1996

UWOMJ Volume 66, No 1, Winter 1996-97

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Paediatrics

INSIDE:
- Paediatric Radiology
- Stress Reactions
- Turner's Syndrome
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Journals, like fashions, change with the times.

At its debut in 1930, the UWO Medical Journal was a paperback-sized volume of about 50 pages, devoted mainly to scientific review articles and, somewhat later, research abstracts and book reviews. Its advertising emphasized medical supplies, including golf clubs, “elixirs”, and the “highly palatable” quick-energy beverage, Vi-Tone. Among the Journal’s early contributors were some unknowns who later rose to celebrity, notably Murray Barr of “Barr-body” fame, who wrote several articles as a student and fledgling physician, including a charming piece on moulding brain models out of clay as a way of learning neuroanatomy.

The Journal’s original format and spare, elegant design survived with only minor changes through the Great Depression and World War II. But by the early fifties, its clinical austerity was softened by a regular feature called “In a Lighter Vein”, which offered local medical humour and poetry. Seldom anthologized, much of this poetry can be found only in the back issues of the Meds Journal. Starting about 1965, the Journal passed through a rapid series of metamorphoses, changing its look almost yearly until, in the late eighties, it had slimmed down to 10 or 15 pages, with sports roundups, social calendars and comics pages called “In Stitches” and “Leisure Seizures”.

Then came a major change behind the scenes. Since its inception, the Journal had been published by the Hippocratic Society, now known as the Hippocratic Council. But in the early nineties the Journal became independent of the Council. Under the new regime, the page count grew, there was a renewed emphasis on educational articles, and each issue was built around a special feature topic to provide a focus. At the same time, we acquired Willow Press as our printer and our advertising was contracted out to View-an-Ad, thus guaranteeing the funds to publish two issues a year.

These changes have resulted in a series of excellent publications. But they have also limited involvement in Journal activities to a handful of students. Moreover, almost all of the articles we have received in recent years have been scientific or clinical. While this type of article will continue to be a focus of the Journal, we have now taken steps to expand our scope by establishing regular columns on Promotion and Prevention, History of Medicine, Ethics, and Medical Myths. The first installment of Promotion and Prevention appears in this issue, and all four columns should be up and running in the next edition. We have brought on four new staff members to seek out and edit material for these sections, but we want to enlarge our contributor base much further, by inviting articles from other faculties or even from outside the University, and by inciting more of our readers to make their marks on these pages.

For the future, we aim to computerize further the Journal’s operations, and to establish a peer-review procedure, which will improve the quality of the contributions and will also expose students to the real-world process of publishing a scientific paper. I hope that all these changes, in the works and yet to come, will increase participation in the Journal and make it a wider forum for the enlightenment of the medical community on scientific, ethical and historical topics.

Our next issue will feature New Technologies in Medicine. If you are interested in writing or doing graphics on this topic, or for any of the regular sections, please contact me or one of the other editors. When your piece is published, mention it in your CV. I urge you to follow Dr Murray Barr’s footsteps to greatness by contributing to the UWO Medical Journal.

Cindy Hawkins,
Editor

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AN INTERVIEW WITH MEDICAL GENETICIST
DR JACK JUNG

by Lisa A. Calder BScH, Meds 2000

“Do you like dinosaurs?” the doctor asks the little boy. A timid 7-year-old sitting on his mom’s lap silently nods.
“What kind of dinosaur is this one?” - Dr Jung points to a model on his desk.
“A long neck”, the child triumphantly replies.
And so a bond is made.

- Dr Jung in the midst of a day of clinical practice at the Regional Medical Genetics Centre (RMGC) of the London Health Science Centre, Westminster Campus.

Medical genetics may not be the first specialty that comes to mind when pondering the possibilities of a career in medicine. Dr Jung hopes that this is changing. Through this interview, one gets a sense of the excitement of being in a ground-breaking field that successfully combines many clinically fascinating issues with fundamental biological questions. This is a profile of a man who truly loves his work as a medical geneticist.

Dr Jack Jung is the director of the Regional Medical Genetics Centre (RMGC), an institution which works in partnership with many programs of the London Health Sciences Centre. He is also a father to two beautiful girls, aged 3 and 7, whose picture he proudly displays in his office. Chat with him for a while, and you’ll soon discover he is also an avid fan of fly fishing.

HOW TO BECOME A MEDICAL GENETICIST 101

Dr Jung began his undergraduate career in the early seventies at the University of British Columbia in a general biology program. His first introductory course to genetics was taught by Dr Tony Griffiths, former president of the Genetics Society of Canada, whose clarity in the presentation of persuasive logic was apparently captivating. Dr Jung was encouraged by Dr Griffiths and another prominent geneticist, Dr David Suzuki, to enter into a program of genetic science. After completing an honours degree in genetics, Dr Jung embarked on what he terms an “adventure” at the University of Calgary in the undergraduate medical degree program. At the time, the medical school was in its infancy; beginning a new curriculum that emphasized self-directed learning to such a degree that examinations were non-mandatory. Students were obliged to write a comprehensive exam at the end of their third year in the program; but the freedom to pursue one’s own learning objectives was much enjoyed by Dr Jung. Upon completing his MD, he pursued specialty training in paediatrics, following which he was invited by Drs Judith Hall and David Smith at the University of Washington to train in medical genetics. Equipped with a Canadian Medical Research Council post-doctoral fellowship, Dr Jung moved to Seattle.

Monoclonal antibodies became the focus of his research in Seattle, as he worked towards identifying specific differentiation proteins hypothesized to be involved in the development of stem cells. The model used for testing this hypothesis was the switching of foetal haemoglobin to adult haemoglobin. Basic science research impressed him and he marvels at how “it is still a major challenge to try and understand very basic biological phenomena”.

Following his fellowships, he eventually found his way to London. He was attracted to London because of its relatively small size, allowing for professional development and the possibility to effect a significant impact. Having now been here for 15 years, he confirms he undoubtedly made the right choice: “It’s a sense of balance that holds me here...balance of personal life with professional, balance within professional work between clinical and academic work and teaching...”

CLINICAL RESEARCH - RELATING CLINICAL SCENARIOS TO BIOLOGY BASICS

Indeed Dr Jung does balance a variety of roles: clinician, teacher, administrator and researcher. The major thrust of Dr Jung’s research has been clinical dysmorphology. He contends that while many associate this area with the study of very rare genetic syndromes, “I feel very strongly that these challenging clinical scenarios are important links to questions of basic (science) research...” He explains that clinical dysmorphology involves the recognition of unusual developmental problems as distinct clinical entities, that
in alliance with basic science can be explored at the molecular level. Dr Jung comments that, "through the use of a combination of molecular, biochemical, and cytogenetic techniques, scientists have been able to link genes to clinical phenotypes identified by clinical dysmorphologists." Dr Jung also pointed out that this kind of knowledge is essential to developing potential therapies for these genetic conditions.

Other avenues of Dr Jung's research have included several studies related to neurofibromatosis (NF), an autosomal dominant disease characterized by subcutaneous benign tumours and cafe-au-lait spots. His work with his colleagues in this area has included characterizing a mutation of the NF-1 gene, developing a polymerase chain reaction (PCR) based approach to molecular and prenatal diagnosis of NF-1 and clarifying the relationship between familial segregation of phenotype and mutations of the NF-1 gene.

Further recent work has looked at the cardiac screening of children with Down's syndrome and, in another study, the genetic predisposition for the severity of foetal alcohol syndrome. In addition, the RMGC is currently involved in a large multicentres clinical trial dealing with breast cancer, that is funded by the American National Institutes of Health. One of the objectives of the trial is to determine the regional frequency of the various types of mutations of BRCA1, a recently discovered breast cancer gene. While the study is anticipated to run for 3-4 years, Dr Jung says that the RMGC and London Regional Cancer Centre have already enrolled over 100 families with a very high incidence of familial cancer. They are currently undergoing genetic analysis.

SOME OF THE PARAMETERS OF CLINICAL GENETICS PRACTICE

While Dr Jung is very involved in genetics research, he indicates that his true love remains with clinical work and teaching. Over the years, many of the exciting advances in genetics have had far-reaching implications. Dr Jung's practice of medical genetics has evolved from being primarily oriented toward paediatric issues to encompassing a significant adult population, who present with questions about familial, hereditary and late onset cancers or neurodegenerative diseases. He also notes that prenatal counselling is evolving and has to keep pace with the rapid developments in very disease-specific molecular genetic technologies.

Another important component of his practice as a medical geneticist is genetic counselling: "I don't think there is any great mystique to genetic counselling - it is based on good principles of medical practice. When patients or families present themselves to a doctor, it's that process of imparting information so that it's understandable to the patient and the family that is important."

SHARING KNOWLEDGE WITH THE NEXT GENERATION

One of the keys to successful genetic counselling is good communication. In observing him interact with his patients and their families, it is clear the Dr Jung is a gifted communicator. This also comes across in the genetics course he teaches in Phase I of the undergraduate medical program at the University of Western Ontario. Dr Jung structures the course such that fundamental genetic principles are illustrated through actual discussions with patients during lectures.

"My personal teaching philosophy is to show real life situations that will help the students understand why the basics need to be understood (for example a biochemical pathway or the structure of DNA). When students get a chance to be faced with real questions being posed by these individuals, it gives importance and relevance for the need to understand basic aspects of biology."

In listening to their stories and watching Dr Jung interact with his patients, first year students are learning about the importance of good communication as well as the basics of genetics. The impact Dr Jung has had on his students is reflected in the teaching awards he has received from the UWO Faculty of Medicine and Department of Paediatrics.
WHAT DOES THE FUTURE HOLD?

When asked what he thinks will be "hot" in genetics in the near future, Dr Jung suggests that some of the research focus will shift from monogenic disorders to polygenic, multifactorial diseases such as the hyperlipidemias, diabetes and hypertension. In addition the fundamentals of cell differentiation and the process of embryological development need to be further understood. Finally he believes genetic diagnostics will expand and develop even more rapidly and that increasing opportunities for gene therapy are not far off the horizon.

In personal terms, one of Dr Jung's future goals is to increase his involvement in medical education. His contagious excitement about his specialty is something he hopes to be able to pass on to others.

"I've always considered myself extremely fortunate because within my chosen specialty, you see clinical problems that frequently pose relevant questions in terms of basic science - it's a bridge that you can't get away from in clinical medidal genetics practice... (It's) more challenging to try and make this connection and I hope more of the younger generation will pursue this..."

HISTORY OF THE REGIONAL MEDICAL GENETICS CENTRE (RMGC), LONDON HEALTH SCIENCES CENTRE

1921-1945 • Dr Madge Macklin provides advice to local physicians on genetic matters. After publishing over 100 genetic-related articles, she is recognized as a pioneer in medical genetics in North America and is elected president of the American Society of Human Genetics in 1959.

1949-1969 • Dr Murray Barr publishes a neurohistological study identifying the sex chromatin body (Barr body) and pointing to its clinical significance. Over next 20 years he brings international recognition to the University of Western Ontario as Dr Barr is established as one of the founders of human cytogenetics.

1965 • One of Ontario's first cytogenetics laboratories is instituted at Victoria Hospital.

1972 • A Genetic Counselling Clinic is established in the Department of Paediatrics at the new University Hospital.

1974 • The Birth Defects Evaluation Clinic is founded at the Victoria Hospital to provide prenatal counselling and genetic amniocentesis.

1980 • UWO Regional Medical Genetics and Birth Defects Service is based at CHWO on South Street. (The service later becomes known as the Regional Medical and Molecular Genetics Program of the London Health Sciences Centre)

1981 • UWO RMGC is accredited for the first time as a "major centre for service" by the Canadian College of Medical Geneticists.

1982 • Windsor Genetics Clinic is established as a direct outreach clinic of the RMGC.

1995 • 420 different physicians in the Southwestern Ontario Region referred patients, couples or families to the RMGC.

1996 • RMGC has seen more than 20,000 patients. The rate of growth in numbers of referred patients has averaged between 15 and 20% in each of the 16 years since the centre was founded.

A stitch in time saves nine" is the central thrust of preventive medicine. It is much easier to employ preventive measures than to deal with the often messy consequences of an uncontrollable disease process. Therefore, if a disease process can be slowed or controlled during the early stages of life, severity of illness can be drastically reduced later on. The paediatrician's role is therefore key to the management of many diseases, not the least of which is cardiovascular disease, which is theoretically preventable by changing certain lifestyle patterns. Healthy habits such as exercise and proper diet, and the avoidance of unhealthy habits such as smoking, should be lifelong lifestyle patterns which should be firmly entrenched as early as possible.

Coronary heart disease is the leading cause of death in North America, responsible for over 500,000 deaths annually. Surprisingly enough, even though these numbers are not typically associated with the paediatric population, deaths are rarely due to a sudden pathological process. Rather, it is the endpoint of a lifetime of damage, a disease process that begins in childhood and early adolescence. It has long been known that fatty streaks, thought to be the pathologic precursors of atherosclerotic plaque, appear in childhood. Young American soldiers who died in the Korean war were shown at autopsy to have disseminated evidence of atherosclerosis. This implies that aggressive early intervention is necessary to fight a disease that spans many decades in its course.

Cholesterol screening has been suggested, although not without controversy, as an early measure to identify candidates for cholesterol-lowering diets. This is controversial due to the fact that cholesterol levels may be high in childhood yet normal and without any pathological consequences later in life. It should nevertheless probably be implemented because a healthy diet early in childhood can have few if any deleterious effects, while promoting healthy lifestyle habits for the future.

Although childhood hypertension is not common, prevention still must be a concern for those who care for children. Children who are obese have higher blood pressure than their lean counterparts. Measures to address the prevention of hypertension should focus on appropriate dietary measures, including reduction of fat and salt. Furthermore, regular aerobic exercise plays an important role in the prevention of hypertension.

Circulating blood lipid levels, cholesterol, physical inactivity, smoking and obesity should all be actively targeted by paediatricians, parents and school administrators. Healthy dietary patterns in children can greatly decrease the risk of heart disease, and therefore nutritional education at home and in school should be a prime concern. To this end, a student organization known as "Health Matters", established by UWO medical students, is planning to engage in a nutritional education program in local elementary schools. Their aim is not simply to inform, using the conventional didactic approach involving the four food groups, but also to change behaviours and attitudes about nutrition through the use of small group teaching. A family-oriented approach including practical nutritional teaching (label reading and recipe modification) combined with behaviour contracting techniques, and an exercise program has proven successful in the modification of cardiovascular risk factors, including being overweight.

