this study, bacteremia was detected in 4.9% of the infected cases and carried grave prognosis. The organism isolated was *Klebsiella pneumoniae* in both cases. The mortality rate was 100% in these 2 patients with positive blood cultures, as compared to the overall mortality rate of 7.3% among the infected patients (Tables 17, 23 & 24).

Latifa *et al.*[52] in his study on CSF shunt infections had said that blood cultures were mostly negative due to the absence of direct access to blood stream.

Odio *et al.*[67] had showed blood cultures positivity in 29% involving 59 infectious episodes in 51 patients.

All the Gram-positive cocci showed 100% sensitivity to vancomycin. *Staphylococcus epidermidis* showed 81.3% sensitivity to ofloxacin, 75% sensitivity to oxacillin, cefotaxime, chloramphenicol and gentamicin. *Staphylococcus aureus* showed 88.9% sensitivity to ofloxacin, 77.8% sensitivity to oxacillin, cefotaxime, gentamicin, chloramphenicol, co-trimoxozole, 66.7% sensitivity to ampicillin. *Micrococcus luteus* and *Enterococcus faecalis* were sensitivity to all drugs (Table 18).

All the Gram-negative bacilli showed 100% sensitivity to Imipenam, cefaperazone-sulbactam with the exception of *Klebsiella pneumoniae which* was 83.3 % sensitive to cefaperazone-sulbactam. *Escherichia coli* showed 80% sensitivity to ofloxacin, amikacin, and chloramphenicol. *Klebsiella pneumoniae* showed 83.3% sensitivity to ofloxacin and chloramphenicol, *Klebsiella oxytoca* were 100% sensitivity to ofloxacin, amikacin, ceftazidime and cefaperazone.

Citrobacter diversus and *Morganella morganii* were sensitive to all drugs. *Pseudomonas aeroginosa* showed 100% sensitivity to amikacin, and *Acinetobacter baumannii* showed 100% sensitivity to ofloxacin, amikacin, ceftazidime and cefaperazone (Table 19).

In our study 22.2% of the isolates were methicillin resistant *Staphylococcus aureus* (MRSA) and 25% of the isolates were methicillin resistant *Staphylococcus epidermidis* (MRSE).

MRSA and MRSE mostly present in old patients and patients who had undergone various other neurosurgical procedures.

In a study by Kuo-Wei Wang *et al.*[51] oxacillin resistant *Staphylococcal* strains accounted for 33% of the episodes.

β-lactamase production was detected in 37.5% of the isolates in *S. epidermidis* and 33.3% of the isolates in *S. aureus* (Table 20).

In our study ESBL producing strains were detected in *Klebsiella pneumoniae* (33.3%) *Escherichia coli* (40%), *Pseudomonas aeroginosa* (20%). one strain of *Klebsiella pneumoniae* showed production of Amp C beta-lactamase (Table 21). These strains were mostly present in cases of multiple shunt revisions and recurrence.

In this study, minimum inhibitory concentration break points of benzyl penicillin for penicillin resistant *Staphylococcus* species were between 8 µg/ml to 32 g/dl (Table 22). MIC breakpoints of ceftazidime resistant Gram-negative bacilli were between 32 g/dl-128 g/dl with MIC_{50} of 128 µg/dl (Table 23).

In our study most strains were sensitive to all drugs suggesting that they have

been derived from patient's residential flora. A few strains were resistant. Those bacteria were isolated from patients who had associated CSF leak, displaced shunt, or wound infection suggesting the possibility of contamination from the environment.

Various studies revealed the source of infection in majority of the cases in cases of Gram-positive shunt infections were commensals of the skin, a result of direct contamination during surgery [3, 78]. In Gram-negative infections, they could probably be introduced during surgery. Another probable mechanism is retrograde infection, in which an asymptomatic perforation of the bowel leads to distal contamination of the VP shunt catheter and retrograde progression of infection.[76, 86.]

Duhaime et al [21] in their study concluded that the bacteria most often associated with shunt infections were airborne in the operating room, and are distributed in the highest concentration near the surgical team.

