Dalhousie Research Day
Winning Abstracts

Each year, the Dalhousie Medical School holds a medical research competition where students present work either as a poster or an oral presentation. The following abstracts are from the presentations judged to be the best in 1997, in both the oral and poster categories.

ORAL PRESENTATIONS

First Place

Non-compensated, Informal Caregivers for Community Acquired Pneumonia

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Background: Although there is a vast amount of research on informal caregivers, the studies are overwhelmingly focused on caregivers of patients who are chronically ill. It is unclear whether the findings of this research can be transferred to caregivers of patients with acute diseases.

Objectives: (1) to describe caregivers and their importance in the management of patients diagnosed with community acquired pneumonia (CAP); (2) to identify predictors of the presence of a caregiver for patients with CAP; and (3) to determine the effects of caregiving on the daily life of the caregiver.

Setting: Four university teaching hospitals and one clinical site with an health maintenance organisation.

Subjects: 712 consecutive patients diagnosed with pneumonia and at low risk for mortality; 191 non-compensated, informal caregivers for these patients.

Design: Prospective observational study (patients) and structured prospective interviews (caregivers) at 7, 30 and 90 days post patient pneumonia diagnosis.

Measurements: Demographics (patients and caregivers), patient outcomes and assistance provided to the patient, functional disability resulting from caregiving and attitudes toward the caregiving role.

Results: 30.3% of patients received caregiver assistance during the 90 day post-diagnosis study period. Patients who were female, married, younger, treated on an inpatient basis or at a higher risk stratum (within low risk) were more likely to have a caregiver (all p < 0.05). The mean age of the caregivers was 44 years and caregivers were more likely to be female (61.2%), employed (55.1%) and the spouse of the patient (57.5%). Caregivers spent a mean of 9.3 hours a week on caregiving activities specific to the pneumonia illness. Inpatients received more types of assistance and more hours of assistance than did outpatients. 67.9% of employed caregivers experienced at least moderate employment interference as a result of caregiving. Caregivers admitted mild functional impairment and mild agreement with negative attitudes toward caregiving. Level of activity restriction was closely correlated with negative attitude scale (R-squared = .978).

Conclusions: A large proportion of low risk patients with CAP identify caregivers during their episode of illness. These caregivers provide considerable assistance and endure life interference as a result of caregiving activities.

Second Place

Increased Expression of Basic Fibroblast Growth Factor (bFGF) in the Neonatal Brain Following Glutamate Induced Neurotoxicity

Janet MacIntyre¹, MD '00, and Michael Wilkinson², MD, PhD

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Glutamate, an excitatory neurotransmitter, is emerging as one of the key factors involved in sexual maturation. Treatment of neonatal rats with glutamate has been shown to induce precocious puberty by an unknown mechanism. Smyth and Wilkinson (1994) demonstrated that a single treatment of GLU (monosodium glutamate) shortly after birth, or treat-
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(2) Full remission rates (HAM-D 0 total < 7) vs. placebo, in a 9-week randomized, double-blind study of venlafaxine XR (n=169), fluoxetine (n=102) and placebo (n=167). The full remission rate at week 9 was nearly twice as high in the venlafaxine XR group as it was in the fluoxetine group, a statistically significant difference (p<0.005) only at that time point.

(3) 9-week randomized, double-blind, placebo-controlled study of 322 patients comparing venlafaxine XR 75 mg and 150 mg and paroxetine 20 mg once-daily. Venlafaxine XR 75 mg was significantly (p<0.05) more effective than paroxetine 20 mg on HAM-D scores at week 1, 2, 4, 6 and 8 and venlafaxine XR 150 mg was significantly (p<0.05) more effective than placebo on the HAM-D at week 4, 6, and 8.

Remission rates with venlafaxine XR 75 and 150 mg were 57% compared with 48% and 44% in the placebo and paroxetine groups, respectively.

(4) In clinical trials, the most commonly observed adverse events associated with the use of Effexor XR (exceeding 5% or greater) and not seen at an equivalent incidence among placebo-treated patients were: abnormal dreams, insomnia, dizziness, dry mouth, nausea, nervousness, somnolence, sweating, and nervousness as well as abnormal ejaculation in men. There was evidence of adaptation to some adverse events with continued therapy (e.g., dizziness and nausea, but less to other effects (e.g., abnormal ejaculation and dry mouth). Some adverse events appeared to be dose-dependent.