Habitual cigarette smoking, tobacco use, and alcohol consumption are reported in one-third of adolescents and young adults. These habits have their roots in early childhood. (Tobacco companies realize that their customer base is dying, and that in order to maintain profits they must recruit a young generation of smokers.) Tobacco companies in the United States have used advertising that appeals to young people. The adorable cartoon figure of 'Joe Camel' portrays to children and young adolescents that smoking is 'cool' and adorable. Even the Marlboro Man appeals to young adolescents through the use of 'cool' images linked to smoking. Legislation in Canada is aimed at limiting cigarette advertising in general, and specifically at limiting marketing ploys aimed at children and young adolescents. Parents, teachers, legislators and paediatricians should collaborate to ensure that the youngest of our population do not succumb to the pitfall of smoking. In young men who die in accidents, the increased occurrence of atherosclerotic lesions in those who smoked tobacco compared with those who had similar cholesterol levels but did not use tobacco demonstrates the need for early intervention.

Paediatricians can also discourage smoking in parents, as passive smoking can also have deleterious consequences. Physicians should take an active role in educating children about the harmful and addictive nature of smoking.

Physical inactivity has become of increasing concern as our society becomes more electronic and consequently sedentary. Physical activity should be promoted at school, not only through physical education, but also through the encouragement of an active lifestyle by parents and physicians. An association has been found

ABOUT THE AUTHOR

Dennis Klironomos is presently a first-year medical student at UWO. Before entering medical school, he completed a Bachelor of Science degree in Anatomy at McGill University.
between viewing television more than 2 hours per day, poor dietary habits, and elevated cholesterol levels in children. Television viewing should be limited to 2 hours or less per day, with a policy of no eating or drinking while watching programs. Furthermore, at least 30 minutes of physical activity 3 days per week, in addition to that obtained from school physical education programs, is essential.

Health promotion and disease prevention is probably as old as the practice of medicine itself. In recent history, the prevention of infectious disease through the use of vaccines, antibiotics and improved antiseptic procedures has been remarkably effective. Almost every new HIV infection is entirely preventable, either through the use of sterile needles, condoms or community-based educational programs about HIV transmission. Thus the importance of preventive medicine cannot be overemphasized. If one contrasts the high cost of hospital care after myocardial infarction with the small price of nutritional counselling, it becomes very evident that primary care and prevention can be the most cost-effective strategy in the promotion of cardiovascular health.

REFERENCES

INTERVENTIONAL RADIOLOGY IN A MODERN HOSPITAL SETTING

by Dimitrios Papadouris, Meds '98

INTRODUCTION

Interventional radiology is a relatively new discipline that offers many services. It has emerged in the last 15 years to provide alternatives to many surgical procedures. The benefits of interventional procedures include local anaesthesia and sedation instead of a general anaesthetic, shorter recovery periods, lower cost and the ability to treat ill patients who are not surgical candidates. Unfortunately, medical education has lagged behind these advances and the majority of medical students, while exposed to diagnostic radiology, are unaware of interventional radiology and the services that it provides. Thus, the focus of this article is to give medical students and clinicians a simple, comprehensive overview of the field.

PERIPHERAL ANGIOGRAPHY AND VASCULAR INTERVENTIONS

The roots of modern interventional radiology are in cardiovascular procedures. Peripheral angiography, first performed in the 1920s, was neither practical nor in widespread use until the 1950s, when the Seldinger method was introduced. Since then, angiography has developed from a purely diagnostic procedure to one that also allows therapeutic interventions. Angioplasty has complication rates lower than surgery and patency rates, in properly selected patients, that are equivalent to those achieved with surgery.

Angiography is used to diagnose primary vascular disease such as vaso-occlusive disease; to define the anatomy in arteriovenous malformations or aneurysms; and to localize small vascular tumours such as pancreatic insulinomas or parathyroid adenomas. Moreover angiography is performed prior to any therapeutic vascular procedure such as balloon angioplasty, thrombolysis, embolization, chemoembolization, stenting or atherectomy. Presurgical angiography is also performed to establish the vascular anatomy before tumour resections, transplants and revascularization procedures.

The absolute contraindication to any of the above procedures is a medically unstable patient. Other relative contraindications include recent myocardial infarct, coagulopathies and pregnancy.

In therapeutic angiography, the tools at the disposal of the radiologist are the angioplasty balloon, and more recently stents and covered stents. Most experience with percutaneous transluminal angioplasty (PTA) has been in the lower extremities and aortoiliac region. Vascular lesions have been classified into four categories ranging from category 1 where balloon angioplasty is the treatment of choice to category 4 where surgery is preferred. This classification is based on the nature of the lesion (stenosis vs. occlusion), its location, and its length. Endovascular stents make many category 3 and 4 lesions amenable to percutaneous therapy. Stents are also used when there is an unsatisfactory PTA result, as is the case in elastic recoil or intimal dissection.

Angioplasty techniques have recently been applied to the arteries of the head and neck. Carotid angioplasty is at present reserved for cases of surgical failure or high risk patients that are not surgical candidates. Vertebral artery angioplasty is successful in properly selected patients with lesions at the origin of the vertebral artery and can be the treatment of choice for these lesions.

Interventional procedures in trauma were classically restricted to diagnostic angiography. Following the institution of less invasive tests such as CT, the use of diagnostic angiography in this setting decreased. At present, therapeutic interventional procedures have a role in selected trauma patients with internal hemorrhage. The goal of arterial embolization therapy is to stop bleeding and stabilize the patient. The use of covered endovascular stents for this purpose has also been described in some centres. The major limitation in the performance of these procedures is the availability of a skilled interventional team, with a rapid response time, 24 hours a day, in an appropriately equipped level 1 trauma center. As the benefits of emergency interventional radiology become apparent, the availability of these services will become more widespread.

Other indications for transcatheter artery embolization, outside the trauma setting, include bronchial artery hemorrhage, obstetrical hemorrhage, gastrointestinal bleeding, arteriovenous malformations, testicular varices, bone tumours, high-flow priapism and chemoembolization of liver tumours.

CENTRAL VENOUS ACCESS

Modern medicine often requires venous access for therapy and diagnosis (blood tests). Therapies that require central venous access (CVA) include haemodialysis, total parenteral nutrition and chemotherapy for microbial or neoplastic disease. As the indications for these therapies continue to increase, the use of CVA will increase.

ABOUT THE AUTHOR

Dimitrios Papadouris is a third year medical student at the University of Western Ontario with a B.Sc. in biochemistry from the University of Toronto. Mr. Papadouris is interested in radiology as a career and has a specific interest in interventional radiology.
Although CVA catheters have traditionally been inserted by surgeons in the operating room (OR), present standard practice in most institutions is to place these catheters radiologically. Advantages of radiological placement over surgical placement include a shorter waiting time (usually less than 24 hours), quicker recovery because general anaesthetics are avoided, and lower cost to the institution because radiological suites do not have the overhead of an OR and a recovery room.

CVA catheters can be placed in various sites including the antecubital veins (usually short-term), subclavian veins, internal jugular veins, hepatic veins and inferior vena cava. The selected route depends on the type of catheter, anticipated duration of access requirement and most importantly, the availability of suitable patent veins.\(^9\)

The long-term CVA catheters used at present have either a subcutaneous tunnel or are attached to a subcutaneous port. The catheter is placed in two steps. First, venous access is achieved using standard percutaneous access techniques and a sheath is placed in the vein. The catheter is then tunnelled subcutaneously and placed in the vein through the sheath. When placing a port, a pocket is created subcutaneously for the port and then the catheter is tunnelled and placed as before.\(^9\)

With the present use of CVA catheters no longer confined to an inpatient setting, outpatients continue with activities of daily living while a CVA catheter is in place. This type of stress has forced catheter design to be improved, reducing thrombotic and infectious complications of long-term CVA.\(^9\)

**GASTROINTESTINAL INTERVENTIONS**

One of the most common GI interventional procedures is placement of gastrostomy or gastrojejunostomy tubes. These procedures are preferentially performed radiologically as surgical placement is associated with delay in starting feedings, increased incidence of aspiration, wound infection and the possibility of a temporarily delayed gastric emptying time.\(^5\)

The major indication for placing a gastrostomy or gastrojejunostomy tube is to provide nutritional support in patients capable of absorbing nutrients enterically when mechanical or functional disorders (e.g. head and neck lesions, neurological disorders) do not allow adequate feeding by mouth.\(^5,10,11\) Other indications include decompression in small bowel obstruction and in conditions associated with decreased gastric motility.\(^5\)

Contraindications for this procedure include the presence of a ventriculoperitoneal shunt (absolute), bleeding disorders, difficult percutaneous access, massive ascites, gastric wall lesions and abdominal varices.\(^5\)

Other GI procedures include caecostomies in children with faecal incontinence and dilatation of enteric strictures. In malignant dysphagia, dilatation of the oesophagus may palliate otherwise inoperable carcinomas of the oesophagus. Other diseases, including primary lung cancers and mediastinal masses, can also compromise the oesophageal lumen. Oesophageal dilatation and covered stent placement, not in widespread use at present, improve quality of life in patients with oesophageal dysphagia and oesophagorespiratory fistula.\(^12\)

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BIOPSY

One of the most frequently performed procedures in interventional radiology is the image-guided needle biopsy. This technique can be used to sample most lesions in the chest, abdomen, pelvis, soft tissues and retroperitoneum. Guidance for biopsy procedures is provided by ultrasound, computed tomography (CT), fluoroscopy, or combinations of the above. Success rates for radiological biopsies are typically very high and complication rates are low because of the use of small calibre needles. In a large series by Parker et al., adequate tissue for histology was obtained in 97% of cases and sampling of target tissue was obtained in 92% of cases when using a biopsy gun.

ABSCESS DRAINAGE

The development of percutaneous drainage as a first-line treatment of abscesses is partially due to advances in cross sectional imaging. Ultrasound and CT can document a safe access route to an abscess, allowing the interventionalist to avoid vital structures while approaching deep seated collections. Successful percutaneous drainage can be attained for abscesses in pelvic, pancreatic, retroperitoneal, hepatic, subphrenic, thoracic, splenic and musculoskeletal locations. Although previously viewed as contraindications to percutaneous treatment, the presence of multiple abscesses, loculations or enteric communications do not preclude treatment radiologically at present. Other types of abscesses which previously would not have been treated percutaneously include lymphoceles, empyemas and amoebic or echinococcal abscesses. When performing fine needle aspiration of an abscess for diagnostic procedures, organs and bowel may be crossed but when placing a drainage catheter a direct access route is preferred. Other patient conditions which require care are coagulopathies and access requiring the transgression of the pleural space.

Most abscesses can be cured with percutaneous therapy. Benign cysts treated percutaneously will often recur and require sclerotherapy to ablate their secretory surfaces. Some complicated abscesses which are multilocular, purulent, contain necrotic tissue or have enteric communications may not be curable by percutaneous means. This situation most often occurs in patients with pancreatic abscesses, or abscesses caused by leaks from enteric anastomoses. In these cases percutaneous therapy is of temporizing benefit, helping the patient recover from the acute illness and allowing the surgeon to plan a definitive surgical cure electively.

BILIARY AND GALBBLADDER INTERVENTIONS

Endoscopic retrograde cholangio-pancreatography (ERCP), performed by endoscopists, is the preferred method for visualizing the biliary ductal system and placing stents for biliary ductal obstruction. When this procedure is unsuccessful or not possible, percutaneous transhepatic cholangiography (PTC) is performed. Although more invasive, PTC offers superior resolution of anatomic abnormalities in the biliary system when compared to other radiological methods (e.g. CT, US or nuclear medicine).

The actual procedure involves placing a needle into an intrahepatic bile duct and then injecting contrast to delineate the ducts. This procedure is easier in a patient with a dilated biliary system but can be accomplished in 85-90% of patients with non-dilated ducts. As biliary infection is prevalent in patients with biliary obstruction, it is important to provide adequate antibiotic coverage with broad spectrum prophylactic antibiotics.

If a PTC shows a biliary obstruction, one can proceed to drain the biliary system percutaneously. Percutaneous drainage is designed to relieve biliary obstruction and associated jaundice, pruritis, biliary sepsis or cholangitis. To achieve drainage, a catheter can be placed in the biliary system through to the duodenum past the obstruction. These catheters have side holes that are positioned above and below the obstruction. Endoprostheses, which achieve drainage in the same manner but are completely internal, can be placed radiologically or endoscopically. The drawback to endoscopic stenting is that often the endoscopist cannot traverse the stricture. In these cases a rendezvous procedure is done where the radiologist places a guidewire percutaneously across the stricture into the duodenum and the endoscopist then inserts the internal stent over this wire.

Biliary stone removal can also be done percutaneously. Both common duct stones and intrahepatic duct stones can be removed using basket extraction, injected dissolvants and cholangioscopic lithotripsy through a percutaneous tract. Transhepatic basket extraction and lithotripsy procedures are done in two stages with a tract being created by using a T tube, allowing this tract to mature for 5-6 weeks and then actually removing the stone.

In the gallbladder, percutaneous cholecystostomies are performed. Indications for cholecystostomy include: drainage of purulent material in a patient who is a poor surgical risk; unexplained sepsis with an abnormal gallbladder on US; to stabilize a patient prior to cholecystectomy; or to remove gallstones. Less commonly, biliary drainage can be achieved in a patient who has a blockage downstream from the cystic duct.

GENITOURINARY INTERVENTIONS

Just as percutaneous transhepatic cholangiography is the initial step in biliary interventions, percutaneous nephrostomy (PN) is the initial step in genitourinary intervention. The PN can be used to drain the renal collecting system in the setting of pyeloureteral obstruction or sepsis. It is also used to gain access to the collecting system for the placement of ureteral stents or to divert urine from the ureters, allowing healing following ureteral injury or fistula.

In the treatment of renal stones, extracorporeal shock wave lithotripsy is the method of choice. In cases of large stones or when complications from
extracorporeal therapy occur (ureteral obstruction), percutaneous intervention is indicated. A PN can be used to debulk large stones prior to lithotripsy and can also provide a passage for fragments post lithotripsy.  

Other aspects of renal intervention include biopsy of lesions, treatment of cysts or abscesses and treatment of post renal transplant complications. All of these indications involve percutaneous methods mentioned previously.