In our study endogenous swabs taken from the external auditory canal, nose, umbilicus revealed *Staphylococcus epidermidis* and *Staphylococcus aureus* which was found to be phenotypically similar with the isolates identified from the CSF samples as the antibiotic susceptibility patterns were the same. This showed that the pathogens would most likely be the resident flora of the skin. Subsequent Phage typing also showed correlation.

In this study environmental sampling done in neurosurgical ward, neurosurgery theatre using swab and open plate method grew *methicillin resistant Staphylococcus strains, Klebsiella pneumoniae* suggesting the possibility *of* nosocomial infections.

Phage typing of the isolate and environmental samples of *Staphylococcus*

aureus done which showed correlation. Phage 622 was the most common. Some strains were untypable.

Infected patients were treated with external ventricular drainage with appropriate antibiotics. An empirical regimen of ampicillin-cloxacillin (500 mg IV BD) followed by treatment based on sensitivity pattern was instituted among most patients. Most of the patients improved with in one week and new shunt was inserted subsequently. 2 patients had recurrence of infection with bacteremia and died subsequently (Table 24).

SUMMARY

- This study was done for a period of 18 months involving 428 patients of both sexes and age group ranging from 0-60 of which 404 were cases who underwent primary shunt insertion and 24 were old cases of shunt insertion who underwent shunt revision.

- A total of 120 cases with shunt malfunction were taken for the study which included 96 cases who had one episode of shunt malfunction among the 404 cases and also the 24 old cases who presented with shunt malfunction during the study period.

- 36 cases were infected after their primary shunt surgery resulting in an infection rate of 8.9%. Two cases had recurrence of infection. In 24 cases with multiple revisions, the infection rate was 20.8%.

- The underlying condition of the patient that necessitated shunt in children were mainly congenital malformations (54.4%), followed by preceding meningitis (21.8%), CNS tumour (15.7%), idiopathic (6%), subarachnoid haemorrhage (2%). In adults CNS tumour (50%) were common followed by preceding meningitis (28.3%) and idiopathic (21.7%).

- Most infections occurred with in one to two months of surgery. 63.9% of infections occurred within one month, 86.1% in 2 months and 94.4% presented within 3 months.

- Young age, less than six months of age was a main risk factor. 13 out of 41 cases were within 6 months of age.

- Infection rates were higher with myelomeningocele (21.4%), preceding meningitis (20%), subarachnoid haemorrhage (20%) in children. In adults the

infection rates were comparatively less.

- Fever, seizures, altered consciousness, CSF leak, displaced shunt were the symptoms most commonly associated with shunt infection. Headache, vomiting, abdominal signs and wound changes were less common symptoms.

- CSF pleocytosis, neutrophilia, low glucose level, high protein level were found in increased frequency with the infected group. Using Chi-square test, the values in infected group was found to be significantly different from the non infected group with $P<0.05$.

- Gram staining was positive in 86.4% of Gram-negative infections as compared to only 33.3% in case of Gram- positive infections.

- The correlation between Gram staining and CSF neutrophilia can be very helpful in choice of antibiotic for empirical therapy.

- The commonest organism isolated was *Staphylococcus epidermidis* (32%) followed by *staphylococcus aureus (*18%), *Klebsiella pneumonia* (12%), *Escherichia coli* (10%), *Pseudomonas aeroginosa* (10%)*, Klebsiella oxytoca* (4%)*, Acinetobacter baumannii* (4%). The remaining organisms isolated were *Micrococcus luteus, Enterococcus faecalis, and Citrobacter diversus all* contributing to about 2%. *Morganella morganii* (2%) was isolated in mixed infection along with *E. coli.* One *Candida albicans* was isolated in a recurrent infection.

- 62.5% episodes of infection were caused by slime producing *Staphylococcus epidermidis*

- Bacteremia was detected in 4.7% of infected cases and carried grave prognosis.

