
Selected published abstracts of Baylor researchers

ADVANCED DRUG DELIVERY REVIEWS

siRNA vs. shRNA: similarities and differences

Rao DD, Vorhies JS, Senzer N, Nemunaitis J

Adv Drug Deliv Rev 2009;61(9):746–759. Reprinted with permission from Elsevier.

RNA interference (RNAi) is a natural process through which expression of a targeted gene can be knocked down with high specificity and selectivity. Using available technology and bioinformatics investigators will soon be able to identify relevant bio molecular tumor network hubs as potential key targets for knockdown approaches. Methods of mediating the RNAi effect involve small interfering RNA (siRNA), short hairpin RNA (shRNA) and bi-functional shRNA. The simplicity of siRNA manufacturing and transient nature of the effect per dose are optimally suited for certain medical disorders (i.e. viral injections). However, using the endogenous processing machinery, optimized shRNA constructs allow for high potency and sustainable effects using low copy numbers resulting in less off-target effects, particularly if embedded in a miRNA scaffold. Bi-functional design may further enhance potency and safety of RNAi-based therapeutics. Remaining challenges include tumor selective delivery vehicles and more complete evaluation of the scope and scale of off-target effects. This review will compare siRNA, shRNA and bi-functional shRNA.

AMERICAN HEART JOURNAL

Influence of patient age and sex on delivery of guideline-recommended heart failure care in the outpatient cardiology practice setting: findings from IMPROVE HF

Yancy CW, Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghade M, Heywood JT, McBride ML, Mehra MR, O'Connor CM, Reynolds D, Walsh MN

Am Heart J 2009;157(4):754–762. Reprinted with permission from Elsevier.

Background: The influence of patient age and sex on delivery of guideline-recommended heart failure (HF) therapies in contemporary outpatient settings has not been well studied. The Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) is a prospective cohort study designed to characterize current management of outpatients with chronic HF and left ventricular ejection fraction $\leq 35\%$.

Methods: Baseline data for eligible patients with systolic HF in a national registry of 167 US outpatient cardiology practices were collected by trained chart abstractors. Data were stratified and analyzed as male/female and by age tertiles with generalized estimating equation models constructed for 7 care measures.

Results: A total of 15,381 patients were enrolled, with 8,770 (71.1%) of these male. Median age of female patients was 72.0 and 70.0 for males. Use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, aldosterone inhibitors, and cardiac resynchronization therapy was not significantly different between male

and female patients, but rates for implantable cardioverter defibrillators, anticoagulation therapy for atrial fibrillation, and HF education were significantly lower for females. After adjusting for patient and practice characteristics, 3 of 7 measures significantly differed by patient sex, and 6 of 7 measures by age. Older patients, particularly older women, were significantly less likely to receive guideline-indicated HF therapies.

Conclusions: Patient age and sex were independently associated with reduced rates of some, but not all, HF therapies in outpatient cardiology practices. Older women are especially at risk. Further research is needed to understand the causes and consequences of these age- and sex-related differences in care.

AMERICAN JOURNAL OF CARDIOLOGY

Comparison of heavier versus lighter operatively excised stenotic aortic valves in adults with aortic stenosis and implications for percutaneous aortic valve implantation without replacement

Roberts WC, Ko JM, Filardo G

Am J Cardiol 2009;104(3):393–405. Reprinted with permission from Elsevier.