CAVAL AND PORTAL VENOUS INTERVENTIONS

Two procedures which have gained popularity recently are percutaneous placement of inferior vena cava (IVC) filters and transjugular intrahepatic portosystemic shunts (TIPS).

Indications for IVC filters include the patient who is refractory to, or has complications associated with, anticoagulant therapy and poses a significant risk of developing a pulmonary embolus. The placement of these filters percutaneously is a straightforward procedure that can be life saving. A recent advancement is the use of temporary or retrievable filters which will be of benefit to patients with reversible conditions.  

Transjugular intrahepatic portosystemic shunts are indicated for portal hypertensive haemorrhagic complications, intractable ascites and in Budd-Chiari syndrome. The procedure involves entering the caval system via the right internal jugular vein and advancing a guidewire into a main hepatic vein with a small calibre catheter. Then, using a needle advanced over the guidewire, the portal system is punctured intrahepatically. The final stage is balloon dilatation of the connecting tract and placement of a stent. A major problem with TIPS is a stenosis rate of 25% at 6 months and about 50% at a year. This necessitates routine follow up of the stent with Doppler US and revision of the procedure if stenosis is found.  

The role of TIPS has yet to be defined. At present it is preferentially used in high-risk patients with variceal hemorrhage who are not responding to endoscopic sclerotherapy. In the future, if long-term patency rates are improved by the use of newer methods, TIPS may have an increased role in treating lower risk patients that require portal system decompression.

CONCLUSION

In the management of the ill patient that may benefit from an interventional procedure, it is important to use the interventionalist as a consultant, much like a surgeon. This will allow the determination of the best treatment modality for the patient be it medical, surgical or interventional.

ACKNOWLEDGEMENT

The author would like to thank Dr Ray McLoughlin, an interventional radiologist at University Hospital, for his help in preparing this manuscript.

REFERENCES

As we walked into Auditorium A of University Hospital on that warm September evening, we were not dissimilar to the archetypal Tin Woodsman, Cowardly Lion, and Scarecrow from the Wizard of Oz. Overwhelmed by looming histology slides, anatomy dissections, and piles of textbooks, we lacked wisdom, heart, and courage, or at least we thought we did. Although we were promised a theatrical forum on ethics, we were unsure what to expect. What we got was a whirlwind tour through what it really means to be a doctor. In our constantly changing society, a physician cannot be cold and scientifically-minded, treating his patients like problems out of a textbook. Physicians must be caring individuals with heightened sensitivity for their patients’ needs, fears, and expectations of them. They must be able to render medical decisions in such a way as to not only accommodate patients’ medical needs, but to involve them as partners in the pursuit of their own health.

We were introduced to these issues by watching a video of a theatrical, musical performance entitled, “The Waiting Room.” The entire production, from musical score to lyrics, was developed by Western medical students under the direction of Dr. Jeff Nisker, the architect of the Yellow Brick Road program. Through song and music, we glanced into the lives of three women waiting to see a doctor. Each woman, while representing a different cultural and temporal framework, was faced by the dilemma of physical self-sacrifice in order to fulfill societal expectation. The characters featured were a modern-day American woman whose desire for physical attractiveness prompted breast augmentation and cancer fear, a Chinese woman forced by family and cultural tradition to bind her feet tightly so she could attract a potential mate, and a woman from Victorian England, who wore society’s corset and was considering oophorectomy to remove mood changes and sexual thoughts. What we witnessed was a portrait of how health-related decisions can be made in the absence of personal choice.

After the video, Dr. Nisker shared his vision of creating a dynamic, multimedia forum for the discussion of bioethical and culturally sensitive issues related to medicine. The goal is to form a program that employs presentations such as plays, literature, theatre and narrative seminars to address complex issues that we, as students and future practitioners, will face. In the ensuing discussion, the class showed a great awareness for the importance of ethical decisions and how they shape medicine. The term informed consent was left aside for the more appropriate phrase informed choice, as physicians should by no means seek to impose their wills on patients, and simply seek a signature on a consent form.

Other issues that surfaced for exploration included female genital mutilation, a common practice in many African countries affecting millions of women. This is an example of how cultures can influence personal health choices; women from these traditions often feel it their duty to undergo such procedures in the name of culturally ascribed practices. Understanding the risks and benefits of a procedure is very important, as cultural factors, gender control issues and the undue influence of role models may skew patients into making personal decisions that they do not want to make. After discussion, we arrived at key factors which we felt were essential for an informed choice. Patients must be educated about their own health concerns, display confidence to make their own choices, be independent or free from coercion, and be competent and autonomous. With these attributes, patients become empowered to make decisions that directly affect their own health. It was acknowledged by the group that it is the physician’s role to provide this empowering atmosphere for the patient.

Linked to the empowerment of the patient is the autonomy of the physician, who, as an individual, has the ability to refuse to perform a treatment such as genital mutilation based on a personal ethical choice. In times of conflict, how do physicians express their right to autonomy without appearing culturally insensitive or discriminative? From the physician’s standpoint, an attitude of placing the decision firmly in the hands of the patient should be the ideal. But, patient autonomy sometimes conflicts with social benefit and in these instances it is probably better to maintain societal values. For example, a patient requesting that her gynaecologist perform a form of female genital mutilation should be refused, even though she may then proceed to have it done under substandard and potentially dangerous conditions.

Overall, the bioethics seminar was well received. Students generally felt that there was a need to bring bioethical health issues into discussion so that they could begin to think about the complexities of their profession. It is important to state that many of the males present felt intimidated by the Waiting Room presentation. Specifically, they felt that men were portrayed to be the sole root of the medical problems that the women faced. Since historically men have controlled society’s imperatives, this juxtaposition is not unreasonable.

The high level of awareness, cultural sensitivity, and analytic ability portrayed by the students outlined the Lynch-pins of this new method of teaching: as medical students passing through a rigorous admissions process, we already possess the skills, scientific and humanitarian, to become good doctors. Just like the Tin Woodsman, Lion, and Scarecrow characters on their journey to Oz, it is simply a matter of discovering attributes within ourselves. The purpose of the Yellow Brick Road program is to maintain and foster our enthusiasm for humanity, compassion, and giving of ourselves to others. These are virtues often lost over a lifetime of board exams and hectic call schedules. Our development of clinical skills need not interfere with our development as human beings.
In this way, the Yellow Brick Road represents the next step in advancing medical education. Following the innovation of problem-based learning, the interactive, multimedia Yellow Brick Road presentations allow for the provocative exchange of ideas regarding the socio-ethical aspects of medicine. The active participation of students in program design and implementation are instrumental in ensuring that each issue becomes incorporated into our “database” of sensitivity and compassion. The philosophy is simple, education through empowerment with bioethical tools leads to a life-long awareness of sensitive issues, and this leads to better doctors. In the context of this program, Western seeks to create a generation of ethically responsible physicians.

As medical schools across Ontario continually revise and redevelop their curricula to embrace the ideals of EFPO and produce graduates who are better prepared to provide medical service to their communities, the need for a program like the Yellow Brick Road becomes apparent. In the newly rediscovered era of patient-centred medicine, this program attempts to form the student-centred curriculum. With sessions already starting to wind their way to medical schools across North America, brick by brick, the Yellow Brick Road is charting new territory and will certainly be coming to a medical school near you in the foreseeable future. Here at Western, we look forward to the upcoming Yellow Brick Road sessions, which will touch on a variety of ethical issues that we, as members of the medical community, will surely encounter in the future.

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The Vision Leader
The problems diagnosed in paediatric radiology are different from those seen in adult radiology, but the method of reading the paediatric film is very similar. An organized approach is the most important part of reading films. One approach is presented in this article, as well as common problems seen on chest, abdominal and bone films.

THE PAEDIATRIC CHEST FILM

One approach to the chest film is the ABC's. Before looking at the image, however, look in the corner at the patient information. Always make sure that you have the correct patient name and the correct date of examination. Look at the age of the patient, as certain diseases are more common in different age groups. Then go on to the ABC's: abdomen, bones (and soft tissues) and chest (lungs, airway, mediastinum, diaphragm).

ABDOMEN

Examine visible abdomen as if you were reading an abdominal film (see below).

BONES AND SOFT TISSUES

It is easy to overlook these, especially if there is a glaring abnormality in the lungs. Make sure that all normal bony anatomy, (i.e. clavicles, ribs, vertebrae) are present. Look for abnormal structure, fractures, and destruction of bone. The spinous processes of the vertebrae are not fused in children under three. Next, look for swelling, foreign bodies, and calcifications in the soft tissues of the neck, thorax, limbs and abdomen. Beware of artifacts such as clothing, jewelry and skin folds.

CHEST

1. Airway: This should be visible in all chest films, from below the nasopharynx to the carina (the division of the trachea into the right and left bronchi). Evaluate for patency, position and size. The trachea normally buckles during expiration in infants. Look for consistent narrowing of the airway, as this may be a clue to extra tracheal masses and vascular rings, as well as tracheal abnormalities. A steeple appearance of the subglottic airway on inspiration, in addition to stridor and a barking cough, is pathognomonic for croup. A thumb-like opacity on lateral views of the upper airways is seen in epiglottitis. However, this diagnosis should be made clinically; the airway may occlude in the time that it takes to radiograph the patient. The trachea lies to the right of the midline. Deviation from this position is an important clue to mediastinal masses as well as differences in hemithoracic pressure. Note the position of the major bronchi.

2. Mediastinum: This is a difficult part of the paediatric chest x-ray, primarily because the thymus obliterates many structures from view. Additionally, because of the fast respiratory rate and inability of the infant to cooperate, it is difficult to get an inspiratory film. Look for position, size and contour of the mediastinal structures. The thymus has a wavy contour and may extend from the thoracic inlet to the diaphragms. It can obscure the lung fields. It should not alter the position of any structures in the chest.

3. Heart: The heart is situated mainly in the left hemithorax. It is difficult to evaluate the heart size on the frontal film because it is not necessarily taken during inspiration. On the lateral film, draw a line from the carina straight down to the diaphragm. This line will intersect an enlarged heart. An enlarged heart will push adjacent structures such as the carina posteriorly. It may indicate congenital heart disease. Tetralogy of Fallot (overriding aorta, right ventricular hypertrophy, right ventricular outflow tract obstruction & ventricular septal defect) causes a boot shaped heart.

Figure 1: A 7-year-old boy with a clinical history of pneumonia. Note the air space disease in the right lower lobe with an air fluid level. This lung abscess resolved with treatment.
4. Great Vessels: The aortic arch and descending aorta should be on the left of the midline. Also look for the left and right pulmonary arteries situated in the lung hila.

5. Esophagus: This is posterior to the trachea. Esophageal air may be normal in the neonate, but is abnormal in older infants and children.

6. Lymph Nodes: In pathologic conditions such as lymphoma, lymph nodes may be visible in the hilar regions of the chest.

7. Lungs: The lungs are the largest and most exciting structure seen on the chest x-ray. There are two fissures in the right lung and one in the left lung. Look for any invasive tubes or monitoring equipment that may hint at the diagnosis or symptoms, and ensure that the lines are correctly placed. The left hilum is slightly higher than the right hilum, and the right hemidiaphragm is slightly higher than the left. A change in this anatomy is frequently pathologic. The heart borders should be sharply defined by the air in the lungs. Fuzzy or obscured borders indicate lung abnormalities such as pneumonia, abscess (fig 1), or atelectasis. Atelectasis results in a decrease in volume of the affected lung, and adjacent fissures will be pulled toward the affected area. Consolidation will not change the lung volume. The location of consolidated lung can be pinpointed by the disappearance of normal anatomy (i.e., the diaphragms are obscured by lower lobe pathology, the left heart border is obscured by lingular pathology, the right lower heart border by right middle lobe pathology and the upper heart borders by upper lobe pathology). The costophrenic angles should be sharp. Rounded angles indicate pleural fluid or thickening. Lung markings (white lines created by bronchi and vasculature) should be most visible in the proximal 2/3 of the lung. If a pneumothorax is present, there will be no vascular markings surrounding the collapsed lung and the perimeter of the lung can be visualized. This is best
seen on expiratory films because decreased aeration makes the lung denser (whiter) compared to black pleural air. Expiratory films are also useful to look for air trapping in foreign body aspiration (fig 2). Other, more subtle lung field abnormalities include respiratory distress syndrome (RDS) and neonatal pneumonia, which often mimics RDS. The lung fields are small, hazy, with a reticular (net-like) pattern caused by interstitial fluid and atelectasis, and there are dilated bronchi. The pattern with neonatal pneumonia is slightly coarser, with better lung expansion and pleural effusions.

THE PAEDIATRIC ABDOMINAL FILM

An orderly approach, similar to that used for the chest film, should be used for the abdominal film. There should be two views of the paediatric abdomen: supine and erect (or decubitus), as well as a frontal chest x-ray.

CHEST

Carefully review any visible chest.

BONES AND SOFT TISSUES

Look at the ribs and pelvis for fractures and dysmorphism. Ensure that the spinal column has a normal contour, particularly in the older child who may have scoliosis. Watch for areas of decreased density in the bone which might signal malignancy, but do not be fooled by overlying bowel gas. Look for the peritoneal fat line (flank stripe) on the supine film. It indicates the edge of the peritoneal cavity and will disappear if edematous (peritoneal inflammation). If the colon is gas filled, it should abut the flank stripe. Space between the two may be due to peritoneal fluid or a solid mass.