- Gram-positive cocci showed 100% sensitivity to Vancomycin, followed by ofloxacin, gentamicin, cefotaxime, oxacillin, ampicillin where as Gram-negative

bacilli showed 100% sensitivity to imipenam followed by cefaperazone-sulbactam, amikacin, ceftazidime, ofloxacin and ampicillin.

- MRSA and MRSE strains accounted for about 22.2% and 25% of the isolates respectively.

- β-lactamase production was detected in 37.5% of the isolates in *S. epidermidis* and 33.3% of the isolates in *S. aureus.* ESBL producing strains were detected in *Klebsiella pneumoniae* (33.3%) *Escherichia coli* (40%)*, Pseudomonas aeroginosa* (20%).

- Amp C beta-lactamase was positive in one strain of Klebsiella *pneumoniae*.

- MIC break points of Benzyl penicillin for penicillin resistant staphylococcal species were between 8µg/ml to 32 g/dl. MIC breakpoints of ceftazidime resistant Gram negative bacilli were between 32 g/dl-128 g/dl.

- The source of infection were mostly skin commensals mostly occurring possibly during surgery. Also the possibility of nosocomial infections should not be ignored.

- Antibiotic use with external ventricular drainage (EVD) followed subsequently by a new shunt placement was the most effective treatment.

- An empirical regimen of ampicillin-cloxacillin(500 mg IV BD) was found to be effective in about 60% of shunt infections

CONCLUSION

- Ventriculoperitoneal shunt infection is a cause of significant morbidity and mortality, causing shunt malfunction and chronic ill health.
- The overall infection rate associated with ventriculoperitoneal shunts was 8.9%.
- Majority of the infections occurred within one to two months of surgery.
- The most frequently isolated organism was *Staphylococcus epidermidis*.
- Young age, cause of hydrocephalus as myelomeningocele, multiple shunt revisions were the main risk factors for shunt infection.
- CSF Gram staining and CSF neutrophil count is of immense help in starting empirical antibiotic therapy.
- Early identification and with the use of appropriate antibiotics both prophylactically as well as long term along with prompt removal of and replacement of the drainage system will ensure a good outcome.
- Surveillance of MRSA and ESBLs are essential to implement strict control measures and antibiotic policies to combat bacterial drug resistance.

BIBLIOGRAPHY

1. Alexa I. Canady, Sandeep Sood, Steven D.Ham. Surgical Management of Hydrocephalus in Children. Henry schmudex, William H Sweet Operative Neurosurgical techniques. Indications, Methods& Results. Third edition, volume 2; 1995; chapter 98:1231-1243.

2. Ammirati M, Raimondi AJ: Cerebrospinal fluid infections in children: A study on the relationship between the etiology of hydrocephalus, age at the time of shunt placement, and infection rate. Childs nerv Sysl 1987; 3: 106-109.

3. Bayston R, Lari J. A study of sources of infection in colonized shunts. Dev Med Child Neurol 1974; 16:16-22.

4. Bayston R, Milner RD Antimicrobial activity of silicone rubber used in hydrocephalus shunts, after impregnation with antimicrobial substances Clin Pathol.1981; Sep; 34(9):1057-62

5. Bayston R, Rodgers J .Role of serological tests in the diagnosis of immune complex disease in infection of ventriculoatrial shunts for hydrocephalus.Eur J Clin Microbiol Infect Dis. 1994 May; 13(5):417-20

6. Bayston R. Microbial colonization of cerebrospinal fluid shunts. Med Lab Sci 1981; 38:259-267.

7. Betty A. Forbes, Daniel F. Sahm, Alice S.Weissfeld. Meningitis and other Infections of the Central Nervous System. Chapter 58 In Bailey& Scott's Diagnostic Microbiology 11th edn.2002; 907-912.

8. Bhatnagar V, George J, Mitra DK, Upadhyaya P. Complications of cerebrospinal fluid shunts. Indian J Pediatr 1983; 50:133-8.

9. Bhatnagar V, Mitra DK, Upadhyaya P. Shunt related infections in hydrocephalic children. Indian pediatr 1986; 23; 255-7.