To better understand aortic valves amenable to percutaneous aortic valve implantation, operatively excised stenotic aortic valves were examined and divided into 2 groups: heavier and lighter valves. Among 2,247 operatively excised stenotic aortic valves in adults aged >20 years without associated mitral stenosis or mitral valve replacement, 1,608 valves were weighed; 1,241 (77%) weighed <4 g, and 367 (23%) weighed ≥ 4 g. Of the valves from 1,038 men, 717 (69%) weighed <4 g, and 321 (31%) weighed ≥ 4 g; of the valves from 570 women, 524 (92%) weighed <4 g, and 46 (8%) weighed ≥ 4 g. The patients with heavier (≥ 4 g) valves had higher transvalvular peak gradients (78 ± 28 vs 55 ± 27 mm Hg, $P < 0.0001$), smaller valve areas (0.69 ± 0.30 vs 0.75 ± 0.27 cm², $P < 0.0001$), and more often congenitally malformed valves (327 of 367 [89%] vs 638 of 1,241 [51%], $P < 0.0001$). In patients aged 81 to 90 years, 44 of the 195 valves (23%) were congenitally unicuspid or bicuspid; in those aged 41 to 50 years, 112 of 128 valves (88%) were congenitally malformed. In conclusion, compared with patients whose stenotic aortic valves weighed <4 g, those with valves weighing ≥ 4 g were younger, had higher transvalvular peak systolic pressure gradients, had smaller valve areas, and usually (about 90%) had congenitally unicuspid or bicuspid valves. It seems reasonable to avoid percutaneous aortic valve implantation in patients with heavily calcified stenotic aortic valves, most of which are either congenitally unicuspid or bicuspid.

Comparison of interpretations of valve structure between cardiac surgeon and cardiac pathologist among adults having isolated aortic valve replacement for aortic valve stenosis (\pm aortic regurgitation)

Roberts WC, Vowels TJ, Ko JM

Am J Cardiol 2009;103(8):1139–1145. Reprinted with permission from Elsevier.

Most studies concerning aortic valve structure in patients having aortic valve replacement have utilized the valve structure (unicuspid, bicuspid, tricuspid) as that called by the cardiac surgeon performing the operation. We determined valve structure of 744 operatively excised stenotic aortic valves submitted to the surgical pathology laboratory of a single hospital over a 6-year period and then compared valve structure determined by a single cardiac pathologist (WCR) with that recorded in the operative report dictated by the operating surgeon. Compared with that determined from examination of the operatively excised valve by the cardiac pathologist, valve structure determined at operation was congruous in 59% (440 of 744 patients), incongruous in 20% (152 of 744), of uncertain structure in 1% (9 of 744), and not mentioned in 19% (143 of 744). Valve structure was virtually always congruous (278 of 280 cases, 99%) in patients with 3-cuspid valves, less so with bicuspid valves (156 of 280, 56%), and infrequently so with unicuspid valves (6 of 41, 15%). In conclusion, in patients having isolated aortic valve replacement for aortic valve stenosis, the structure of the valve by the operating surgeon was similar (99%) to that described by 1 of us (WCR) when a 3-cuspid aortic valve was excised, but less so when a congenitally unicuspid (15%) or bicuspid (56%) valve was excised.

Measurement of functional capacity requirements to aid in development of an occupation-specific rehabilitation training program to help firefighters with cardiac disease safely return to work

Adams J, Roberts J, Simms K, Cheng D, Hartman J, Bartlett C

Am J Cardiol 2009;103(6):762–765. Reprinted with permission from Elsevier.

We designed a study to measure the functional capacity requirements of firefighters to aid in the development of an occupation-specific training program in cardiac rehabilitation; 23 healthy male firefighters with no history of heart disease completed a fire and rescue obstacle course that simulated 7 common firefighting tasks. They wore complete personal protective equipment and portable metabolic instruments that included a data collection mask. We monitored each subject's oxygen consumption (VO_2) and working heart rate, then calculated age-predicted maximum heart rates ($220 - \text{age}$) and training target heart rates (85% of age-predicted maximum heart rate). During performance of the obstacle course, the subjects' mean working heart rates and peak heart rates were higher than the calculated training target heart rates ($t_{22} = 5.69$ [working vs target, $P < 0.001$] and $t_{22} = 15.14$ [peak vs target, $P < 0.001$]). These findings, with mean results for peak VO_2 (3,447 mL/min) and metabolic equivalents (11.9 METs), show that our subjects' functional capacity greatly exceeded that typically attained by patients in traditional cardiac rehabilitation programs (5 to 8 METs). In conclusion, our results indicate the need for intense, occupation-specific cardiac rehabilitation training that will help firefighters safely return to work after a cardiac event.

AMERICAN JOURNAL OF GASTROENTEROLOGY

Intestinal and renal effects of low-volume phosphate and sulfate cathartic solutions designed for cleansing the colon: pathophysiological studies in five normal subjects

Patel V, Nicar M, Emmett M, Asplin J, Maguire JA, Santa Ana CA, Fordtran JS

Am J Gastroenterol 2009;104(4):953–965. Reprinted by permission from MacMillan Publishers Ltd.