ABDOMEN

Free peritoneal air is always abnormal. It can be seen below the diaphragm and above the liver and stomach bubble on an erect film. If there are only small amounts of air, it may be easier to see it on a left lateral decubitus film as a thin line above the liver. A "football sign" may be seen; the lace of the football is the falciform ligament (normally invisible) highlighted by a football-shaped lucency of free air. The kidneys are 10-12 cm long and located at the T12-L2 level, the right being slightly lower than the left. Their outlines can be seen faintly on either side of the iliopsoas shadows. It is important to look for stones and other calcifications in the kidneys and along the path of the ureters as well as in other areas of the abdomen. Decide where the calcification is and determine its character. Ill-defined margins, irregular outline, and punctate calcifications are ominous signs, possibly indicative of malignant neoplasm. An appendicolith may appear in the right lower quadrant as a cause for appendicitis. In clinically obscure cases, appendicitis may be diagnosed by
ultrasound. A thickened appendiceal wall +/- an appendicolith will be seen (fig 3). Examining the bowel gas pattern is an important part of abdominal radiographic evaluation. Look at the position, contour and size of the gas pattern. The large bowel frames the peritoneal cavity, with the small bowel situated centrally. In infants, this may be the only clue to distinguishing small from large bowel. The caecum, which has a larger diameter than the rest of the bowel, should be in the right lower quadrant. Displacement may be due to malrotation of the gut. Make sure that the gastric bubble is under the left hemidiaphragm for similar reasons. The bowel walls, highlighted by air within the lumen, should be smooth and regular. Irregularity may denote inflammation from diseases such as Crohn’s disease, which has a cobblestone appearance. Physiologically, there should be less than three air fluid levels. There are occasionally more in infants and young children. These show up as menisci between the black (hypodense) air and the white (opaque, dense) fluid. Multiple air fluid levels may denote mechanical obstruction such as volvulus or Hirschsprung’s disease (colonic aganglionosis) (fig 4). The double bubble sign (2 air-filled adjacent areas of bowel) is seen with proximal obstruction such as duodenal atresia. If a mechanical obstruction has been present for some time, bowel distal to the obstruction will be devoid of air. A paralytic ileus is identified by dilated loops of bowel. A single loop of dilated bowel is called a “sentinel loop” and is associated with disease of a specific organ in a localized area, such as in pancreatitis. Pyloric stenosis is not diagnosed on plain film, however, the stenotic pylorus is visible with ultrasound (fig 5).

THE PAEDIATRIC SKELETAL FILM

As with other types of films, approach the bone film methodically. Always get at least two views; the cortex is circumferential, while the plain film presents only a 2-dimensional view.

Look at the soft tissues, joint space and bone. Long bones, such as the femur, have four parts. The diaphysis is the shaft. The metaphysis, at the ends of the diaphysis, is attached to the epiphyseal plate. The epiphysis articulates in the joint. Bone age can be approximated by comparing hand and wrist x-rays to those in an atlas. Different epiphyses ossify (become roentgenographically visible) at different ages.

Observe the alignment of the bones. Malalignment of the bones with respect to each other may indicate dislocation. Bone density is difficult to estimate on plain film due to differences in film exposure, but asymmetry or inconsistency within a bone may indicate a lytic process. Look at the continuity of the bony cortex and the trabecular pattern. Children’s bones are more flexible than adult’s, and a slight cortical or trabecular discontinuity may be the only sign of fracture. The greenstick fracture is manifested by a bowing of a long bone with a discontinuity of the cortex (the fracture) on the convexity. Buckling of the cortex is seen in a torus fracture. The periosteum (the metabolically active covering of long bones) is not normally seen except in 2-6 month old infants. A visible periosteum indicates periosteal reaction to trauma. It is loosely applied to the paediatric diaphysis
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and with trauma, it can be lifted off the bone. It will then form a thick layer of new bone within 7-14 days. This reaction can be used to date a fracture. The periosteum is more tightly applied to the metaphysis. A twisting injury can cause corner and bucket handle fractures - a thin wedge of bone is torn from the rim of the metaphysis and resembles a corner of bone torn off or the handle of a bucket (Fig 6). Multiple fractures at different stages of healing, rib, corner and bucket handle fractures are virtually pathognomonic for child abuse. Fractures that involve the physis are classified under the Salter-Harris classification.

All fractures should be described with respect to type (open or closed), site, pattern (transverse vs. spiral, compression vs. greenstick; fragmentation), and displacement (apposition, angulation, rotation and length). Some fractures such as supracondylar (elbow) fractures are difficult to see on plain film. A clue to their existence is elevation of the articular fat pads - the sail sign. The lucent fat pad resembles a sail on the distal humeral metaphysis.

Developmental dysplasia of the hip is a common problem best seen with sonography because the hip joint is not fully ossified in infants. The acetabulum appears flat instead of being cupped to fit the femoral head.

The most important thing to remember about reading paediatric radiographs is to do so methodically. Knowledge of the pathology and clinical progression of a disease will help in the identification of pertinent radiologic signs.

REFERENCES
ZYPREXA® (olanzapine tablets)

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Pharmacodynamic Properties: ZYPREXA® (olanzapine), a thienobenzodiazepine, is an antipsychotic, displaying high receptor affinity in binding to serotonine 5-HT2A (Ki = 4 and 10 mg/day) and dopamine D2 receptors (Ki = 1.9-2.5 nM), adrenergic a1 (Ki = 10 nM) and histamine H1 (Ki = 7 nM) receptors. In behavioral paradigm predictive of antipsychotic activity, olanzapine reduced conditioned avoidance response in rats as determined by a hole board test. Olanzapine was also statistically significantly superior to haloperidol on the Montgomery-Asberg Depression Rating Scale (MADRS). The validity of this scale in patients with schizophrenia, however, is not established.

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Pharmacokinetics: For ZYPREXA tablets, peak plasma concentrations of olanzapine were achieved within 4-7 hours following a single dose of 20 mg/day OD. ZVPREXA (1 mg/day OD) was statistically significantly superior to haloperidol on the BPRS total, BPRS positive psychotom, the CGI-S scale, the Positive and Negative Syndrome Scale (PANSS) total, the PANSS positive subscale, and the PANSS negative subscale. ZYPREXA 1 mg/day OD, and haloperidol (15 mg/day) on a BID schedule. There were no statistically significant differences between groups on efficacy measures in the 10 mg/day OD ZYPREXA group compared to placebo. The 10 mg/day OD ZYPREXA group was statistically significantly superior to ZYPREXA 1 mg, on the BPRS positive psychotom cluster, PANSS negative subscale, and the CGI-S scale.
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Olanzapine

Novel antipsychotic power for routine use
For patients who have known or suspected hepatic dysfunction prior to starting ZYPREXA, standard clinical assessment, including measurement of transaminase levels is recommended. Patients with severe hepatic dysfunction may be more susceptible to the effects of ZYPREXA, as well as for patients who develop signs and symptoms suggestive of a new onset liver disorder during ZYPREXA therapy.

Hematologic indices: There were no data to suggest ZYPREXA adversely affected bone marrow function, even in patients with a history of clozapine-associated neutropenia or leucopenia. ZYPREXA was associated with a 5.7% incidence of transient treatment-emergent reductions of eosinophil counts above the normal range. Elevations were not associated with any symptoms, identifiable allergic phenomena, or changes in other hematologic indices.

Hyperprolactinemia: As with other drugs that block dopamine D2, and serotonin 5-HT2 receptors, olanzapine may elevate prolactin levels. Elevations associated with ZYPREXA treatment are generally mild and may not require discontinuation of therapy.

Since tissue culture experiments indicate that approximately one third of human breast cancers are progestin-dependent, ZYPREXA treatment was evaluated in patients with breast cancer. Olanzapine has been detected in breast milk, and other drugs used in the treatment of breast cancer has been advised when breastfeeding is necessary.

ZVPREXA was associated with a 0.6% incidence of persistent transaminase elevations with a mean elevation of 5.4 kg.

Weight Gain: Olanzapine was associated with weight gain during clinical trials. Patients treated at higher doses (15 ± 2.5 mg/day) had the greatest mean weight gain. However, a categorization of patients at baseline on the basis of body mass index (BMI) revealed a significantly greater effect in patients with normal BMI and weight gain continued for the patients with a BMI of 15-20 kg/m^2.

Antiemetic Effect: Olanzapine inhibited dopamine antagonist effects, olanzapine may have an anxiolytic effect. Such an effect may mask signs of toxicity due to overdosage of other drugs, or may mask symptoms of disease such as brain tumor or intestinal obstruction.

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been reported with olanzapine use. Appropriate cooling measures are advised when prescribing ZYPREXA for patients will be experiencing conditions which may contribute to an elevation of core body temperature, exposure to high heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Suicide: The possibility of suicide or attempted suicide is inherent in psychosis, and thus suicide supervision and appropriate clinical management of high-risk patients should accompany drug therapy.

Drug Interactions: Given the primary CNS effects of ZYPREXA, caution should be used when it is taken in combination with other centrally-acting drugs and alcohol. As it exhibits in vitro dopamine antagonism, ZYPREXA may antagonize the effects of levodopa and dopamine agonists.

Because of its potential for inducing hypotension, olanzapine may enhance the effects of certain antihypertensive agents.

Potential for Other Drugs to Affect ZYPREXA: ZYPREXA metabolism by CYP3A4. Olanzapine is also metabolized by CYP2D6 and CYP2C19. In vitro studies with human microsomes, olanzapine was shown to inhibit CYP3A4 and CYP2C19, and olanzapine inhibited CYP2D6, CYP2C9, and CYP2C11. Potential interactions with ZYPREXA should be considered when prescribing ZYPREXA.

Pregnancy: There are no adequate and well-controlled studies in pregnant women. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with ZYPREXA. If the patient becomes pregnant while receiving ZYPREXA, the drug should be used only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery: Parturition in rats was not affected by olanzapine. The effect of ZYPREXA on labor and delivery in humans is not known.

Lactation: Olanzapine is excreted in human milk. Patients should be advised not to breast feed an infant if they are taking ZYPREXA.

Geriatrics: The number of patients 65 years of age or over, with schizophrenia or related disorders, exposed to ZYPREXA was not available. In elderly patients, ZYPREXA should not be used without adequate clinical trials showing the drug to be safe and effective in this population.

Renal and Hepatic Impairment: Small single-dose clinical pharmacology studies (see PHARMA- MONOCLINIC, Pharmacokinetics, and DOSAGE AND ADMINISTRATION) indicate that ZYPREXA has not been evaluated in patients with a history of myocarial infarction or hepatic dysfunction. Use in patients with concomitant disease is limited. Clinical experience with olanzapine in patients with renal failure has been limited. Caution is advised when prescribing ZYPREXA in elderly patients or patients with conditions that may affect renal function or hepatic function.

Use in Patients with Concomitant Illness: Clinical experience with olanzapine in patients with concomitant illness is limited. Caution is advised when using ZYPREXA in patients with diseases or conditions that may be affected by the metabo- lism of olanzapine (see PHARMACOLOGY, Pharmacokinetics, and DOSAGE AND ADMINISTRATION).

ZYPREXA has not been evaluated in patients with a history of myocarial infarction or hepatic dysfunction. In myocarial infarction or hepatic dysfunction. Use in patients with concomitant disease is limited. Clinical experience with olanzapine in patients with renal failure has been limited. Caution is advised when prescribing ZYPREXA in elderly patients or patients with conditions that may affect renal function or hepatic function.

As ZYPREXA demonstrated anticholinergic activity in vitro, caution is advised when prescribing for patients with symptomatic prostatic enlargement, narrow-angle glaucoma or paralytic ileus and related conditions.

In clinical trials, a single case of pre-existing interstitial hypertension exacerbated.

ADVERSE REACTIONS

The stated frequencies of adverse events represent the proportion of individuals who experienced at least one treatment-emergent adverse event in the clinical trials. The adverse events were reported during therapy by the investigator without distinguishing them by severity.

Commonly Observed Adverse Events in Placebo-Controlled Clinical Trials: The following are treatment-related adverse events, derived from Table I, commonly occurred in acute ZYPREXA therapy. For at least 5% of patients, the adverse event occurred more often in the ZYPREXA group compared to the placebo group.

1) Nervous System: Headache, dizziness, constipation, anxiety, and weight gain were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

2) Gastrointestinal System: Constipation, diarrhea, nausea, vomiting, pyrexia, and dyspepsia were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

3) Respiratory System: Cough, pharyngitis, and rhinitis were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

4) Skin and Appendages: Rash, pruritus, and redness were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

5) Special Senses: Tinnitus, nystagmus, and diplopia were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

6) Urogenital System: Dysuria, vaginitis, and vulvar pruritus were the most common adverse events. The incidence of these events was not significantly different between the ZYPREXA and placebo groups.

The most frequent adverse events were:

1) Headache (5%)
2) Dizziness (5%)
3) Constipation (5%)
4) Anorexia (5%)
5) Nausea (5%)
6) Vomiting (5%)
7) Fatigue (5%)
8) Vertigo (5%)
9) Insomnia (5%)
10) Sleep disturbances (5%)

In clinical trials, the adverse events were reported during therapy by the investigator without distinguishing them by severity.

The incidence of adverse events in placebo-controlled clinical trials was generally similar to that in clinical trials with ZYPREXA and placebo.
Incidence of Weight Changes in Placebo-Controlled Clinical Trials: During acute therapy (up to 6 weeks) in controlled clinical trials comparing ZYPREXA with placebo in the treatment of schizophrenia, the percentages of patients with weight gain >7% of baseline body weight at any time were 20% for ZYPREXA and 3% for placebo, which was a statistically significant difference. The average weight gain during acute therapy in patients treated with ZYPREXA was 2.8 kg. However, a categorization of patients at baseline on the basis of body mass index (BMI) revealed a significantly greater effect in patients with low BMI compared to normal or overweight patients. In long-term extension trials, weight gain tended to level off after 6-8 months of treatment, with an average gain of 5.4 kg (see PRECAUTIONS).

Incidence of Vital Sign Changes in Placebo-Controlled Clinical Trials: In placebo-controlled clinical trials, orthostatic hypotension (greater than 30 mm decrease in systolic blood pressure) occurred with an incidence of 5% in olanzapine-treated patients compared to 2% in placebo-treated patients (see vital sign measurements collected only after 3-7 days of treatment). Olanzapine was associated with a mean baseline to endpoint increase in heart rate of 2.4 beats per minute compared to no change among placebo-treated patients (see PRECAUTIONS).

Incidence of Laboratory Changes in Placebo-Controlled Clinical Trials: Olanzapine was associated with asymptomatic increases in SGPT, SGOT, and GGT (see PRECAUTIONS). Olanzapine is also associated with generally mild increases in serum prolan, which usually decreases with continued drug treatment. Olanzapine is also associated with asymptomatic increases of eosinophils and uric acid (see PRECAUTIONS), and with decreases in serum bicarbonate.

Incidence of ECG Changes in Placebo-Controlled Clinical Trials: Between-group comparisons for pooled dose-response trials revealed no statistically significant olanzapine/placebo differences in the proportions of patients experiencing potentially important changes in ECG parameters, including QT, QTc, and PR intervals.

Dose-Dependent Adverse Events in Fixed-Dose Clinical Trials: Dose-relatedness of adverse events was assessed using data from a clinical trial with a fixed dosage range. Table 2 enumerates the treatment-emergent adverse events in which there was a statistically significantly increasing dose response in this clinical trial.