10. Bruce A Kaufman, Infections of cerebrospinal Fluid Shunts.,W.M. Scheld, R.J. Whitley and D.T.Durack, Infections of the Central Nervous System 2nd ed.1997 ;Chapter 29:555-577.

11. Bullock R, van Dellen JR, Ketelbey W, Reinach SG. A double-blind placebo-controlled trial of perioperative prophylactic antibiotics for elective neurosurgery. J Neurosurg. 1988 Nov; 69(5):687-91

12. Caldarelli M, Di Rocco C, La Marca F. Shunt Complications in the first postoperative year in children with meningomyelocele. Childs Nerv Syst. 1996 Dec; 12(12); 748-54.

13. Casey ATH, Kimmings EJ, Klein Lugtebeld AD et al: The long term outlook for hydrocephalus in children. A ten-year cohort study of 155 patients. Pediatr Neurosurg 27:63-70, 1997.

14. Cheng- chou Lan, Tal-Tong Wong, Shu- Jen Chen, Muh-Lii Liang, Ren-Bin Tang. Early diagnosis of ventriculoperitoneal shunts infections and malfunctions in children with hydrocephalus. J Microbiol Immunol Infect 2003; 36; 47-50.

15. Choux M, Genitori L, Lang D, Lena G. Shunt implantation: reducing the incidence of shunt infection**.** Childs Nerv Syst. 1997 Nov-Dec;13(11-12):584-7

16. Christensen GD, Simpson WA, Bisno AL, Beachey EH.Adherence of slime-producing strains of Staphylococcus epidermidis to smooth surfaces.Infect Immun. 1982 Jul; 37(1):318-26

17. Colle JG, Duguid P, Fraser G, Marmion BP, A. Simmons. Laboratory strategy in the diagnosis of infective syndromes, Chapter 4. In: Mackie & Mc cartney practical Medical Microbiology. 14th edn. 1996; 53-94.

18. Dallacasa P, Dappazzo A, Galassi E, Sandri F, Cocchi G, Masi M. Cerebrospinal fluid shunt infections in infants. Childs Nerv Syst. 1995 nov; 11(11):643-8

19. Davidoff LM.Treatment of hydrocephalus. Historical review and description of a new method. Arch Surg 1945: 51:1-14.

20. Diaz-Mitoma F, Harding GK, Hoban DJ, Roberts RS, Low DE. Clinical significance of a test for slime production in ventriculoperitoneal shunt infections caused by coagulase-negative staphylococci.

21. Duhaime AC, Bonner K, McGowan KL, Schut L, Sutton LN, Plotkin S. Distribution of bacteria in the operating room environment and its relation to ventricular shunt infections: a prospective study. Childs Nerv Syst. 1991 Aug; 7(4):211-4.

22. Elizabeth B.Claus, Charles Duncan. Shunt Infection. H. Richard wims. Youmans Neurological surgery. Fifth edition. Volume 3. Chapter 217; 3419-3425.

23. Elmer W. Koneman, Stephen D. Allen, William M .Janda, Paul C. Schrenckenberger, Washington C. Winn. The Family Micrococcaceae: Taxonomy and Clinical Significance. Colour and atlas and textbook of Diagnostic Microbiology. 5th edn 1997; 540-549

24. Ersahin Y, Mutiuer S, Guzelbag E. Cerebrospinal fluid shunt infections. J Neurosurg Sci. 1994 Sep; 38(3):161-5

25. Fan-Harvard P, Nahata MC. Treatment and prevention of infections of cerebrospinal fluid shunts. Clin pharm.1987; 6:866-868.

26. Filka J Huttova M, Tuharsky j, Sagat T, Kranlinsky K, Kremery V Jr. Nosocomial meningitis in children after ventriculoperitoneal shunt insertion. Acta padiatr 1999; 88:576-8

27. Forrest DM, Cooper DGW. Complications of ventriculoatrial shunts: a review. J Neurosurg. 1968; 29; 506-512.

28. Forward KR, Fewer HD, Stiver HG. Cerebrospinal fluid shunt infections. A Review of 35 infections in 32 patients. J Neurosurg. 1983 Sep; 59(3):389-94.