Objectives: Ingestion of a concentrated low-volume phosphate solution produces copious diarrhea, which cleanses the colon, but it occasionally causes renal failure due to calcium phosphate precipitation in renal tubules. We hypothesized that a concentrated low-volume sulfate solution would be an equally effective cathartic, and that urine produced after sulfate would have less tendency to precipitate calcium salts than urine produced after phosphate.

Methods: Hydrated subjects ingested 75 mL of phosphosoda or an equimolar dose of sulfate salts in a small volume of solution. Four liters of PEG (polyethylene glycol) lavage solution was the control. All solutions were administered in split doses, 10 h apart. Propensity of urine to precipitate at pH 6.4 (the pH of renal tubular fluid) was assessed by determining the minimal calcium concentration that caused precipitation.

Results: Average diarrheal stool weight was 2,004 g after phosphate, 2,854 g after sulfate, and 3,021 g after PEG ($P \leq 0.001$). Average calcium concentration (in mg/dL) required to induce urine precipitation at pH 6.4 was 43 after PEG, 10 after PO_4 , and 187 after SO_4 ($P = 0.009$).

Conclusions: (i) In equimolar doses, sulfate produced 42% more diarrheal stool weight than phosphate. (ii) Phosphate increased the propensity for calcium salt precipitation in urine at pH 6.4, whereas sulfate did not. (iii) These results suggest that a hypertonic low-volume sulfate solution would be an effective cathartic for colon cleansing and that sulfate-induced catharsis would be less likely than phosphate catharsis to produce calcium salt deposition in renal tubules.

AMERICAN JOURNAL OF NURSING

Leech therapy

Yantis MA, O'Toole KN, Ring P

Am J Nurs 2009;109(4):36–42. Reprinted with permission.

Leech therapy is experiencing a resurgence in health care today, primarily in plastic and reconstructive surgery as a treatment for venous congestion, which can threaten surgical outcomes. Most nurses have had no formal training in administering the therapy or in maintaining *Hirudo medicinalis*, the species of freshwater worm used therapeutically. Yet nurses may be expected to participate in this therapy in a variety of clinical settings and can use these guidelines for the safe and effective use of the leech in treatment.

CLINICAL LYMPHOMA AND MYELOMA

Waldenström's macroglobulinemia: hyperviscosity syndrome and cryoglobulinemia

Stone MJ

Clin Lymphoma Myeloma 2009;9(1):97–99. Reprinted with permission of Cancer Information Group; permission conveyed through Copyright Clearance Center, Inc.

Hyperviscosity syndrome (HVS) is a common manifestation of Waldenström's macroglobulinemia (WM). Patients with HVS have skin and mucosal bleeding, retinopathy with visual disturbances, and a variety of neurologic disorders. HVS can be diagnosed from physical examination by identifying the characteristic retinal venous engorgement ("sausaging") on fundoscopic inspection. HVS can be accurately monitored with an Ostwald tube and reversed by plasmapheresis.

Cryoglobulins precipitate or gel at temperatures <37°C and dissolve on re-warming. They may be composed of single or multiple components. Most cryoglobulins are mixed monoclonal IgM-polyclonal IgG immune complexes and many are associated with hepatitis C viral infection. Monoclonal macroglobulin autoreactive antibodies are included among the “IgM-related” disorders that influence the clinical presentation and natural history of WM.

CURRENT OPINION IN CARDIOLOGY

Percutaneous mitral valve therapy: When? Which patients?

Mack M

Curr Opin Cardiol 2009;24(2):125–129. Reprinted with permission from Lippincott Williams & Wilkins.

Purpose of review: Transcatheter management of valvular heart disease is an emerging area of intense interest. Patients with mitral regurgitation present a large clinical unmet need for therapeutic advances.

Recent findings: A large randomized, pivotal trial of one device, which performs an edge-to-edge repair, has recently completed enrollment and is awaiting all patients to reach the primary clinical endpoint. A host of other devices are still in preclinical or early clinical feasibility trials after having undergone device iteration. Clinical trials with two devices have been stopped because of disappointing early results.