(5) 75 mg/day is the recommended dosage for most patients. Dosage adjustment is necessary in patients with hepatic or renal impairment. Treatment with venlafaxine has also been associated with modest but sustained increases in blood pressure.

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The recommended treatment dose is 75 mg per day divided in one or two divided doses, taken with food. If the expected clinical response does not occur after a few weeks, a gradual dose increase to 150 mg per day is recommended. If needed, the dose may be further increased to 375 mg per day. It is recommended to be taken around the same time each day. In elderly patients, a gradual dose increase to 150 mg per day is recommended. If needed, the dose may be further increased to 375 mg per day. It is recommended to be taken around the same time each day. It is recommended to be taken around the same time each day.

**EFEXOR XR Capsules:**
A slower rate of drug release is achieved in the extended-release formulation of EFEXOR XR capsules. This provides a lower and more consistent drug level, which allows for fewer daily doses. It is recommended to be taken at the same time each day.

**DOSEAGE AND ADMINISTRATION:**

EFEXOR XR is contraindicated in patients with a history of QTc prolongation or in those with known electrolyte abnormalities. It is also contraindicated in patients with a history of uncontrolled or severe arrhythmias.

**Pregnancy and Lactation:**
EFEXOR XR is not recommended for use during pregnancy or lactation. It is not known if EFEXOR XR is excreted in human milk. If the use of EFEXOR XR is considered, the potential benefits should be weighed against the potential risks.

**Geriatric Use:**
EFEXOR XR was not studied in patients 65 years of age or older. It is recommended to use with caution in elderly patients and to use the lowest effective dose.

**ADVERSE REACTIONS:**

**Cardiovascular System:**
- Hypertension
- Palpitations
- Bradycardia

**Central Nervous System:**
- Dizziness
- Somnolence
- Headache

**Gastrointestinal System:**
- Constipation
- Diarrhea

**Hematologic System:**
- Eosinophilia

**Other Adverse Reactions:**
- Headache
- Mild elevation of liver enzymes

**Laboratory Tests:**
- Periodic measurement of liver function tests and complete blood count is recommended. It is recommended to perform these tests at the start of treatment and every 6 to 8 weeks during treatment.

**Discontinuation of EFEXOR XR Therapy:**
It is recommended to gradually taper the dose over a period of 1 to 2 weeks to avoid withdrawal symptoms. If symptoms occur, they should be treated with a lower dose of EFEXOR XR.

**Pharmacokinetics:**
EFEXOR XR has a longer duration of action compared to EFEXOR Tablets due to the extended-release formulation. The pharmacokinetics are linear over the dose range of 75 to 375 mg.

**EREfExOR:**
EFEXOR XR is a once-daily extended-release formulation of EFEXOR that provides a lower and more consistent drug level, which allows for fewer daily doses. It is recommended to be taken at the same time each day.

**Ventricular Tachycardia:**
Patients with ventricular tachycardia are at increased risk of developing ventricular tachycardia. It is recommended to use EFEXOR XR with caution in patients with ventricular tachycardia.

**Drug Interactions:**
EFEXOR XR can interact with other medications, including warfarin, digoxin, and phenytoin. It is recommended to use with caution and monitor for adverse effects.

**Special Populations:**
EFEXOR XR is not recommended for use in children or adolescents due to insufficient data on its safety and efficacy in this population.

**Dosage Forms:**
EFEXOR XR is available in 75 mg, 150 mg, and 375 mg capsules.

**How Supplied:**
EFEXOR XR is supplied in bottles of 100 capsules. It is recommended to take the capsules whole, without breaking or crushing them.

**Package Information:**
The package inserts of EFEXOR XR should be reviewed before use.

**Burden of Illness:**
EFEXOR XR is associated with a reduction in symptoms of depression and anxiety. It is recommended to provide patient education on the importance of consistent medication use and the potential benefits of EFEXOR XR.