29. Frame PT, Watanakunakorn C, McLaurin RL, Khodadad G .Penetration of nafcillin, methicillin, and cefazolin into human brain tissue. Neurosurgery. 1983 Feb; 12(2):142-7

30. Gardner P, Leipzig T, Philips P. Infections of central nervous system shunts. Med Clin North Am 1985 Mar; 69(2):297-314.

31. Gardner P,Leipzig TJ,Sadigh M .Infections of mechanical cerebrospinal fluid shunts. Curr Clin Top Infect Dis 1988; 9: 185-214.

32. Gargritu; Gulati V.L; Arora Usha. Extended spectrum beta-lactamases production by *Pseudomonas aeroginosa* isolated from surgical wound infections and its resistance pattern. Department of Microbiology, Govt. Medical college, Amristar(Pb). BP-25. MICROCON-2005.

33. George R, Leibrock L, Epstein M. Long term analysis of cerebrospinal fluid shunt infections: a 25 year experience. J Neurosurg. 1979; 51:804-811.

34. Georgiade NG, King EH, Harris WA, Tenery JH, Schlech BA. Effect of three proteinaceous foreign materials on infected and sub infected wound models. Surgery 1975; 77:569-576

35. Geraghty J, Feely M Antibiotic prophylaxis in neurosurgery. A randomized controlled trial.J Neurosurg. 1984 Apr; 60(4):724-6.

36. Gombert ME, Landesman SH, Corrado ML, Stein SC, Melvin ET, Cummings M. Vancomycin and rifampin therapy for Staphylococcus epidermidis meningitis associated with CSF shunts: report of three cases.J Neurosurg. 1981 Oct; 55(4):633-6

37. Guevara JA, Zuccaro G, Revisan A, Denoya CD. Bacterial adhesion to cerebrospinal fluid shunts. J Neurosurg. 1987 Sep; 67 (3): 438-45.

38. Haines SJ, Taylor F. Prophylactic methicillin for shunt operations: effects on incidence of malfunction and infection. Child's Brain. 1982; 10:10-22.

39. Haines SJ, Walters BC. Antibiotic prophylaxis for cerebrospinal fluid shunts: a metanalysis. Neurosurgery. 1994 Jan; 34(1):87-9

40. Harold L. Rekate, M.D., W. Bruce Cherny, M.D. Pathophysiology, Diagnosis, and Clinical Features of Hydrocephalus in Infants and Children. George T Tindall, Paul R.Cooper, Daniel Barrow. The Practice Of Neurosurgery, 1996; Volume III. Chapter 179; 2679-2705.

41. Ishak MA, Groschel DHM, Mandel GL et al: Association of slime with the pathogenicity of coagulase negative staphylococci causing nosocomial septicemia. J Clin Microbiol 22:1025-1029,1985.

42. Jagadish Chander. Laboratory Diagnosis of Fungal Diseases, Section I. 2nd edn., 2002; 40-53.

43. James HE, Waish JW, Wilson HD, Connor JD, Bean JR, Tibbs PA.

Prospective randomized study of theraphy in cerebrospinal fluid shunt infection. Neurosurgery 1980; 7:459-463.

44. James HE, Waish JW, Wilson HD, Connor JD. The management of cerebrospinal fluid shunt infections- a clinical experience. Acta Neurochir (Wein) 1981; 59:157-166.

45. James HE, Wilson HD, Connor JD, Walsh JW Intraventricular cerebrospinal fluid antibiotic concentrations in patients with intraventricular infections. Neurosurgery. 1982 Jan; 10(1):50-4.

46. Joseph H. Piatt, Jr.Hydrocephalus Treatment. Robert H.wilkins, Setti S.Rengachary Neurosurgery. 1996; 366:3633-3643

51. Wang KW, Chang WN, Shih TY, Huang CR, Tsai NW, Chang CS, Chuang YC, Liliang PC, Su TM, Rau CS, Tsai YD, Cheng BC, Hung PL, Chang CJ, Lu CH. Infection of cerebrospinal fluid shunts: causative pathogens, clinical features, and outcomes. J. Infect. Dis., 57, 44-48,2004.