Summary: Although the field of transcatheter treatment of aortic stenosis is proceeding at a brisk pace with commercial approval of two devices in Europe, percutaneous treatment of mitral regurgitation has progressed at a much more measured pace because of varying cause of the disease, complexity of valvular anatomy, imaging, and delivery issues.

HUMAN IMMUNOLOGY

Understanding human myeloid dendritic cell subsets for the rational design of novel vaccines

Klechevsky E, Liu M, Morita R, Banchereau R, Thompson-Snipes L, Palucka AK, Ueno H, Banchereau J

Hum Immunol 2009;70(5):281–288. Reprinted with permission from Elsevier.

Dendritic cells (DCs) orchestrate a repertoire of immune responses that endows resistance to infection and tolerance to self. Understanding the principles by which DCs control immunity and tolerance has provided a rich basis for studying and improving clinical outcome of human disease treatment. Several features contribute to the complexity of the DC system. Among these, plasticity and existence of subsets are prominent determinants to the quality of the elicited immune responses. Indeed, different DC subsets are distributed in peripheral tissues and the blood and display different microbial receptors, surface molecules and cytokine expression, all of which influence the immunologic outcome. The biologic *raison d'être* for separate DC subsets has been the focus of many studies including our own and is being reviewed with an emphasis on human skin DCs.

JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool

Farley E, Masrou S, McKey J, Menter A

J Am Acad Dermatol 2009;60(6):1024–1031. Reprinted with permission from Elsevier and the American Academy of Dermatology, Inc.

Background: Palmoplantar psoriasis is associated with significant quality-of-life issues. Its epidemiology and phenotypical expression remain ill defined.

Objective: We reviewed the literature and our clinical experience and developed a new quality-of-life assessment tool.

Methods: We conducted a retrospective review of 150 patients with palmoplantar psoriasis.

Results: In all, 78 (52%) patients displayed predominantly hyperkeratotic palmoplantar lesions, 24 (16%) pustular, 18 (12%) combination, and 30 (20%) had an indeterminate phenotype. In 27 (18%) patients, lesions were confined to the palms and soles. A new quality-of-life index was constructed to characterize disease severity. In all, 27 (18%) had mild, 72 (48%) moderate, and 51 (34%) severe disease involvement. Palmoplantar disease severity appeared independent from the degree of body surface area involvement.

Limitations: This was a retrospective review. The quality-of-life index remains to be statistically verified in prospective clinical studies.

Conclusion: Defining morphologic subtypes together with the use of a specific quality-of-life assessment tool in patients with palmoplantar psoriasis will improve our understanding and treatment of this recalcitrant form of psoriasis.

JOURNAL OF CLINICAL ONCOLOGY

Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US Oncology Research Trial 9735

Jones S, Holmes FA, O'Shaughnessy J, Blum JL, Vukelja SJ, McIntyre KJ, Pippin JE, Bordelon JH, Kirby RL, Sandbach J, Hyman WJ, Richards DA, Mennel RG, Boehm KA, Meyer WG, Asmar L, Mackey D, Riedel S, Muss H, Savin MA

J Clin Oncol 2009;27(8):1177–1183. Reprinted with permission. © 2009 American Society of Clinical Oncology. All rights reserved.

Purpose: We previously reported that four cycles of docetaxel/cyclophosphamide (TC) produced superior disease-free survival (DFS) compared with four cycles of doxorubicin/cyclophosphamide (AC) in early breast cancer. Older women are under-represented in adjuvant chemotherapy trials. In our trial 16% of patients were ≥65 years. We now report 7-year results for DFS and overall survival (OS) as well as the impact of age, hormone receptor status, and *HER2* status on outcome and toxicity.

Patients and methods: Patients were randomly assigned to receive either four cycles of standard-dose AC (60/600 mg/m²; n = 510), or TC (75/600 mg/m²; n = 506), administered by intravenous infusion every 3 weeks.