**References:**
ment with NMDA, a GLU agonist, after weaning, resulted in the premature induction of puberty. The mechanism by which GLU mediates this process has not been elucidated. We hypothesize that GLU may induce precocious puberty by: (1) neurotoxic removal of inhibitory cells of the GnRH system and/or (2) acceleration of normal development, perhaps via growth factors. One such factor is basic fibroblast growth factor (bFGF). The objective of this study was to examine the distribution of bFGF in the brain of the neonatal female rat following glutamate treatment.

Neonatal rats, on postnatal day 2 (P2), received a single sc injection of either saline solution (control) or monosodium glutamate (MSG) at a dose of 4 mg MSG/g body weight. Starting on P3, two or three animals from both experimental groups were collected and sacrificed at 2-day intervals up to the age of P9. The expression of bFGF in the neonatal brain was examined using immunocytochemical procedures. bFGF was visualized in the dorsomedial nucleus, ventromedial nucleus and arcuate nucleus of the hypothalamus, within the hippocampus and diffusely throughout the cerebral cortex of both MSG treated and control animals. Following treatment with MSG on P2, bFGF immunoreactivity in the arcuate nucleus increased between P4 and P9 compared to control animals. By P9 the difference between bFGF immunoreactivity observed in the arcuate nucleus of MSG treated and control animals had decreased. These data suggest that bFGF may be one component of the neural reorganization that leads to precocious puberty.

In conclusion, the present study determined bFGF was present in several specific regions of the neonatal brain. Treatment with MSG resulted in an increase in bFGF expression within the arcuate nucleus. These results support the possibility that the expression of bFGF following a GLU-induced lesion in the hypothalamus promotes the precocious maturation of GnRH neurons and partially stimulates the onset of precocious puberty.

Janet MacIntyre is a third year medical student at Dalhousie University. Funding for this study was supported by a Dalhousie Medical School Summer Studentship (Elizabeth Rafuse Studentship) and grants from the Medical Research Council of Canada and the IWK-Grace Foundation.

Third Place

Isolation of Two Genes from S. cerevisiae: Role in Phosphatidylcholine Reacylation

Janice Chisholm, BSc, MD '00, and Christopher McMaster, PhD

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2 Atlantic Research Centre, Department of Pediatrics, IWK-Grace Health Centre

The accumulation of unsaturated fatty acyl species within the backbone of phosphatidylcholine (PtdCho) is regulated by the activity and substrate specificity of lysoPtdCho acyltransferase. Neither the cDNA nor the gene for the lysoPtdCho acyltransferase have been isolated from any source. In this study, two approaches were used to attempt to isolate and characterize the gene in the eukaryotic yeast S. cerevisiae. The first approach was the development of a colony autoradiography assay specific for lysoPtdCho acyltransferase activity. Attempts to optimize this assay were unsuccessful, as specificity for only lysoPtdCho acyltransferase activity was not possible. The second approach used to isolate and characterize the gene was via computer algorithms to identify tentative active site motifs, in the known genome of S. cerevisiae, that are associated with acyltransferase reactions. The results of this, coupled with the known biochemical characteristics of lysoPtdCho acyltransferase, yielded two sequences, YBL011w and YKR067w. The genes were then amplified and transformed into wild type yeast cells under high copy (Yep).

Based on known biochemical properties of lysoPtdCho acyltransferase activity, coupled with the presence of a motif common to other glycerolipid acyltransferase enzymes, it is predicted that these two genes are good candidates for coding of glycerolipid acyltransferase activities themselves. Although this remains to be proven biochemically, this study has yielded the cloned genes that can be used as a set of molecular tools for analysis of the encoded products.

Janice Chisholm is a third year medical student at Dalhousie University. She graduated from Bishop's University in 1996 with a BSc (Hon) in biochemistry.