## Table 2

### Dose-Dependent Adverse Events in a Fixed Dose Range, Placebo-Controlled Clinical Trial

<table>
<thead>
<tr>
<th>Percentage of Patients Reporting Event</th>
<th>Placebo</th>
<th>ZYPREXA 2.5 mg/day</th>
<th>ZYPREXA 5 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>6%</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1%</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Abnormal Liver Function</td>
<td>0%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>0%</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Acute Pain</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Vaginal Bleeding</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Incidence of Treatment-Emergent Extrapyramidal Symptoms in Placebo-Controlled Trials: Table 3 enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by categorical analyses of formal rating scales during acute therapy in a controlled clinical trial comparing olanzapine at 3 fixed dosage ranges with placebo in the treatment of schizophrenia.

### Table 3

#### Treatment-Emergent Extrapyramidal Symptoms As Assessed By Rating Scales

<table>
<thead>
<tr>
<th>Incidence In A Fixed Dose Range, Placebo-Controlled Clinical Trial - Acute Phase</th>
<th>Percentage of Patients</th>
<th>ZYPREXA 2.5 mg/day</th>
<th>ZYPREXA 5 mg/day</th>
<th>ZYPREXA 10 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akathisia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Dystonia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Abnormality, Extrapyramidal</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Akathisia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Dystonia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Incidence of Treatment-Emergent Extrapyramidal Symptoms Assessed by Adverse Events

### Table 4

#### Treatment-Emergent Extrapyramidal Symptoms Assessed by Adverse Events

<table>
<thead>
<tr>
<th>Incidence In a Fixed Dose Range, Placebo-Controlled Clinical Trial - Acute Phase</th>
<th>Percentage of Patients Reporting Event</th>
<th>Placebo</th>
<th>ZYPREXA 2.5 mg/day</th>
<th>ZYPREXA 5 mg/day</th>
<th>ZYPREXA 10 mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akathisia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Dystonia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Abnormality, Extrapyramidal</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**SYMPTOMS AND TREATMENT OF OVERDOSE**

Experience with ZYPREXA® (olanzapine) in overdose is limited. In clinical trials, accidental or intentional acute overdose of ZYPREXA was identified in 67 patients. In the patient taking the largest ingested amount, 300 mg, the only symptoms reported were drowsiness and slurred speech. In the limited number of patients who were evaluated in the hospital, and in the patient taking 300 mg, there were no observations indicating an adverse change in laboratory analyses or ECG. Vital signs usually returned to normal levels following overdoses.

Based on animal data, the predicted symptoms would reflect an exaggeration of the drug's known pharmacological actions. Symptoms may include somnolence, mydriasis, blurred vision, respiratory depression, hypotension, and possible extrapyramidal disturbances (see also ANIMAL TOXICOLOGY).

There is no specific antidote to ZYPREXA; therefore, appropriate supportive measures should be initiated, while possible medical intervention should be considered.

In case of acute overdose, establish and maintain an airway and ensure adequate oxygenation and ventilation. The use of activated charcoal should be considered because the concomitant administration of activated charcoal was shown to reduce the oral bioavailability of ZYPREXA by 50% to 60%. Gastric lavage (after intubation, if patient is unconscious) may also be considered.

Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents such as norepinephrine (do not use epinephrine, dopamine or other sympathomimetic agents with beta-agonist activity since beta stimulation may worsen hypotension in the setting of alpha blockade induced by ZYPREXA). Cardiac monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

Close medical supervision and monitoring should continue until the patient recovers.

**DOSE AND ADMINISTRATION**

(see also CLINICAL PHARMACOLOGY)

**Adults:** ZYPREXA® (olanzapine) should be administered on a once-a-day schedule without regard to meals, generally beginning with 5 to 10 mg, with a target dose of 10 mg/day within several days. Further dosage adjustments, if indicated, should generally occur at intervals of not less than 1 week, since steady state for ZYPREXA would not be achieved for approximately 1 week in the typical patient. When dosage increments are necessary, dose increments/ decrements of 5 mg QD are recommended. An increase to a dose greater than target dose of 10 mg/day (i.e., to a dose of 15 mg/day or greater) is normally recommended only after clinical assessment.

In clinical trials a dose range of 5-20 mg/day was studied (see CLINICAL TRIALS). The safety and efficacy of doses above 20 mg/day have not been evaluated.

**The elderly or debilitated patient:** In clinical trials, 44 patients with schizophrenia or related disorders, 65 years of age or over, with no evidence of extrapyramidal symptoms, were treated with ZYPREXA. (See PRECAUTIONS; see also PHARMACOLOGY Special Populations). Given the limited experience with ZYPREXA in the elderly, and the higher incidence of concomitant illness and concomitant medication in this population, ZYPREXA should be used with caution.

The recommended starting dose is 5 mg in patients who are elderly, debilitated, who have a predisposition to hypotensive reactions, who otherwise exhibit a combination of factors that may result in slower metabolism of ZYPREXA (e.g., nonsmoking females), or who may be pharmacodynamically more sensitive to ZYPREXA. When indicated, dose escalation should be performed with caution in these patients.

**Patients with Hepatic and/or Renal Impairment:** As clinical experience is lacking in these patients, the lower initial starting dose and slower titration to initial target dose should be considered. Further dose escalation, when indicated, should be conservative (see PRECAUTIONS; see also PHARMACOLOGY Special Populations).

**Maintenance Therapy:** It is recommended, that responding patients be continued on ZYPREXA at the lowest dose needed to maintain remission. Patients should be reassessed periodically to determine the need for maintenance treatment. While there is no body of evidence available to answer the question of how long the patient should be treated with ZYPREXA, the effectiveness of maintenance treatment is well established for many other antipsychotic drugs.

**PHARMACEUTICAL INFORMATION**

**DRUG SUBSTANCE:**

- **Trade Name:** ZYPREXA®
- **Proper Name:** Olanzapine

- **Chemical Name:** 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-phenanthrene[2,3-b][1,5]benzodiazepine

- **Molecular Formula:** C26H27N5S

- **Molecular Weight:** 371.44

**Description:** Olanzapine is an antipsychotic agent of the thienobenzodiazepine class. It is a yellow crystalline solid, which is soluble in n-Propanol and practically insoluble in water.

**pK_a:** 5.00 and 7.40 in Dimethylformamide/Water (60:40, v/v)

**Melting Point:** 195 ± 2°C

**COMPOSITION:**

Each ZYPREXA (olanzapine) tablet contains the equivalent active amount of 5 mg (16 μmol), 7.5 mg (24 μmol), or 10 mg (32 μmol) of olanzapine. Inactive ingredients include carrageenan, color mixture white (hydroxypropyl methylcellulose, titanium dioxide, polyethylene glycol, and polysorbate 80), crospovidone, FD&C Blue No. 2 Aluminum Lake, hydroxypropyl methylcellulose, lactose, magnesium stearate, and microcrystalline cellulose.

**STABILITY AND STORAGE RECOMMENDATIONS:**

Store tablets at 20°-25°C. Protect from light and moisture.

**AVAILABLE DOSAGE FORMS:**

All tablets are white, round, film-coated, and imprinted in blue ink with "LILLY" and the tablet identification code. Each strength is available in amber HDPE bottles of 60 tablets.

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**Product Monograph available on request. October 15, 1996.**
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STRESS REACTIONS OF THE DISTAL RADIAL EPIPHYSEAL PLATES IN YOUNG GYMNASTS

by Lynda Newkirk, Meds 2000

ABSTRACT

This paper is a report on stress injuries to the distal radial epiphyses of young gymnasts. These injuries are common in young gymnasts as a result of the repetitive, upper-limb weight-bearing characteristic of the sport. The topic is introduced with reference to the case of an eight-year-old gymnast with damage to the distal epiphyseal plate of her left radius. Pathogenesis, diagnosis, treatment, epidemiology, etiology, prognosis, implications, and prevention of stress injuries to the distal radial epiphyses are discussed.

INTRODUCTION

As a result of upper-limb weight bearing, the wrists of young gymnasts are exposed to unusually large amounts of stress. The stress from repetitive, high-impact loading may damage their distal radial epiphyseal plates. This damage may occur as a stress fracture, or as a stress reaction characterized by irregularity of the metaphyseal margin, widening, cystic changes, and sclerosis of the epiphyseal plate. Damage to the epiphysis warrants concern as it may lead to premature closure of the epiphyseal plate and disrupted growth. It is important that gymnastics coaches, parents, and physicians understand the risks, implications, and symptoms of these stress injuries, in order that any such injury be recognized and treated early. The goal of this paper is to provide information on all aspects of stress injuries to the distal radial epiphysis.

CASE STUDY

In February 1995, an eight-year-old elite, female gymnast presented with left wrist pain. In January 1994, the gymnast fell off the uneven parallel bars and landed on an outstretched arm, forcing her wrist into hyperextension. Plain film radiographs showed a Salter Type II fracture of the distal radius. The fracture was treated by means of cast immobilization for three weeks. Repeat x-rays taken at the end of the month showed a small amount of periosteal bone formation over the dorsal surface of the radius, and otherwise little change.

The injury occurred during the athlete's fourth year of participation in gymnastics. She was also involved in dance and karate. At the time of the injury, she was training at gymnastics for approximately 18 hours per week. Following the removal of her cast, the gymnast did physiotherapy and gradually, over a period of one month, returned to her full training schedule. In January of 1995, while training 18-20 hours per week, the gymnast was experiencing wrist pain during workouts. She noticed a bump on the dorsum of her wrist. Repeat x-rays showed irregularity of the epiphysis and slight dorsal tilting of the distal radius. The radiograph also showed slight attenuation of the ulnar aspect of the epiphysis, suggesting disturbed growth. It was recommended that if pain continued despite these measures, she should terminate her participation in gymnastics and place more emphasis on dance. It was also recommended that if her condition improved and she was able to increase her training pain-free, she should train less than 12-14 hours per week. Upon re-examination in September of 1995, she reported that training for three consecutive days aggravated her wrist. She could, however, train for 3 hours a day on alternate days (a total of 12 hours per week) without any discomfort.

DISCUSSION

PATHOGENESIS

The epiphyseal plate is a cartilaginous disk between the epiphysis and metaphysis. Here cartilage cells proliferate and calcify during endochondral ossification. The cartilage of the epiphyseal plate is one of the weakest skeletal structures in the young athlete. It is estimated to be 2 to 5 times more likely to sustain injury than the joint capsule and other ligaments. Consequently, it is susceptible to both acute and chronic injuries. When fractured, the epiphyseal plate tends to separate between

ABOUT THE AUTHOR

Lynda Newkirk is a first-year medical student at UWO. Prior to entering medical school she completed a Bachelor of Human Kinetics degree at the University of British Columbia.


**Feature Section**

the calcified and uncalcified cartilage at the metaphyseal junction. This area is avascular, and consequently, there should be a limited amount of swelling associated with its fracture. When injured, the epiphyseal plate tends to widen due to continued production of cartilage cells despite disturbed bone formation. Other stress-related changes include cystic changes (usually on the metaphyseal aspect of plate), sclerosis, irregularity of the metaphyseal margin, widening of the epiphysis, and a hazy appearance of the epiphyseal plate on radiographs.

**DIFFERENTIAL DIAGNOSIS**

In diagnosing chronic wrist pain in a young gymnast one must consider a number of possible injuries. Some of these include stress reaction or stress fracture of the distal radial epiphysis, ligament injury, chondromalacia, tendonitis, degenerative joint disease, stress fracture of the radius, ulna, or a carpal bone, tumour, cartilage damage, and damage to the triangular fibrocartilage complex. The physical exam may enable the physician to diagnose the presence or absence of tendonitis; however, further diagnoses will require investigative techniques. The plain film radiograph may not show stress fractures, but it will show signs of stress reactions in the epiphyseal plate. It has been suggested that information from a technetium-99 bone scan is of little use in the diagnosis of epiphyseal plate injuries: A normal epiphyseal plate has high uptake, and injured epiphyses have been found to show uptake which is normal for the patient's age. However, the bone scan may be useful in eliminating other possible diagnoses. Mandelbaum et al. suggest that MRI is particularly useful in the diagnosis of gymnastics wrist injuries as it effectively differentiates between and shows damage to various types of structures and tissues.

A diagnosis of a stress fracture or stress reaction of the distal radial epiphyseal plate can be made based on the following: exposure to a stress mechanism, such as repetitive weight-bearing, localized pain and tenderness over the distal radial epiphysis, pain in response to forced dorsiflexion and sometimes with radial or ulnar deviation, minimal swelling, and radiographs showing a fracture or other stress related changes as described previously. The gymnast in this case study had a history, physical findings, and radiographs consistent with disruption of the epiphyseal plate as a result of an acute fracture of the epiphysis and continued exposure to stress.

**TREATMENT**

Treatment of injuries to the distal radial epiphyseal plate should begin conservatively, including rest from weight-bearing, non-steroidal anti-inflammatory drugs, physical therapy using multiple modalities, and ice. Some injuries may require temporary cessation of gymnastics and immobilization. As a guideline, weight-bearing should be avoided until the wrist is no longer tender to touch and there is no pain with forced range of motion, especially in dorsiflexion. The athlete should undertake a strengthening program for upper body and wrists, keeping activity within a pain-free limit. Return to activity should be gradual and progressive, allowing time for the body to adapt to stress. To protect the wrist from further damage, the wrist can be taped, or the gymnast can be fitted with a rigid wrist brace. These methods will help the gymnast to avoid excessive hyperextension of the wrist.

**EPIDEMIOLOGY**

A study of 100 provincial and national level gymnasts showed a high injury rate amongst the participants, with 155 acute and 124 chronic injuries sustained over 40 months. In this study, 4.5% (7) of the acute injuries were fractures of the forearm or wrist, and 1.6% (2) of the chronic injuries were distal radial stress fractures. Despite having a high injury rate, the sport of gymnastics is very popular, with an estimated 600,000 participants in the United States alone.

Recently, there has been a trend toward early participation in gymnastics which has sparked special concerns. Prepubescent athletes have open growth plates which are susceptible to damage. This damage may have significant long-term effects.

Damage to the distal radial epiphysis has been identified as a common problem for gymnasts. Stress changes of the distal radial epiphyseal plates were obvious in 10% of gymnasts at the World Championship Gymnastics Competition in Rotterdam in 1987, and in 11 of 21 (42%) high performance gymnasts studied by Roy. Epiphyseal plate fractures are most often reported in competitive gymnasts, but also occur in individuals at lower skill levels.