Results: The median age in women younger than 65, was 50 years (range, 27 to 64) and for women ≥ 65 was 69 years (range, 65 to 77). Baseline characteristics in the two age subgroups were generally well matched, except that older women tended to have more lymph node involvement. At a median of 7 years follow-up, the difference in DFS between TC and AC was significant (81% TC v 75% AC; $P = .033$; hazard ratio [HR], 0.74; 95% CI 0.56 to 0.98) as was OS (87% TC v 82% AC; $P = .032$; HR, 0.69; 95% CI, 0.50 to 0.97). TC was superior in older patients as well as younger patients. There was no interaction of hormone-receptor status or HER-2 status and treatment. Older women experienced more febrile neutropenia with TC and more anemia with AC.

Conclusion: With longer follow-up, four cycles of TC was superior to standard AC (DFS and OS) and was a tolerable regimen in both older and younger patients.

JOURNAL OF IMMUNOLOGY

CD2 distinguishes two subsets of human plasmacytoid dendritic cells with distinct phenotype and functions

Matsui T, Connolly JE, Michnevitz M, Chaussabel D, Yu CI, Glaser C, Tindle S, Pypaert M, Freitas H, Piqueras B, Banchereau J, Palucka AK

J Immunol 2009;182(11):6815–6823. Copyright © The American Association of Immunologists, Inc. Reprinted with permission.

Plasmacytoid dendritic cells (pDCs) are key regulators of antiviral immunity. They rapidly secrete IFN- α and cross-present viral Ags, thereby launching adaptive immunity. In this study, we show that activated human pDCs inhibit replication of cancer cells and kill them in a contact-dependent fashion. Expression of CD2 distinguishes two pDC subsets with distinct phenotype and function. Both subsets secrete IFN- α and express granzyme B and TRAIL. CD2^{high} pDCs uniquely express lysozyme and can be found in tonsils and in tumors. Both subsets launch recall T cell responses. However, CD2^{high} pDCs secrete higher levels of IL12p40, express higher levels of costimulatory molecule CD80, and are more efficient in triggering proliferation of naive allogeneic T cells. Thus, human blood pDCs are composed of subsets with specific phenotype and functions.

LIVER TRANSPLANTATION

Improved results of transplantation for hepatocellular carcinoma: a report from the International Registry of Hepatic Tumors in Liver Transplantation

Onaca N, Davis GL, Jennings LW, Goldstein RM, Klintmalm GB

Liver Transpl 2009;15(6):574–580. Copyright © 2009, American Association for the Study of Liver Diseases. Reprinted with permission of John Wiley & Sons, Inc.

Improved outcome after liver transplantation (LTX) for hepatocellular carcinoma (HCC) made LTX a legitimate treatment of the disease. We analyzed trends of LTX for HCC with tumors known before transplantation in 902 patients in a large international registry across 3 periods: 1983–1990, 1991–1996, and 1997–2005. Patient survival improved gradually across eras, with 5-year survival rates of 25.3%, 44.4%, and 67.8%, respectively ($P < 0.0001$), and the 5-year tumor recurrence rate declined from 59% to 41.3% and 15%, respectively

($P < 0.0001$). The number of HCC nodules and tumor size decreased over time, and there were fewer moderately or poorly differentiated tumors. Tumors > 5 cm decreased from 54.5% to 31.7% and 11.7%, respectively ($P < 0.0001$), and LTX with ≥ 4 nodules decreased from 38.9% to 23.5% and 15.1%, respectively ($P = 0.0044$). Poorly differentiated tumors decreased from 37.2% to 31.8% and 20.3%, respectively ($P = 0.0005$). Tumor microvascular invasion remained at 21.2% to 23.8% despite changes in patient selection over time ($P = 0.7124$). Stepwise Cox regression analysis ($n = 502$) showed significant risk for tumor recurrence and patient survival for transplants before 1997 (hazard ratio [HR], 1.82 and 1.88, respectively), tumor size > 6 cm (HR, 2.09 and 1.76), microvascular invasion (HR, 1.75 and 1.69, respectively), and alpha-fetoprotein > 200 (HR, 2.45 and 2.32, respectively). In conclusion, outcome after LTX for HCC has improved continuously over the past 20 years. Improved perioperative care and better patient selection may partially explain the improved outcome after LTX for HCC.