POSTER PRESENTATIONS

First Place

β-Adrenergic Receptors in Fetal Rabbit Lung: Characterization and Ontogeny Studies

Philip Wornell, BSc (Hon), MD '00, Kathleen Landymore, MD, PhD, Margaret Oulton, PhD

1 Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia
2 Department of Obstetrics and Gynaecology, IWK-Grace Health Centre and Faculty of Medicine, Dalhousie University
3 Department of Physiology and Biophysics, Faculty of Medicine, Dalhousie University

The tissue punch technique using the hydrophilic radioligand [3H]CGP-12177 was used to characterize β-adrenergic receptors in fetal rabbit lung and quantify the development of this receptor population during early ontogeny. [3H]CGP binding to the lung punches was saturable, rapid,
reversible, linearly related to punch number at 30°C and reached equilibrium at this temperature by 1 h. The results of the ontogeny study indicated that the number of β-adrenergic receptors in rabbit lung increases progressively during gestation between days 24 and 30 and that this increase continues after birth during early postnatal life. The affinity of this population of receptors remains the same throughout this period. The tissue punch technique using the hydrophilic radioligand [3H]CGP-12177 is suitable for the study of β-adrenergic receptor binding in fetal lung tissue. Involving minimal tissue disruption, this technique represents a more physiologically relevant alternative to those techniques involving tissue homogenization and centrifugation.

Philip Wornell graduated from Dalhousie University in 1996 with a BSc combined Honours degree in Biochemistry and Microbiology. During the summer of 1998, he continued his research under the supervision of Drs. Landymore and Oulton, using the tissue punch technique to determine the effects of maternal hormone administration on the development of beta adrenergic receptors in the fetal rabbit lung. At this time, his career choices include internal medicine, pediatrics and family medicine. Philip hopes to be involved in research throughout his career.

Second Place

Choice of Antibiotic for the Empiric Treatment of Community-Acquired Pneumonia: Results of a Survey of Nova Scotia General Practitioners

Jacob Pendergrast1, BSc, MD '99, Tom Marrie2, MD, FRCPC

1 Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia
2 Department of Medicine, Division of Infectious Diseases, QEII Health Sciences Centre

Introduction: Community-acquired pneumonia (CAP) is one of the most prevalent infectious diseases in North America and is responsible for significant mortality and morbidity. Although effective treatment depends greatly on targeting antibiotic therapy towards a specific pathogen, physicians must often initiate therapy empirically, without culture and sensitivity data. As a result, there is a large variation in the types of antibiotics prescribed for CAP. By understanding the factors that predict which antibiotic a physician will choose, programs aimed at rationalizing antibiotic prescription can be made more effective.

Methods: Questionnaires were mailed during the spring of 1997 to the 841 general practitioners registered with the Medical Society of Nova Scotia. The questionnaires were based on three hypothetical cases of CAP in which a definite pathogen was not known. The first case was a 17-year-old male with an uncomplicated pneumonia and a chest x-ray showing a lobar infiltrate. The second case was a 66 year-old man with a smoking history and a Gram stain showing Gram-positive diplococci. The third case was a 45-year-old woman with a severe pneumonia requiring ICU admission whose chest x-ray revealed bilateral infiltrates. Respondents were asked to choose an antibiotic for each case and indicate the reason for their choice using a series of Likert scales. One half of the surveys included a series of knowledge-testing questions on microbiology.

Results: 188 questionnaires were returned (22.4%). For the first case, respondent choice of antibiotic correlated with respondent age, graduation year, and CCFP training. Choice also depended on the importance respondents expressed with regards to: desire to cover a specific pathogen; antimicrobial resistance; and drug side effects. For the second case, antibiotic choice depended on the importance respondents attached to: the patient's general health and smoking status; antimicrobial resistance; experience with similar cases; cost-effectiveness; and number of pathogens targeted. For the third case, the only significant predictor of antibiotic choice was respondent familiarity with the case.

Conclusion: As case complexity increased, there was greater variation in the antibiotics chosen, and decreasing consensus between general practitioners and infectious diseases specialists. The more familiar a respondent was with a particular case of pneumonia, the more explicit the decision-making strategy underlying their choice of antibiotic. Overall, general practitioners prescribed appropriately for straightforward cases of CAP, and demonstrated a good understanding of the relevant microbiology.

Jacob Pendergrast is a final year medical student at Dalhousie University. He received a BA (Hon) in history and philosophy from McGill University in 1995. He is enrolled in the BSc (Med) programme. His research interests include physician practice patterns and disease epidemiology.

Third Place

Cardiac Surgery In Octogenarians: Can Elderly Patients Benefit?