47. Kestle JR, Hoffman HJ, Soloniuk D, Humphreys RP, Drake JM, Hendrick EB. A concerted effort to prevent shunt infection. Childs Nerv Syst. 1993 Jun;9(3):163-5.

48. Keutcher TR, Mealey J.Long term results after ventriculoatrial and ventriculoperitoneal shunting for infantile hydrocephalus. J neurosurg. 1979; 50:179-186.

49. Kontny U, hofling B, Gujahr P, Voth d, Schwarz M, Schmitt HJ. CSF shunt infections in children. Infection 1993 Mar-Apr; 21(2):89-92

50. Kulkarni AV, Drake JM, Lamberti-Pasculli M**.** Cerebrospinal fluid shunt infection: a prospective study of risk factors. J Neurosurg. 2001 Jun: 94(6):1019-20

51. Wang KW, Chang WN, Shih TY, Huang CR, Tsai NW, Chang CS, Chuang YC, Liliang PC, Su TM, Rau CS, Tsai YD, Cheng BC, Hung PL, Chang CJ, Lu CH. Infection of cerebrospinal fluid shunts: causative pathogens, clinical features, and outcomes. J. Infect. Dis., 57,44-48,2004

52. Latifa T.F. Yeung M.D. Cerebrospinal Fluid Shunt Infections The hospital

For Sick Children Toronta, Ontaio Canada , May 14,1998.

53. Leake ES, Gristina AG, Wright MJ. Scanning and transmission electron microscope as tools for the study of phagocytosis of bacteria adherent to hard surfaces. J Leukoc Biol 1984;35:527-534.

54. Lowy FD, hammer SM. Staphlococcus epidermidis infections. Ann Intern med 1983; 99:834-839.

55. Mayhall, C.G., Archer, N.H., Lamb, V.A., Spadora, A. C., Baggett, J.W., wrd, J.D. and narayanan, R.K.(1984): Ventriculostomy-related infections. A prospective epidemiologic study.N.Engl. J. Med., 310,553-559

56. McCullough Dc, kane JG, Presper JH, et al. Antibiotic prophylaxis in ventricular shunt surgery. Child's brain.1980; 7:182-189.

57. McGirt MJ, Zaas A, Fuchs HE, George TM, Kaye K, Sexton DJ. Risk factors for pediatric ventriculoperitoneal shunt infection and predictors of infectious pathogens**.** Clin Infect Dis. 2003 Apr 1; 36(7):858-62.

58. Meirovitch J, Kitai-Cohen Y, Keren G, Fiendler G, Rubistein E. Cerebrospinal fluid shunt infections in children. Pediatr Infect Dis J. 1987 Oct; 6(10):921-4.

59. Miles RS, Amyes SG. Laboratory control of antimicrobial theraphy, Chapter 8. In: Mackie & Mc cartney practical Medical Microbiology. 14th edn. 1996; 151-178

60. Molke Borgbjerg B, Gjerris F, Albeck MJ, Borgesen SE. Frequency of infections after shunting of hydrocephalus. An analysis of 884 shunts. Ugeskr Laeger.1997 May 5:159(19):2867-71

61. Mollman HD, Haines SJ. Risk factors for postoperative neurosurgical wound infection. J Neurosurg 1986; 64:902-906.

62. Monica Cheesbrough. Examination of cerebrospinal fluid, Chapter 7 in District laboratory practice in Tropical Countries.Part 2.2002; 116-124.

63. Morisette I, Gourdeau M, Francoeur J. CSF Shunt infections: a fifteen year experience with emphasis on management and outcome. Can J Neurol Sci. 1993 may; 20(2); 118-22.