Twenty years' follow-up of portal vein conduits in liver transplantation

Nikitin D, Jennings LW, Khan T, Vasani S, Ruiz R, Sanchez EQ, Chinnakotla S, Levy MF, Goldstein RM, Klintmalm GB

Liver Transpl 2009;15(4):400–406. Copyright © 2009, American Association for the Study of Liver Diseases. Reprinted with permission of John Wiley & Sons, Inc.

Portal vein problems remain a formidable challenge in liver transplantation. In select situations, a portal vein conduit can provide a solution. No long-term results have been reported. This study was designed to assess the impact of portal vein conduits on graft survival after liver transplantation and the safety of portal vein conduits and to establish the long-term results (up to 20 years) of portal vein conduits. Data from 2370 adult liver transplants were prospectively collected into a computerized research database and analyzed. All portal vein conduits were constructed from the donor iliac vein obtained at the liver retrieval. Portal vein conduits were required in 35 (1.5%) first transplants. The long-term (up to 20 years of follow-up) graft survival after liver transplantation using portal vein conduits was excellent and comparable to that of the control group. The graft survival was 65% with the conduit versus 66% without the conduit at 5 years of follow-up, 58% versus 51% at 10 years, and 48% versus 35% at 15 years. There was a higher rate (8.6% versus 1.4%) of portal vein thrombosis after the portal vein conduit, and the majority occurred in the first 3 months after transplantation. For the same time period, there was no statistically significant difference in graft survival or patient survival for the retransplants with and without portal vein conduits. There was no statistically significant difference in graft survival or patient survival for the transplants with portal vein conduits and with portal vein thrombectomy. In conclusion, portal vein conduits can be used safely for liver transplantation with no negative impact on long-term graft survival or patient survival. Despite the higher rate of portal vein thrombosis in the immediate postoperative period, excellent long-term results can be obtained.

Post-liver transplant survival in hepatitis C patients is improving over time

O'Leary JG, Randall H, Onaca N, Jennings L, Klintmalm GB, Davis GL

Liver Transpl 2009;15(4):360–368. Copyright © 2009, American Association for the Study of Liver Diseases. Reprinted with permission of John Wiley & Sons, Inc.

Outcomes after orthotopic liver transplantation for chronic hepatitis C have been reported to be worsening over the last 2 decades. We analyzed our center's experience over 15 years to identify trends in post-orthotopic liver transplantation survival in patients with and without hepatitis C virus infection. Patient survival and graft survival among adult primary orthotopic liver transplantation recipients who survived more than 90 days from January 1991 to June 2006 at the Baylor Regional Transplant Institute (n = 1901) were evaluated by Kaplan-Meier analysis. Those with or without hepatitis C virus infection were analyzed by era: era 1, 1991–1994 (n = 473); era 2, 1995–1998 (n = 421); era 3, 1999–2002 (n = 498); and era 4, 2003–2006 (n = 512). Differences in eras with disparate survivals were assessed by univariate and multivariable analysis. Overall, patient survival and graft survival were significantly lower among hepatitis C virus infection recipients compared to those without hepatitis C virus infection ($P < 0.001$). This difference was dependent on the era of transplantation, with progressive improvement in hepatitis C virus patient ($P < 0.001$) and graft ($P < 0.001$) survival in sequential eras. Several factors accounted for this improvement, notably better selection of hepatocellular carcinoma patients and fewer late cytomegalovirus infections. Improvement occurred despite an increase in the ages of both donors and recipients. In conclusion, posttransplant survival after orthotopic liver transplantation for chronic hepatitis C has improved significantly over the last 15 years despite demographic changes in patients and grafts that have been previously shown to impair survival. A major reason for this improvement is better selection of patients with concurrent hepatocellular carcinoma and fewer late cytomegalovirus infections, although other factors may play a role as well.

OTOLARYNGOLOGY—HEAD AND NECK SURGERY

Endoscopic transantral repair of orbital floor fractures

Ducic Y, Verret DJ

Otolaryngol Head Neck Surg 2009;140(6):849–854. Reprinted with permission from Elsevier and the American Academy of Otolaryngology–Head and Neck Surgery.

Objective: To review our technique of endoscopic transantral repair of orbital floor fractures.

Study design: Case series with chart review.