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AETIOLOGY

Factors related to the occurrence of injuries to the distal radial epiphysis in gymnasts include the nature of the skills and the sport, the amount of exposure, and the equipment.

Many gymnastic skills involve high-impact loading on the upper extremities. For example, the compressive ground reaction forces experienced during a back handspring (a fundamental and frequently repeated skill) may be up to 2.4 times body weight.1 Repeated compressive forces have been indicated as the primary cause of chronic wrist injuries in gymnasts.2,3 Other contributing factors include a combination of hyperextension and ulnar deviation during vaulting and tumbling (especially during skills involving rotation or twisting), and the torques applied through the wrists during balance beam and pommel horse activities. In these activities the hands are fixed while the rest of the body rotates around them.2,3 Many gymnastics skills involve flight. The nature of these flight moves favour the prepubescent gymnast.4 This has resulted in early participation, with young gymnasts training up to thirty hours per week and exposing their growing bones to high levels of repetitive physical loading.2,3,4 Consequently there is a high risk of growth plate injuries in young gymnasts.

Gymnastics is by nature a repetitive sport. Gymnasts repeat skills and routines time and time again, striving for perfection.2,3 As a result, their bodies experience repetitive microtrauma. This trauma may result in stress fractures. Fractures of the distal radial epiphysis of gymnasts are commonly stress fractures caused by overuse,2,3,5 but can also result from acute injury, such as in this case where the gymnast fell onto an outstretched arm. An injury whose onset is acute may be aggravated and kept from healing by continued exposure to stress. Some exercise has been found to be beneficial, promoting bone growth and hypertrophy, but the inflammation, disruption of normal growth, and degenerative changes in the bones of competitive gymnasts show that these athletes' bodies are being stressed beyond their tolerance level.6 The epiphyseal plate is a weak area of growing bone and is consequently a common site of injuries.

Injuries to the distal radial epiphyses of gymnasts were found to be related to exposure. Literature citing wrist pain in gymnasts describes pain occurring, for the most part, in gymnasts training between 15 and 30 hours per week.1,2,3,4,5 The risk of injury was found to be directly proportional to the skill level.11 This was suggested to be a result of increased training hours and the execution of riskier and more difficult skills at higher levels of training.11

Equipment was also indicated as a contributing factor to wrist injuries. It was suggested that the use of soft mats may exaggerate dorsiflexion.2 Also, the use of dowel grips on bars transfers forces from the hands to the wrists.7 Floor exercise, beam, and pommel horse are most often indicated as causing pain, likely as a result of the torques and forces applied through the wrists during these activities.2,3

PROGNOSIS, IMPLICATIONS, AND PREVENTION

Wrist pain results in loss of training time and consequently decreased performance.6 More seriously, injuries to the distal radial epiphysis may result in premature closure of the epiphyseal plate and/or disruption of growth.1,2,3,4 With ongoing, normal growth of the ulna, this may lead to positive ulnar variance. In current literature there is admitted uncertainty concerning whether or not the exposure of gymnasts' wrists to repetitive microtrauma will result in permanent damage, and at what level of training the stress becomes too much for the bones to handle. However, studies of world-class and collegiate gymnasts show that both adolescent and adult gymnasts have highly significant levels of positive ulnar variance when compared to non-athlete control groups.7 This suggests that participation in competitive gymnastics at the collegiate and international level does disrupt the growth of the radius, and that this damage is long-term. Furthermore, positive ulnar variance has been implicated as a predisposing factor in damage to the triangular fibrocartilage, ulnar impaction syndrome, cystic changes in the triquetrum, chondromalacia, degenerative arthritis of the ulnar compartment, and osteomalacia of the ulnar carpal.7,8 We can therefore conclude that damage to the distal radial epiphysis in gymnasts is a serious injury with potentially life-long consequences.
On a more positive note, it has been found that if the growth plate injury is diagnosed early and the athlete responds quickly with conservative treatment, the prognosis for recovery is very good.2

Stress reactions to the distal radial epiphyses of gymnasts are a small part of a much larger issue. They reflect physical stress. Young gymnasts also experience emotional stress associated with learning high-risk moves, travelling, and competing. They are under intense pressure to win brought upon by their coaches, their parents, and society.12 We must ask ourselves if this is right. Should children be exposed to this magnitude of physical and emotional stress? How much competition and training is too much? Should children participate in a sport at a level which may result in lifelong damage? Would these children be better off participating in a variety of sports?12 What can we do to help? These are difficult questions to answer. Society puts a great deal of emphasis on winning, and winning major athletic events is associated with much prestige. Society’s “win at all costs” attitude would be hard to change.12

If we are unable to change the outcome-oriented approach to athletics, perhaps we can at least control the process of training and reduce the number of injuries. This prevention will begin with the education of coaches, parents, and gymnasts regarding the risks associated with gymnastics and how they may be avoided. Proper conditioning programs which develop strength and flexibility should be implemented at all levels of training.9 Increases in training should be gradual and cyclic in nature, allowing the body time to adapt to new stresses. Gymnasts with open growth plates in their wrists should not use dowel grips.7 During practice, they should alternate between swinging and weight-bearing events.45 They should learn and practice correct falling and landing techniques. The presence of trained, knowledgeable, experienced spotters and the proper use of safety equipment (such as mats and spotting belts) are highly recommended.11 It is also important that exposure is limited to less than 15 hours per week, and that gymnasts do not participate when in pain.45 Finally, rapid diagnosis and treatment of both chronic and acute injuries is essential.5

CONCLUSION

Inflammation, disruption of normal processes of growth, and degenerative changes in bone reflect that the bodies of competitive gymnasts are being physically stressed beyond their tolerance level. Damage to the epiphyseal plate is common in gymnasts, and while early diagnosis and conservative treatment of the injury has a good prognosis for recovery, if left untreated the injury may have serious, lifelong effects. Steps must be taken to prevent epiphyseal plate injuries in young athletes. These steps include education of coaches, parents, and gymnasts, a safe training environment, and limiting exposure to weight-bearing by the upper extremities.

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This paper was peer-reviewed at the University of British Columbia, and was reviewed by Dr Connie LeBrun at the Fowler-Kennedy Sports Medicine Centre.

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In 1938, a syndrome was identified in which there was sexual immaturity, small stature, and skeletal abnormalities due to a full or partial deletion of the X chromosome in somatic cells. One of the most widely studied aspects of this disorder is its associated neurocognitive and behavioural differences. Many competing theories have been proposed to account for the specific neuroanatomical areas in which there are anomalies, as well as the bases for the production of such impairments in brain, behaviour, and ability.

NEUROCOGNITONAL DIFFERENCES

In developmental neuropsychological deficits, such as those produced by Turner's syndrome, there is no contrast between a previous state and the present one. Only the final result of the deficit and the individual's attempt to compensate are exhibited. Thus, psychology has been slow to accept and identify such cases. Turner's patients most predominantly display five major cognitional differences, as compared to normal subjects.

PERFORMANCE VS. VERBAL IQS

The Wechsler IQ scales are used as a measure of basic cognitive function. These tests have a distinct advantage: they provide separate scores for verbal and performance subtests, as well as overall IQ. Previous neuropsychological studies of patients diagnosed clinically and cytogenetically as Turner's syndrome have indicated that Wechsler performance IQs in the disorder ranged significantly lower than the verbal IQs (Figure 1 illustrates the IQ results found in Temple and Carney's study). Other authors have also noted that on the Wechsler Performance IQ test low scores were over represented for Turner's girls.

VISUOSPATIAL ABILITY

Researchers have found that instead of an overall mental deficiency, which was often ascribed to Turner's patients, there are specific non verbal cognitive impairments that include difficulty with visuospatial tasks such as perception of left and right and visuomotor drawing. In normal children, a sex
difference is evident between males and females on both Object Assembly and Block Design subtests of the Wechsler Intelligence Test for Children (Revised), with girls performing more poorly than boys. Results of a study by Temple and Carney supported previous findings that in Turner's patients, this sex difference was exaggerated, producing an even greater deficiency for Turner's girls in those Wechsler subtests.

The basic impairment may be associated with mental processing and sequencing of rotational shape transformations in the spatial dimensions of up down, left right and back front. In daily activities, this deficit in rotational transformation is manifested as a handicap in map reading, drawing floor plans, following travel directions, and recognizing facial expression changes. Ironically, the rotational transformation disability is not a handicap in learning to read, and in fact it may be an advantage. Owing to this impairment, the shapes of letters and words maintain their meaning by remaining static and unrotated. Such a cognitive ability specific to Turner's girls could contribute to an easier process of learning to read and thus could be an explanation for their high verbal abilities.

More generally, individuals with Turner's syndrome have performed worse on a variety of visuospatial processing tasks such as spatial reasoning and extrapersonal space, visual memory, mazes, visual sequencing and discrimination, and design copying.

MEMORY

In one study, Turner's subjects underwent neuropsychological testing in order to determine the hormonal constraints which govern non verbal memory processes. Results showed that subjects had memory deficits for non verbal materials within three perceptual areas: visual, auditory, and tactile. This type of memory impairment was attributed to an alteration in the processing of the material to be remembered. Waber also found deficiencies in Turner's patients for the houses and faces components of the Face Recognition test, illustrating that Turner's patients have a visual memory deficit for non verbal materials.

NUMERICAL ABILITY

The Wechsler test has also shown that a relative difficulty with numbers, a form of dyscalculia, is associated with the syndrome. Results of Waber's study also supported this finding by showing that Turner's syndrome subjects scored significantly lower on overall mathematics achievement, numerical reasoning, and geometry and symbols. Analysis of math processing mechanisms revealed that areas which involved mathematical concepts seemed to be compromised to a greater degree than computational areas. Multiplication was the least affected. The previous deficiency in rotational transformation also serves as a handicap in certain mathematical tasks, especially geometry.
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THE IMPACT OF MOSAICISM ON COGNITIVE DEFICIENCIES

Mosaicism in Turner's syndrome genotypes is a condition characterized by a combination of normal and abnormal cell lines. It is suggested that various aspects of the syndrome's cognitive effects may be less severe among those with mosaicism. Thus, the behavioral phenotype of Turner's patients with mosaic genotypes is less deviant from the normal pattern than is that of pure 45XO. Mosaicism is found to cause a less dramatic expression of the syndrome, as occurs in other genetic disorders.

UNDERLYING CAUSES OF NEUROCOGNITONAL AND ANATOMICAL DIFFERENCES

Many studies have implicated various neuroanatomical areas in which impairments might result in the pattern of the cognitive deficits described above. However, the underlying mechanism(s) through which these impairments are produced are still vague. Three main theories as to the cause of brain, behavioral, and cognitive differences for those afflicted with Turner's syndrome are proposed.

GENETIC

Individuals with Turner's syndrome, who lack the genetic material provided by the X chromosome, are thought to be predisposed to certain cerebral anomalies. These defects are predominantly localized to the most recently developed cortical regions. The disturbances in function are evident in those cognitive processes associated with these brain areas, specifically the posterior right hemisphere.

MATURATIONAL DELAY

Waber proposed the idea of maturational delay as a cause of neuropsychological differences in Turner's girls. This hypothesis stems from the notion that this syndrome is a developmental disorder. Thus, it is of interest to note that the performance of these individuals qualitatively resembles that of the prepubertal child. These patients exhibit an immature pattern of performance, and this immaturity translates into other areas of cognitive and perceptual functioning as well. For example, the inability to perceive right and left on another person could reflect a maturational delay, since these processes strikingly improve between the ages of six and ten in normal subjects.

Empirically, there is also electrophysiological evidence to support this hypothesis. It has been noted that adult Turner's syndrome patients display an averaged evoked response which is most similar to that of female children between the ages of six and nine. This finding has been most readily attributed to the postulated immaturity of the cerebral cortex.

HORMONAL

Evidence from laboratory studies indicates that gonadal hormones play a crucial role in the normal cerebral maturation of many mammalian species. In applying this hypothesis to human studies, and more specifically to Turner's patient studies, it is difficult to separate the effects of the genetic anomalies cited previously from the effects of hormonal absence.

However, sex hormones, which are missing as a result of ovarian dysgenesis, may serve as key factors. A lack of hormones at a critical period of embryonic development could exert an influence on the evolving central nervous systems. Money proposed that this process of hormonal influence is involved in the neural mechanisms of territoriality and territorial defence, which are sex differentiated, being stronger in the male. A connection between these behaviours and spatial ability is then made by postulating the existence of a hormonal mechanism within the period of fetal development which might consequently affect space perception as it relates to territorial behaviour.

These three theories, proposed to attribute causality of neurocognitonal deficits and neuroanatomical anomalies to specific mechanisms, are not complete by any means. Each fails to take into account certain aspects of the condition. None mention the effect of environmental influences, most likely because Turner's syndrome is looked at in such a biological and genetic manner. Rove discusses the implications of certain environmental factors, citing a 1987 study by Bender, Linden, and Robinson which showed that children with sex chromosome abnormalities (including Turner's) from poorly functioning families were more impaired in...
their intellectual and psychosocial development than were those from better functioning families. Thus, when comparing levels of function in Turner's patients, it is important to consider the specific environmental and familial background of each girl.

Each of these theories - genetic, maturational delay, and hormonal - offers only part of an explanation of the causal chain. Chromosomal abnormalities can alter brain development because they can lead to deviations from normal hormonal levels and sensitivity. Alterations in hormone exposure, in turn, can lead to differential brain development which manifests itself as cognitive and behavioural impairments. In this context, environmental influences also act to determine the extent of hormonal effects, and thus the severity of deficiencies.

Turner's syndrome, like so many other biological and genetic disorders which reveal neurocognitional alterations, is the result of a dynamic relationship between genetics, endocrinology, and environment. Each factor serves to magnify or diminish the consequences of this mysterious disorder. Through its study, we may learn to aid those afflicted with it, and to develop a better understanding of the remarkable functions of the mind and body.