64. Myers MG, Schoenbaum SC. Shunt fluid aspiration Am J Dis Child 1975; 129:220-222.

65. Nelson D. Cerebrospinal fluid shunt infections. Pediatr Infect dis J 3(3):830-832, 1984

66. Noetzel MJ, Baker RP. Shunt fluid examination: risks and benefits in the evaluation of shunt malfunction and infection.J Neurosurg. 1984 Aug; 61(2):328-32

67. Odio C, McCracken GH, Nelson JD: CSF shunt infections in pediatrics. Am J Dis Children ,1984; 138: 1103-1108.

68. Patrick A. Roth, Alan R. Cohen: management of hydrocephalus in infants and children. George T. Tindell, Paul R. Cooper, Daniel L. Barrow. The practice of Neurosurgery, 1996; Chapter 180, 2707-2728.

69. Paul. M. kanev Jonas M. Sheehan. Reflections on Shunt infection. Pediatr Neurosurg 2003; 39: 285-290.

70. Pezotta S, Locatelli D, Bonfantifogliarini R, Bruschi L, RondiniG. Shunt in high-risk newborns. Child's Nerv System 1987; 3; 114-116.

71. Pope IK, Quinn MW, Bayston R. Morbidity and outcome of shunted hydrocephalus. Z Kinderchir. 1990; 45:29-31.

72. Pople IK, Bayston R, Hayward RD. Infection of cerebrospinal fluid shunts in infants: a study of etiological factors J Neurosurg. 1992 Jul; 77(1):29-36

73. Raimondi AJ, Robinson JS, Kuwarmura K. Complications of ventriculo-peritoneal shunting and a critical comparison of the three-piece and one-piece systems. Child's brain 1977; 3:321:342.

74. Renier D, LacombeJ, Pierre-kahn A, Sainte-Rose C, Hirsch JF, Facyors causing acute shunt infection. Computer analysis of 1174 operations. J neurosurg.1984 Dec; 61(6):1072-1078.

75. Rotim K, Miklic P, Paladino J, Melada A, Marcikic M, Scap M. Reducing the incidence of infection in pediatric cerebrospinal fluid shunt operations Childs Nerv Syst. 1997 Nov-Dec; 13(11-12):584-7

76. Rubin RC, Ghatak NR, Kisudhipan P. Asymptomatic perforated viscus and

Gram negative ventriculitis as a complication of valve regulated ventriculoperitoneal shunts. J Neurosurg 1972; 37:616-8.

77. Rush DS, Walsh JW, Belin RP, Pulito AR. Ventricular sepsis and abdominally related complications in children with cerebrospinal fluid shunts. Surgery 1985 Apr; 97(4):420

78. Sarguna P, Lakshmi :Ventriculoperitoneal shunt infections. Indian J Med Microbiol. 2006 Jan; 24(1):52-4.

79. Schmidt K, Gjerris F, Osgaard O, Hvidberg EF, Kristiansen JE, Dahlerup B, Kruse-Larsen C. Antibiotic prophylaxis in cerebrospinal fluid shunting: a prospective randomized trial in 152 hydrocephalic patients.Neurosurgery. 1985 Jul; 17(1):1-5

80. Schoenbaum Sc, Gardner P, Schillito J. Infections of cerebrospinal fluid shunts: epidemiology, clinical manifestations, and therapy. Infect Dis May; 131(15):543-52

81. Sells CJ, Shurtleff DB, Loeser JD. Gram –negative cerebrospinal fluid shunt-associated infections. Paediatr 1977; 59:614-618.

82. Shaprio S, Boaz J, Kleiman M, Kaisbeck J, Mealey J. Origin of organisms infecting ventricular shunts. Neurosurgery. 1988 may; 22(5); 868-72

83. Shurtleff DB, Stuntz JT, Hayden PW. Experience with 1201 cerebrospinal fluid shunt procedures. Pediatr Neurosci. 1985-86; 12(1):49-57.

84 Singhal S, Mathur T, Khan S, Upadhyay DJ, Chugh S, Gaind R, RattanA:Evaluation of methods for AmpC beta-lactamase in gram negative clinical isolates from tertiary care hospitals. Indian 2005 Apr; 23(2):120-4.