Deborah Fruitman1, BSc (Hon), MD '00, Carolyn MacDougall2, RN and David B. Ross2, MD, FRCSC

1 Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia
2 Department of Surgery, Division of Cardiovascular Surgery, QE II Health Sciences Centre

Purpose: Increasing numbers of the very old are developing cardiovascular disease and presenting for surgery. While risk factors and outcomes for perioperative events have been described, there is little information regarding quality of life following hospital discharge in this group.

Methods: From March 1995 to February 1997, 127 patients ≥ 80 years at operation (mean age 83±2.5 years, range 80-92) were entered into the cardiac surgery database and
analysed retrospectively. The RAND SF-36 Health Survey
1.0 and the Seattle Angina Questionnaire were used to assess
quality of life by telephone interview (mean follow-up
15.7±6.9 months). No patient was lost to follow-up.

Results: Operations included isolated CABG (65.4%),
CABG + Valve (15.8%), and isolated valve replacement
(14.2%). Preoperatively, 63.8% were in NYHA Class IV.
Thirty-day mortality was 7.9% and actuarial survival was 83%  
(70% CI, 79% to 87%) at one year and 80% (70% CI, 75% to
85%) at two years. Ninety-five patients (92.2%) were in
NYHA Class I or II at follow-up. All but one patient im-
proved by at least one functional class following surgery.
RAND SF-36 scores were equal to or better than for the gen-
eral population of age ≥ 65 years. Patients showed lower
scores in physical functioning (62.9±27.1) and vitality
(58.1±21.7), but had very good scores for emotional well-
being (85.0±18.0), role limitations due to emotional health
(89.3±27.4) and social functioning (84.9±25.1). Seattle An-
gina Questionnaire scores for anginal frequency (92.3±18.9),
stability (94.4±18.9) and exertional capacity (86.8±25.1) in-
dicated good relief of symptoms. Of the survivors, 83.7%  
were living in their own home, 74.8% rated their health as
good/excellent, and 82.5% would undergo cardiac surgery
again in retrospect.

Conclusion: Despite being a high risk group for car-
diac surgery, octogenarians can undergo cardiac surgery at a
reasonable risk and show remarkable improvement in their
symptoms. Elderly patients benefit from improved functional
status and quality of life following surgery.

Debbie Fruitman received her BSc (Hon) in biology
and nutrition studies from the University of Guelph in 1994.
Her current research interests are in pediatrics. She is pres-
cently working on a project involving complex congenital heart
disease. Her career goals include pediatrics and internal
medicine. Debbie wishes to combine her future clinical prac-
tice with research.
**LANOXIN®, (digoxin) Cardiac glycoside**

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**Indications**
2. Atrial fibrillation with rapid ventricular response.
3. Atrial flutter.
4. Paroxysmal atrial tachycardia.

**Contraindications**
1. Ventricular fibrillation.
2. A need for permanent disconnection of other digitalis preparations usually constitutes a contraindication to digoxin.
3. Allergy to digoxin, though rare, may occur. It may not be limited to all digitalis preparations, and another may be tried.

**Warnings**
1. Dosage must be carefully titrated. Patients with renal insufficiency or severe carditis are especially sensitive and may require reduced dosages.
2. Newborn infants display considerable variability in their tolerance to digoxin. Premature and immature infants are particularly sensitive, and dosage must not only be reduced but must be individualized according to their degree of maturity. NOTE: Digitalis glycosides are an important cause of accidental poisoning in children.
3. Anorexia, nausea, vomiting and arrhythmias may accompany heart failure or may be indications of digitalis intoxication. Clinical evaluation of the cause of the symptoms should be attempted before further digitalis administration. If the possibility of intoxication cannot be excluded, cardiac glycosides should be temporarily withheld, if permitted by the clinical situation.
4. Heart failure accompanying acute glomerulonephritis requires extreme care in digitalization. Relatively low loading and maintenance doses and concomitant use of antihypertensive drugs may be necessary and careful monitoring is essential. Digoxin should be discontinued as soon as possible, especially if a therapeutic trial does not result in improvement.
5. Patients with severe carditis, such as carditis associated with rheumatic fever or viral myocarditis, are especially sensitive to digoxin-induced disturbances of rhythm.