REFERENCES


Second-Line Therapy for Otitis Media

There has been a lot of debate regarding the ideal treatment of acute otitis media (AOM) in children. Most parties have agreed that amoxicillin is probably the best first-line therapy. However, until recently there has been little consensus as to which treatment is ideal when first-line therapy is not effective. The efficacy of an antimicrobial is assessed by culturing middle ear fluid before and after administration of a drug. Based on the results of several studies, the Ontario Antimicrobial Review Panel provided recommendations for management of AOM (Appendix 1). Recommended first-line therapy is amoxicillin or pivampicillin. Second-line therapy is TMP/SMX (trimethoprim/ sulfamethoxazole), ER/SX (erythromycin/ sulfisoxazole), AM/CL (amoxicillin/ clavulanate), cefixime, cefaclor, or CFXAX (cefuroxime axetil).

What are the pathogens?

Decisions regarding choice of antimicrobial agent are partly based on the most likely pathogen. The most probable organisms in AOM in children are: S. pneumonia (~35%), H. influenza (~25%), M. catarrhalis (~15%), Strep. Group A, S. aureus, Gram-negative rods, anaerobes or viruses.1

Why amoxicillin for first-line management?

The goal of therapy is to target the most likely organism. More than 90% of AOM in healthy children will resolve with amoxicillin.2 In addition, amoxicillin has a reasonable cost, acceptable flavour and a relatively low rate of adverse effects.

Why do symptoms persist?

Prior to initiating second-line therapy, reasons for symptom persistence should be considered. Possible reasons include concurrent viral infection, bacterial resistance to first-line therapy, failure to eradicate sensitive bacteria, middle ear effusion, poor host defences or noncompliance. This last factor may be due to physician errors (not explaining side effects), pharmacist errors (incorrect labeling) or parental factors (drug cost).

Why is second-line therapy used?

There are two major reasons for initiating second-line therapy. In some situations, incomplete treatment of AOM may have undesirable consequences (e.g. mastoiditis or meningitis). Children with severe symptoms, who are young and febrile or immunocompromised are especially prone to this.

Secondly, an episode of AOM might involve organisms that are resistant to first-line therapy. Children whose symptoms persist beyond 48-72 hours, who have a new AOM during first-line prophylactic therapy, or who have had an AOM unresponsive to amoxicillin within the past 2 months may harbour resistant organisms.

Strains of H. influenza, M. catarrhalis (and S. aureus) are resistant to first-line therapy because they produce β-lactamase (an enzyme), which hydrolyses many of the penicillins. In vitro, up to 40% of H. influenzae, and 90% of M. catarrhalis produce β-lactamase.1 Up to 16% of treatment failures are due to β-lactamase production. Effective second-line therapy includes AM/CL (CL=clavulanic acid is a β-lactamase inhibitor), ER/SX (erythromycin alone is ineffective), or TMP/SMX.

Some strains of S. pneumonia display antibiotic resistance. In vitro, up to 40% of Pneumococci were resistant to TMP/SMX.6 In addition, S. pneumonia may acquire resistance to penicillins, secondary to changes in penicillin binding proteins. AM/CL would be an effective second-line therapy. S. pneumonia are infrequently resistant to erythromycin, or cephalosporins.

CEPHALOSPORINS ARE EFFECTIVE AGAINST MOST GRAM NEGATIVE BACILLI

SIDE EFFECTS

Every drug used to treat AOM has the potential to cause side effects (most commonly GI upset and rashes). Amoxicillin causes the fewest side effects. However, the addition of Clavulanic acid increases the occurrence of diarrhoea. Nausea, vomiting and gastritis are relatively common with erythromycin. Sulpha drugs are rarely associated with Stevens-Johnson syndrome and bone marrow suppression.

DOSAGE

Some of the cephalosporins and TMP/SMX have the advantage of twice daily dosing, compared to dosing three times a day common to many of the second-line therapies.

ABOUT THE AUTHOR

Richard Levine is a fourth year medical student at UWO. Before entering Medical School, he studied Life Sciences at Queen's University. He will be starting his Residency in July 1997.
### Appendix 1. Management of acute otitis media in children

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Cost per day ($/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-Line</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>40 mg/kg/d, divided q8h</td>
<td>0.03</td>
</tr>
<tr>
<td>Pivampicillin</td>
<td>4060 mg/kg/d, divided q12h</td>
<td>0.070.11</td>
</tr>
<tr>
<td><strong>Second-Line</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP/SMX (Trimethoprim/Sulfamethoxazole)</td>
<td>812 mg/kg/d, divided q12h</td>
<td>0.020.03</td>
</tr>
<tr>
<td>ER/SX (Erythromycin/Sulfisoxazole)</td>
<td>40 mg/kg/d, divided q6h</td>
<td>0.0010</td>
</tr>
<tr>
<td>AM/CL (Amoxicillin/Clavulanate)</td>
<td>40 mg/kg/d, divided q8h</td>
<td>0.15</td>
</tr>
<tr>
<td>Cefixime</td>
<td>8 mg/kg/d, divided q122h</td>
<td>0.130.23</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>40 mg/kg/d, divided q812h</td>
<td>0.17</td>
</tr>
<tr>
<td>CFXAX (Cefuroxime axetil)</td>
<td>not in children &lt;12 years old</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Third-Line</strong></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>half the usual therapeutic dose bid</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prophylaxis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP/SMX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pivampicillin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### THE CEPHALOSPORINS

Despite being one of the better tasting preparations, cephalosporins are relatively expensive. In addition, Cefaclor is less effective than some other antibiotics, and Cefixime is not very effective against Pneumococci. Cefixime is very useful while travelling, because it does not require refrigeration.

### MANAGEMENT PLAN

Once the diagnosis of AOM is made, first-line therapy (amoxicillin or pivampicillin) is initiated for 7-10 days. If the patient is allergic to penicillin than a suitable second-line therapy can be initiated (ER/SX, TMP/SMX). If after 7-10 days symptoms have subsided, then treatment is complete.

If symptoms fail to improve within 48-72 hours, then bacterial resistance is likely, and a switch to a suitable second-line therapy is indicated. AM/CL, or ER/SX, TMP/SMX could be used against β-lactamase producing strains. Of these, TMP/SMX is the least expensive, cephalosporins are the most expensive. However, if penicillin resistant S. pneumonia is suspected then TMP/SMX may not be effective. If, at 48-72 hours, the child is toxic or experiencing complications then myringotomy and or tympanocentesis (with culture and sensitivity to identify the pathogen) should be considered.

Relapse (reinfection with the same organism) within 4 days of discontinuing therapy should be treated as failure to respond to therapy. However, recurrence (infection with a new organism) 5 to 14 days after discontinuing therapy should be treated with first-line antibiotics.

Persistence of effusion, or tympanic membrane inflammation (despite resolution of otalgia) after 10-14 days can be managed by continuing the same therapy for 14 to 21 days in total. Alternatively, the patient can be observed without antibiotics. Persistence is often viral in origin, but predisposes to bacterial infection.

Three or more infections in 6 months or 4 infections per year without chronic effusions between episodes is treated acutely as failure to respond. This is followed by chemoprophylaxis and or tympanostomy and myringotomy. C&S results are used to guide further management.

### CONCLUSION

Despite increasing resistance to antimicrobial therapy, most children with acute otitis media should respond to amoxicillin within 48-72 hours. If this is not the case then infection with resistant S. pneumonia, H. influenza or M. catarrhalis should be suspected. Second-line therapy with TMP/SMX ER/SX or AM/CL can be initiated depending on the suspected pathogen. Cephalosporins are an expensive alternative. If there is persistent or recurrent fever or otalgia then tympanocentesis or myringotomy can be used to guide antimicrobial therapy.

### ACKNOWLEDGEMENT

The author would like to thank Dr Duncan MacRae, Department of Otolaryngology, Victoria Hospital Westminster Campus, London, Ontario.

### REFERENCES

A 2-year-old male child is brought by his mother to the Emergency Department at 0400h. The mother describes an episode during which the child stopped breathing, turned red, and was gagging. She was afraid he might die.

PLEASE STOP AND ANSWER THE FOLLOWING QUESTIONS:

1. Name the condition.
2. Define the condition.
3. What is your differential diagnosis?

On examination, the child has a temperature of 37.5, BP 95/60, and HR 75. He is slightly cyanosed. Head and neck examination normal. No signs of airway obstruction. Chest exam normal. Neurological exam unremarkable.

PLEASE STOP AND ANSWER THE FOLLOWING QUESTIONS:

4. What are normal BP and HR for a 2-year-old?
5. Explain the bradycardia.
6. Explain the cyanosis.

The child is admitted to hospital, a complete workup is ordered and he is monitored for several nights. Pain is never observed by hospital staff. ASSUME that, despite exhausting all available diagnostic means, no pathological explanation for the initial pain was found.

PLEASE STOP AND THINK ABOUT THIS QUESTION:

7. What do you do now?

The mother is a 26-year-old unemployed single parent. Her parents put her up for adoption when she was 5 years old, and she has not been in contact with them since. She lives alone because her husband left a year ago and is seeking a divorce. They had one other child that died of SIDS. She feels depressed and lonely. In the past year her son has been admitted to hospital for multiple problems including failure to thrive, lethargy and recurrent diarrhoea. Throughout the interview he insists that she is a "good parent" and that she "loves her son". She also comments that she "doesn’t know what she’d do without the doctor's help". A psychiatric consult is ordered.

PLEASE STOP AND ANSWER THE FOLLOWING QUESTIONS:

8. What rare psychiatric disorder does this scenario suggest?
9. Describe the condition.
10. How could pain, failure to thrive, lethargy, and diarrhoea be exogenously induced?
11. What is the role of the physician in this situation?
12. Discuss principles of intervention.

The mother is currently under psychiatric care and the child will reside in a foster-home indefinitely until her recovery.
1. Apparent Life-Threatening Event (ALTE).

2. An episode characterized by apnoea (central or obstructive), change in colour (usually cyanosis or pallor, occasionally erythema or plethora), change in muscle tone (limpness or stiffness), and choking or gagging. The episode is frightening to the observer. In some cases the observer fears that the infant has died. Previously used terms include "aborted crib death" or "near-miss SIDS".

3. Common causes of ALTE (from Most to Least Common) include: Gastroesophageal Reflux (GER); Neurologic (seizure disorder); Infectious (meningitis); Respiratory (respiratory syncytial virus (RSV), pertussis, pneumonia, congenital central hypoventilation syndrome (CCHS)); Airway Abnormality or Obstruction; Vasovagal Syndrome; Cardiac (Wolff-Parkinson-White syndrome, arrhythmia), Metabolic-Endocrinologic; Munchausen Syndrome by Proxy.

4. Normal BP 90/60 & HR 110 in the 1-2 year age group.

5. Bradycardia is defined as abnormally slow heart rate. The combination of repeated episodes of apnoea and hypoxia eventually slows the heart rate, an effect mediated by the vagus nerve.

6. Cyanosis is defined as blue, grey, or purple discoloration of the skin due to reduced haemoglobin in the blood. Caused by hypoxia and hypercapnia secondary to any condition interfering with air entry into the respiratory tract.

7. Whenever comprehensive physical examination and investigations fail to reveal the aetiology of childhood disorders such as apnoea or an ALTE, non-medical causes must be considered. Obtain a detailed psychosocial history of the mother.

8. Munchausen Syndrome by Proxy (MSP).

9. MSP is a recently described rare form of child abuse in which a caregiver (almost always the mother) fabricates or induces symptoms in a child in order to attract medical attention. The condition is understood in terms of the mother’s need for a relationship with a physician that is rooted in a profound sense of early abandonment. The infant in this sadomasochistic interaction is dehumanized and used as a fetishistic object to control the relationship. MSP is a serious form of child abuse that may remain undetected for years. Victims suffer serious physical and psychological damage and sometimes even death.

10. Apnoea (smothering), failure to thrive (starvation), lethargy (dehydration, malnutrition), diarrhoea (laxatives).

11. Physicians must be aware that MSP exists, can present in the form of anything, and should be considered as a diagnosis in cases that do not make medical sense. MSP is a severe form of child abuse and must be reported to local Child Protection Service when the child is endangered. Physicians play a key role in identifying these children and recommending the best course of action to the rest of the system.

12. After the condition is confirmed, a multidisciplinary team aims to protect the abused child and change the pathological parent-child relationship. Comorbid psychiatric conditions in the illness perpetrators and psychological manifestations in the children must be addressed.
You have a new patient, an 18-year-old woman, who has recently married and wishes to begin family planning. She has a history of Tetralogy of Fallot with surgery having been performed in early childhood. She wants to know if she is at risk of having a child with a congenital heart defect and what can be done to increase her chances of having a healthy child.

1. What further information is necessary before you can answer her questions? She has been relatively healthy and does not drink or smoke. She is on no medications. Although she has had intermittent complaints of dyspnoea and chest pain, a recent treadmill exercise ECG showed excellent endurance to physical effort. She is followed annually by her cardiologist who feels there is no contraindication to pregnancy. Her family history is negative for any individuals with congenital heart defect or other congenital malformations.

2. What is her risk of having a child with:
   (a) congenital heart defect?
   (b) neural tube defect?
   (c) Trisomy 21?

3. What general and specific recommendations would you have regarding management of a pregnancy?

   A year later, she returns, two months pregnant, having been on folic acid supplements. Fetal echocardiogram at 18 weeks demonstrates the presence of hypoplastic left heart syndrome. She and her husband are counselled regarding the extremely poor prognosis for their baby and they elect to continue the pregnancy. Their daughter is born at term weighing 5 pounds and dies at 3 days of age.

4. Has her recurrence risk for congenital heart defect changed in view of this history?

   Two years later, she is again pregnant and you follow the previous plan of management. This time the fetal echocardiogram reveals an apparently normal fetal heart. She gives birth at term to a 6 lb. 2 oz son. At his 1 month checkup, you detect a heart murmur. The child is found to have a patent ductus arteriosus (PDA). The parents are reassured that this is a minor congenital heart defect but he requires surgical repair.

5. Are you becoming suspicious that there may be some underlying genetic disorder or is this mother just unlucky?

   Your patient becomes pregnant for the third time. A routine ultrasound detects only one kidney but fetal echocardiogram is normal. She delivers a healthy 6 lb. 2 oz boy. As a precaution, you refer him for a cardiology assessment and he is found to have a small ventricular septal defect. His maternal grandmother now comes to see you and insists there must be a reason for all of the heart defects in this family. You start to reassess the situation. Now that you think of it, there do seem to be more than just heart problems.

   The child with the PDA has been slow to talk and it is difficult to understand his speech. His mother states that she herself required speech therapy throughout school and her speech is still quite hypernasal. She describes herself as a "slow learner". The baby with the VSD and unilateral renal agenesis tends to regurgitate frequently through his nose.