Methods: All orbital floor fractures treated with the outlined technique from 1998 to 2007 were reviewed in a retrospective fashion. Demographic data, surgical outcomes, and complications were gathered from available patient charts.

Results: A total of 63 patients were treated with the described technique (44 male, 19 female). Thirty-nine patients underwent autograft placement from the anterior maxillary sinus wall harvest/exposure. Fourteen patients underwent placement of various alloplasts, and the remaining 10 patients underwent reduction of the contents and floor repositioning. Two patients underwent repeat repair due to inadequacy

of initial repair. Both of these complications occurred in the subgroup of patients who underwent simple repositioning. There were no cases of blindness, permanent new diplopia, ectropion, entropion, or new infraorbital anesthesia.

Conclusions: The described technique of endoscopic repair of orbital floor fractures represents a precise method of fracture repair that results in excellent outcomes with minimal morbidity in the majority of patients. It allows for immediate fracture repair without the need to wait for periorbital edema to settle. It also allows for clear visualization of the entire fracture for precise graft placement.

PHARMACOLOGY AND THERAPEUTICS

Fabry disease

Schiffmann R

Pharmacol Ther 2009;122(1):65–77. Reprinted with permission from Elsevier.

Fabry disease, an X-linked disorder of glycosphingolipids that is caused by the deficiency of α -galactosidase A, is associated with dysfunction of many cell types and includes a systemic vasculopathy. As a result, patients have a markedly increased risk of developing small-fiber peripheral neuropathy, stroke, myriad cardiac manifestations and chronic renal disease. Virtually all complications of Fabry disease are non-specific in nature and clinically indistinguishable from similar abnormalities that occur in the context of more common disorders in the general population. Although Fabry disease was originally thought to be very rare, recent studies have found a much higher incidence of mutations of the *GLA* gene, suggesting that this disorder is under-diagnosed. Although the etiology of Fabry disease has been known for many years, the mechanism by which the accumulating α -D-galactosyl moieties cause this multi-organ disorder has only recently been studied and is yet to be completely elucidated. Specific therapy for Fabry disease has been developed in the last few years but its role in the management of the disorder is still being investigated. Fortunately, standard 'non-specific' medical and surgical therapy is effective in slowing deterioration or compensating for organ failure in patients with Fabry disease. All these aspects are discussed in detail in the present review.

TRANSPLANTATION

Evidence for induced expression of HLA class II on human islets: possible mechanism for HLA sensitization in transplant recipients

Jackson AM, Connolly JE, Matsumoto S, Noguchi H, Onaca N, Levy MF, Naziruddin B

Transplantation 2009;87(4):500–506. Reprinted with permission from Lippincott Williams & Wilkins.

Recent reports have shown that islet transplant recipients develop antibodies against donor human leukocyte antigen (HLA) class I and II. Because human islets do not express HLA class II under normal conditions, mechanisms underlying induction of the anti-class II response are unclear. We hypothesized that under inflammatory conditions, islets will have induced expression of HLA class II leading to sensitization. Isolated human islets were divided into two groups. Group 1 was cultured at 37°C as control; group 2 was cultured similarly

in presence of tumor necrosis factor alpha and interferon gamma. After treatment, islets were analyzed for expression of HLA class II using real-time polymerase chain reaction, immunofluorescence and flow cytometry. Furthermore, serum from an islet transplant recipient who developed anti-class II antibody was tested by flow cytometry for immunoglobulin (Ig) binding to cytokine-stimulated islets. Real-time polymerase chain reaction analysis for gene transcripts of class II transactivator, *HLA-DR α* , and *HLA-DR α 1* showed maximum 9.38-, 18.95-, and 46.5-fold increase, respectively, in group 2 when

compared with control at 24 hr. Cytokine treatment increased HLA class II expression markedly on both alpha and beta cells in islets as evidenced by fluorescent imaging and flow cytometric analysis. When patient serum was analyzed by flow cytometry, both IgM and IgG binding was observed in cytokine-treated, HLA class II matched islet cells alone. We conclude that inflammation leads to induced expression of HLA class II on transplanted islet cells potentially causing antidonor sensitization and adversely impacting islet transplant outcomes.

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