**Precautions**
Digitalization with a long-acting cardiac glycoside during the previous two weeks, or the presence of moderate or severe renal impairment may enhance digoxin toxicity. Patients with acute myocardial infarction, severe pulmonary disease or advanced heart failure may be unusually sensitive to digoxin-induced disturbances of rhythm.

Hypokalemia sensitizes the myocardium to digitalis, and toxicity is apt to develop even with the usual dosage. Hypomagnesemia and hypercalcemia may also increase sensitivity to cardiac glycosides. Hypokalemia may nullify the effects of digoxin and should be corrected before a full digitalizing dose is given.

Quinidine, verapamil and some antibiotics may cause increased serum digoxin concentrations.

Atrial arrhythmias associated with hypermetabolic states are particularly resistant to digitalis therapy. Care must be taken to avoid digitalis toxicity if digoxin is used to help control the arrhythmia.

Special care is necessary when using cardiac glycosides during cardiac overdrive or in patients with incomplete AV block, Wolff-Parkinson-White syndrome and atrial fibrillation.

Patients with chronic congestive pericarditis or heart failure from amyloid heart disease often respond poorly.

Patients with idiopathic hypertrophic subaortic stenosis or sinus tachycardia should receive digoxin only when severe heart failure is present.

Differences in bioavailability of parenteral preparations, elixirs and tablets must be taken into account when transferring patients from one dosage form to another.

Periodic assessment of serum electrolytes and renal function is recommended.

Digoxin should be given to pregnant women only when clearly needed. Digoxin is excreted in human milk but the amount is small and should have no pharmacological effect upon the infant. Nevertheless, caution is advised in these circumstances.

**Adverse Reactions**
The overall incidence of adverse reactions has been reported as 5 to 20% with 15 to 20% of them being considered serious (1 to 4% of patients receiving digoxin).

Cardiac — Approximately 50% of all adverse reactions. Largely ventricular premature contractions, or ventricular tachycardia. Atroventricular dissociation, AV block and complete heart block may occur. In children atrial tachycardias, with or without block, and junctional (nodal) tachycardia are more common.

Gastrointestinal — Anorexia, nausea, vomiting and diarrhea.

CNS — Blurred or yellow vision, headache, weakness, apathy and psychosis.

Other — Gynecomastia. Note: For severe or complete heart block due to digitalis intoxication and not primarily related to supraventricular tachycardia do not use potassium. Lidocaine, procainamide and propanolol may be useful. Temporary ventricular pacing may be beneficial.

**Dosage and Administration**
Digitalization should always be individualized. The following serves as a guideline only. For more information consult the Prescribing Information.

**Rapid Digitalization**
In previously undigitized patients a single oral dose of 0.5 to 0.75 mg usually produces a detectable effect within 2 hours, and becomes maximal in 2 to 6 hours. Additional doses of 0.125 to 0.25 mg may be given at 6 to 8 hour intervals, until an adequate effect is noted.

The usual daily maintenance dose is 0.25 mg, based on a body weight of 70 kg and a Cor of 60 mL/min.

For doses in infants and children consult the Prescribing Information.

**Measurement of serum digoxin concentration** is important in determining the state of digitalization.

**Availability**
LANOXIN® (Digoxin) Tablets, 0.0625 mg (62.5 µg); Bottles of 100 tablets: imprinted with LANOXIN and USA (peach).

LANOXIN® (Digoxin) Tablets, scored 0.125 mg (125 µg); Bottles of 100 and 1000 tablets: imprinted with LANOXIN and Y38 (yellow).

LANOXIN® (Digoxin) Tablets, scored 0.25 mg (250 µg); Bottles of 100 and 1000 tablets: imprinted with LANOXIN and X34 (white).

LANOXIN® (Digoxin) Tablets, scored 0.5 mg (500 µg) per mL; Bottles of 115 mL with calibrated dropper.

LANOXIN® (Digoxin) Injection, 0.25 mg (250 µg) per mL; Bottles of 10 ampules; 0.5 mg (500 µg) in 2 mL; Boxes of 10 ampules.

LANOXIN® (Digoxin) Injection Pediatric, 0.05 mg (50 µg) per mL; Boxes of 10 ampules.

**REFERENCES**