85. Spanu G, Karussos G, Adinolfi D, BonFanti N. An analysis of cerebrospinal fluid shunt infections in adults. A Clinical experience of twelve years. Acta Neurochir (wein). 1986; 80(3-4):79-82

86. Stamos JK, Kaufman BA, Yogev R. Ventriculoperitoneal shunt infections with Gram negative bacteria. Neurosurgery 1983; 33:858-62.

87. Stephen J. Haines. Shunt infections. Principles and Practice of Pediatric Neurosurgery. Edited by L.Albright, I.Pollack, and D.Adelson, 1999;1177-1185.

88. Sugarman B. Infections and prosthetic devices. Am J med 1986; 81(suppl):78-84.

89. Venes JL . Control of shunt infections-report of 150 consecutive cases.J Neurosurg 1976; 45; 311-314.

90. Venes JL. Infections of CSF shunt and intracranial pressure monitoring devices. Infect Dis Clin North Am. 1989; 3:289-299.

91. Wald SL, McLaurin RL. Cerebrospinal fluid antibiotic levels during treatment of shunt infections.J Neurosurg. 1980 Jan; 52(1):41-6.

92. Walters BC. Cerebrospinal fluid shunt infections. Neurosurg Clin North Am. 1992; 3:387-401.

93. WaltersBC, Hoffman HJ, Hendrick EB, Humphreys RP. Cerebrospinal fluid shunt infection. Influences on initial management and subsequent outcome. J Neurosurg. 1984 May; 60(5):1014-21.

94. Williams DG, Hayes J, McCools. Shunt infections in children: Presentation and management. J. Neurosci. Nurs. 1996 Jun, 28(3): 155-162.

95. Yogev R. Cerebrospinal fluid shunt infections; a personal view. Pediatr Infect Dis J 1985;4:113-118.

96. Young RF, Lawner PM Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. J Neurosurg. 1987 May; 66(5):701-5

97. Younger JJ, Christensen GD, Bartel DL, Simmons JCH, Barret FF. Coagulase-negative staphylococci isolated from cerebrospinal fluid shunts: importance of slime production, species identification, and shunt removal to clinical outcome. J Infect Dis 1987; 156:548-554.

98. Ziemmrli W, Waldvogel FA, Vandaux P, Nydegger UE. Pathogenesis of foreign body infection: description and characteristics of an animal model. J Infect Dis 1982; 146:4:487-497.

PROFORMA

A STUDY ON VENTRICULOPERITONEAL SHUNT INFECTIONS

Name : No :

Age : Sex :

Address :

History of Presenting illness

H/o. Fever

H/o. Seizures

H/o. Disturbed consciousness

H/o. Hydrocephalus

H/o. Abdominal signs - fullness, pain, vomiting, poor appetite

H/o. Septic Shock

H/o. Incessant Cry

H/o. Shunt dysfunction

H/o. Underlying pathology like brain tumour, ICH, SCH, Craniotomy, Head injury

H/o. Use of antacid and H_2 blocking agents

H/o. Previous shunt revision

Date of Shunt Procedure Done:

Duration between shunt insertion
and shunt infection

O/E

General Examination

Consciousness

Pupils equally reacting to light

Anterior fontanelle

Head circumference

Heart rate

Sensory system

Motor system

Cranial nerve examination

Local examination

Erythema or induration along the shunt tract

Wound changes

Investigations

I. Biochemical analysis
CSF - Glucose, proteins and Pandy's test for globulin

II. CSF Cell count - Total count and differential count

III. Microbiological study

i) CSF or shunt tip
   a) Direct Gram stain
   b) Culture and sensitivity - aerobic, anaerobic and fungal

ii) Blood - Culture and sensitivity

iii) Skin surface swabs for endogenous source of infection - culture and sensitivity.

iv) Environmental samples for exogenous source of infection - culture and sensitivity.

Follow up of the patient:

i) History of relapse

ii) History of recurrence

iii) Outcome