6. What type of problem is suggested by these symptoms?

   On looking closely at the mother and two children, you note that they share some physical characteristics. They are not strikingly dysmorphic but they do have small ears and hypertelorism (increased distance between the pupils). Mother has a long nose and high nasal bridge.

7. What is your diagnosis?

8. What tests will you order to confirm this diagnosis?

9. Now that you have a definite diagnosis, what is the recurrence risk?

10. Does this alter your plan of management for future pregnancies?

11. Your patient’s sister is now pregnant and very worried about her risk of having a child with congenital heart defect. What can you tell her?

12. Is this just another one of those esoteric cases that you’ll never see in practice?
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Problem Solving

ANSWERS TO CASE STUDY

1. Family history of congenital heart defects, other congenital malformations, recurrent miscarriages or stillbirths
   History of smoking/alcohol intake
   Exercise tolerance, recent cardiac evaluation

2. (a) In general, the risk of having a child with congenital heart defect if one parent is affected is approximately 1 in 30 (3%).
   (b) Based on her negative family history, her risk of having a child with neural tube defect is the same as that of the general population, approximately 1 in 800.
   (c) Her risk of having a child with Trisomy 21 depends on her age at delivery. At a maternal age of 20 years, the risk is about 1 in 1650.

3. GENERAL:
   (i) periconceptional folic acid supplements at a daily dose of 1 mg PO to decrease the risk for neural tube defect.
   (ii) maternal serum screening at 15 1/2 weeks to screen for risk of neural tube defect and Down syndrome.

SPECIFIC:
   (iii) fetal echocardiogram at 18 weeks to screen for major cardiac malformations.
   (iv) careful monitoring of her cardiac status and SBE prophylaxis for any dental extractions and potentially septic surgical procedures.

4. Yes. With an affected mother and child, the recurrence risk is definitely increased to at least 10%.

5. Patent ductus arteriosus is quite common in premature infants, and usually closes spontaneously or with the aid of indomethacin. However, PDA is rare in term infants. You should now be considering very strongly the possibility of a specific underlying diagnosis.

6. Velopharyngeal insufficiency. You should look for evidence of any palatal problems such as a cleft palate (overt or submucous) or bifid uvula. On examination, mother does have a submucous cleft palate.

7. The combination of velopharyngeal insufficiency with submucous cleft palate, cardiac defect, learning problems, and facial features section (long nose with prominent nasal root, ear anomalies) is typical for Shprintzen (velocardiofacial) syndrome, first described in 1978. In 1992, Shprintzen syndrome was found to be associated with a deletion of part of the long arm of chromosome 22. Other congenital malformation syndromes which may have the same 22q11.2 deletion include DiGeorge syndrome and CHARGE association. All of these disorders are now grouped under the acronym of CATCH 22 which describes the various systems that may be affected, i.e. Cardiac, Abnormal facies, Thymic hypoplasia, Cleft palate, Hypocalcemia (due to hypoparathyroidism). Affected structures are all derivatives of the third and fourth pharyngeal pouches. There is considerable intrafamilial variation (as demonstrated by this case history) as well as interfamilial variation. In the most severe cases, a newborn may present with hypocalcemic seizures, recurrent infections due to decreased T cell function, and major congenital heart defect. Much milder cases may not be diagnosed until a child is investigated for learning problems and speech delay.

8. Occasionally, the deletion may be detected on routine chromosome karyotyping, especially if you indicate that you are interested in the 22q region. However, in the majority of cases, special request must be made for a FISH (Fluorescence In-Situ Hybridization) study, again specifying the 22q region. The cytogenetics laboratory will prepare a metaphase chromosome spread, hybridize to a 22q11.2 DNA probe, and utilize a fluorescent marker to determine whether or not there is a deletion (see illustration).

9. In this family, the mother was proven to have a 22q11.2 deletion which occurred de novo (neither of her parents had the deletion). Both of her sons (and likely her daughter) inherited the deletion. In any future pregnancy, she will have a 50% risk of passing on the deletion. Similarly, her affected children will have a 50% risk of passing on the deletion to their offspring.

10. Chorionic villus sampling at 10 to 12 weeks or amniocentesis at 15 to 18 weeks could be offered to determine if the fetus has inherited the deletion and, if so, fetal echocardiogram would be indicated to determine the severity of congenital heart defect.

11. Since this is a de novo deletion in your patient, her unaffected sister has the same risk as that of the general population for having a child with congenital heart defect. No special prenatal investigations are indicated for the sister.

12. No. Deletions of 22q have been found in up to 5% of all newborns with heart defects and may represent the most common chromosome abnormality after Down syndrome (Trisomy 21). The spectrum of problems seen in CATCH 22
results in many different specialists having the opportunity of assessing and diagnosing a patient: ENT, cardiology, plastic surgery, endocrinology, neurology, immunology. Undoubtedly, there are many undiagnosed cases, particularly as this deletion syndrome is just starting to be recognized.

ACKNOWLEDGEMENTS

I would like to thank Dr Yao Shan Fan for graciously providing a photo of the cytogenetic findings. Dr Yao Shan Fan is the Director of the Regional Cytogenetics Laboratory, London Health Sciences Centre.

REFERENCES


Ω
The Vocabulary Section of this issue was compiled with the help of health care providers in the area of paediatric medicine from seven different countries. The forum for this exchange of ideas was an Internet chat channel called International Pediatric Chat. The website for this organization can be found at the following URL: http://www.pedschat.com. Instructions on how to access the chat channel are provided at that site. Below is an excerpt from this innovative new service.

"International Pediatric Chat (IPC) is an organization of pediatric professionals who use live Internet typing, voice chat, and hopefully someday video conferencing as a means of communicating with each other. It was started May 16, 1996 by Dr Julius Edlavitch from Minneapolis, Minnesota. It is like a giant doctors’ lounge where pediatricians, pediatric nurse practitioners, pediatric specialists, pediatric nurses, and other medical professionals interested in children meet. Below are some of the benefits and features section of IPC.

- live socialization of the members on a regular basis to develop professional friendships never before possible
- professionals can drop into this lounge on a 24 hour a day basis, 7 days a week, to share medical and personal information
- medical education sessions with international perspectives promote free thinking and help professionals approach some of their dilemmas with new and culturally diverse perspectives
- need help? 24 hours 7 days a week, pediatric professionals can get live help from others; one can share cases like never before”.

**PAEDIATRIC MEDICAL VOCABULARY**

1. **LANUGO**
   a. fetal hair
   b. an endemic granulomatous disease
   c. a bundle of fibers in the immature CNS
   d. ubiquitous colour of neonates’ eyes

2. **PRUNE-BELLY DISEASE**
   a. diarrhea
   b. congenital truncal maroon discoloration
   c. Eagle Barrett Syndrome
   d. eponym for appearance of baby’s skin after prolonged immersion in bath water

3. **NIPPLE CONFUSION**
   a. a.k.a. Triple nipple disease
   b. infant thinks his/her nostrils are nipples
   c. infant is born with extra nipples
   d. infant refuses mother’s nipple after experiencing bottle

4. **DIASTEMATOMYELIA**
   a. hernia of rectus muscle
   b. an unusual constitutional susceptibility to a particular disease
   c. anomaly resulting in Tethered Cord Syndrome
   d. the rest period of the cardiac cycle of a neonate, prior to systolic muscle contraction

5. **SYNOPHYRS**
   a. converging brain cells
   b. secondary sensations accompanying actual perceptions
   c. congenital fusion of the testes into one mass
   d. eyebrows that meet in the midline

6. **HURLER DISEASE**
   a. overuse syndrome typified by synovitis of biceps brachialis muscle
   b. congenital lysosomal storage disease
   c. a.k.a. congenital pyloric stenosis
   d. plague to hit Blue Jay pitchers in 1994 season

7. **MONGOLIAN SPOTS**
   a. dermatitis associated with Mongolism (Trisomy 21)
   b. certain bars and restaurants found on Richmond St.
   c. transient blue/black pigmented macules
   d. neonatal red raised lesion

8. **TRICHOTILLOMANIA**
   a. compulsive mischievous behaviour
   b. affective disorder triggered by Trichomonas
   c. compulsive pulling out of one’s hair
   d. meaningless repetition of words and phrases

9. **TALIPES EQUINOVARUS**
   a. flatfoot
   b. clubfoot
   c. fear of horses
   d. congenital lesion at level of cauda equina

10. **ELEKTRA COMPLEX**
    a. Pseudo-Freudian condition of morbid daughter-father attachment
    b. Nintendo-caused thumb synovitis
    c. side effect in some paediatric electroconvulsive therapy recipients
    d. complex of eschar and gangrenous tissue after an electric burn

**ABOUT THE AUTHOR**

Jordan B. Solman is a third-year medical student with a BSc from the University of Toronto. He is interested in paediatric surgery.
NORVASC (amlodipine besylate/pfizer)

**Brief Prescribing Information**

**NORVASC** (amlodipine besylate)

**Tablets 2.5, 5 and 10 mg**

**ACTION AND CLINICAL PHARMACOLOGY**

NORVASC (amlodipine besylate) is a calcium ion influx blocker (calcium entry blocker or calcium antagonist).

**INDICATIONS AND CLINICAL USE**

**Hypertension**

NORVASC (amlodipine besylate) is indicated in the treatment of mild to moderate essential hypertension. NORVASC should normally be used in those patients in whom treatment with diuretics or beta-blockers was found ineffective or has been associated with unacceptable adverse effects. NORVASC can be tried as an initial agent in those patients in whom the use of diuretics and/or beta-blockers is contraindicated or in patients with medical conditions in which these drugs frequently cause serious adverse effects. Combination of NORVASC with a beta-blocker, a diuretic or an antihypertensive agent is an established approach to treating hypertension.

**Chronic Stable Angina**

NORVASC is also indicated for the management of chronic stable angina (rest-induced angina) in patients who have symptomatic despite adequate doses of beta-blockers and/or organic nitrates who do not tolerate those agents. NORVASC may be tried in combination with beta-blockers in chronic stable angina patients in normal ventricular function. When such concomitant therapy is introduced, care must be taken to monitor blood pressure and pulse to detect early indications of hypotension or sinus bradycardia. Hypotension may occur when the drug is suddenly discontinued or following the abrupt withdrawal of other antihypertensive agents. Hypotension and/or bradycardia may occur in the elderly. Although these phenomena have not been systematically studied, the elderly appear to be especially susceptible to postural hypotension with this class of drugs, and should be monitored closely for such events.

**CONTRAINDICATIONS**

NORVASC (amlodipine besylate) is contraindicated in patients with hypersensitivity to the drug or other dihydropyridines and in patients with severe hypotension and allergic reactions (less than 90 mmHg systolic).

**WARNINGS**

**Use in Patients with Congestive Heart Failure**

NORVASC (amlodipine besylate) in patients with heart failure has not been established. Caution should therefore be exercised when using NORVASC in patients with compromised ventricular function, particularly in combination with a beta-blocker. In a controlled clinical trial using a small number of patients with stable heart failure (NYHA Class III), addition of NORVASC to digoxin and diuretic therapy with or without angiotensin converting enzyme inhibitors did not lead to an attenuation of heart failure symptoms in patients treated.

**Increased Angina and/or Myocardial Infarction**

Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed ischemia with increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

**Outflow Obstruction (Aortic Stenosis)**

NORVASC should be used with caution in the presence of fixed left ventricular outflow obstruction (aortic stenosis).

**Use in Patients with Impaired Hepatic Function**

There are no adequate studies in patients with liver dysfunction and dosage recommendations have not been established. In a small number of patients with mild to moderate hepatic impairment given single dose of 5 mg, no major differences were observed. However, because of the potential for drug accumulation in patients with impaired hepatic function, the dosage should be reduced to 2.5 mg once daily.

**Peripheral Edema**

Mild to moderate peripheral edema was the most common adverse event in the clinical trials (see ADVERSE REACTIONS). The incidence of peripheral edema was dose-dependent and ranged in frequency from 3.0% to 10.8%.

**Use in Pregnancy**

Although amlodipine was not teratogenic in the rat and rabbit some dihydropyridine compounds have been found to be teratogenic in other species. What do the second generation agents gives no protection against the dangers of abrupt beta-blocker withdrawal and such withdrawal should be avoided. There is no evidence of hypotension but tachycardia (180 bpm) was observed. (pecase administered 3.5 hours after ingestion and on subsequent observation no sequelae were noted.)

**Use in Elderly or in Patients with Impaired Renal Function**

The recommended initial dose in patients over 65 years of age or patients with impaired renal function is 5 mg once daily. If the dose has increased after 1-2 weeks to a maximum dose of 10 mg once daily.

**STORAGE**

Shelf-stable 5-7°C. Protect from light.

**REFERENCES**

ANSWERS TO PAEDIATRIC VOCABULARY

1. a) The fine hair on the body of a fetus.

2. c) Also known by the eponym Eagle Barrett Syndrome; congenital anomaly which gives the abdomen a wrinkled appearance resembling dried fruit; consists of bilateral megaureter, hydronephrosis, and may include megabladder, bilateral cryptorchidism, and/or megaurethra.

3. d) Because of different mechanics involved in sucking from a bottle, an infant switched to breast feeding may refuse to latch onto the mother’s nipple.

4. c) A malformation in which the spinal cord is split by bone spicules or a fibrous band. This condition and a lipomatous tumor produce Tethered cord syndrome, with resultant abnormalities of distal sensation, gait, and bladder or bowel function.

5. d) A term used to describe the specific dysmorphology of the face in which the eyebrows meet in the midline.

6. b) Deficiency of the enzyme alpha-L-Iduronidase is associated with kyphosis and profound loss of CNS function. Onset is at about 1 year; the cornea appears cloudy, and hepatosplenomegaly is present.

7. c) Mongolian spots are transient dark blue to black pigmented macules seen over the lower back and buttock in as many as 90% of black, Indian, and oriental infants.

8. c) This is a condition in which one is compelled to pull out one’s hair as a means of relieving the anxiety caused by persistent intrusive thoughts.

9. b) Clubfoot may be congenital, teratologic, or positional. Examination of the infant clubfoot demonstrates hindfoot equinus and varus, forefoot adduction, and variable rigidity.

10. a) This a Freudian condition which is roughly parallel to the gender-reversed Oedipal complex; a female child’s morbid attachment to the parent of the opposite sex, and her jealousy towards the parent of the same sex.
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