

# Hot Articles

“May|2017”

Health Science



**Title:** [Targeted Radionuclide Therapy: An Evolution Toward Precision Cancer Treatment](#)

**Author:** Hossein Jadvar | American Journal of Roentgenology

**Journal:** American Journal of Roentgenology

**Volume:** May 2, 2017 (Ahead of Print)

**Doi:** 10.2214/AJR.17.18264

### Abstract

**OBJECTIVE.** This article reviews recent developments in targeted radionuclide therapy (TRT) approaches directed to malignant liver lesions, bone metastases, neuroendocrine tumors, and castrate-resistant metastatic prostate cancer and discusses challenges and opportunities in this field.

**CONCLUSION.** TRT has been employed since the first radioiodine thyroid treatment almost 75 years ago. Progress in the understanding of the complex underlying biology of cancer and advances in radiochemistry science, multimodal imaging techniques including the concept of “see and treat” within the framework of theranostics, and universal traction with the notion of precision medicine have all contributed to a resurgence of TRT.

### Database

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**Title:** [Encapsulation of ritonavir in solid lipid nanoparticles: in-vitro anti-HIV-1 activity using lentiviral particles](#)  
**Author:** Farzaneh Javan, Alireza Vatanara, Kayhan Azadmanesh, Mohsen Nabi-Meibodi and Mehdi shakouri  
**Journal:** Journal of Pharmacy and Pharmacology  
**Volume:** Early View: First published: 4 May 2017  
**Doi:** 10.1111/jphp.12737

## Abstract

### Objectives

In this study, ritonavir was entrapped into solid lipid nanoparticles (SLNs) employing two production methods. The prepared SLNs were characterized and antiretroviral activity was investigated for more efficient formulation.

### Methods

Ritonavir-loaded SLNs were produced by solvent emulsification evaporation (SE) and double emulsion methods (DE), and the effects of Tween80 and poloxamer188 as external phase surfactant were compared. Prepared SLNs were characterized in terms of size, surface charge, entrapment efficiency (EE), release profile and thermal behaviour. Moreover, the activity of drug-loaded SLNs was investigated on the lentiviral-based pseudo-HIV-1 particles.

### Key findings

The average size of negatively charged SLNs was 170–250 nm with polydispersity index (PDI) of 0.2. The most EE% was about 53.2% achieved by DE method in the presence of poloxamer188. It was found that addition of poloxamer188 in the process led to increased entrapment efficiency and particle size. The in-vitro antiviral experiment showed ritonavir SLNs can actively maintain inhibition of virus production as well as free drug.

### Conclusions

In this study, we showed the SLNs not only can encapsulate ritonavir efficiently but also can maintain its antiviral activity and modulate drug release as promising nanocarrier.

## Database

Wiley Online Library

**Title:** [Critical appraisal of clinical practice guidelines for adult cancer patients with febrile neutropenia](#)  
**Author:** Ziad G. Nasr, Safae Abu Yousef, Farah Jibril and Kyle J. Wilby  
**Journal:** International Journal of Pharmacy Practice  
**Volume:** Version of Record online: 27 MAR 2017  
**Doi:** 10.1111/ijpp.12357

## Abstract

### Objectives

To critically appraise published international clinical practice guidelines (CPGs) for management of febrile neutropenia in adult patients with cancer and to determine opportunities for improved development and reporting.

### Methods

A literature search identified CPGs for adult cancer patients with febrile neutropenia. Four independent assessors evaluated each included CPG according to the Appraisal of Guidelines for Research and Evaluation II instrument. Standardized scores were calculated for each guideline and polled collectively. Reliability of assessment was determined using a two-way random model intraclass correlation coefficients.

### Key findings

Eight CPGs were independently evaluated by four assessors. Collectively, the highest scoring domain was editorial independence (83.3), followed by clarity of presentation (55.4), scope and purpose (53.4), stakeholder involvement (53.1), rigour of development (52.7) and applicability (47.8). Overall assessments ranged from 28.6 to 96.4 of 100 possible points. Three (37.5%) guidelines were recommended for use without alterations, two (25%) guidelines were recommended with alterations, and three (37.5%) guidelines were not recommended for implementation into practice. Reliability varied between guidelines with intraclass correlation coefficients ranging from 0.41 to 0.82.

### Conclusions

Clinical practice guidelines for febrile neutropenia in adult patients with cancer were moderately rated with a 37.5% of guidelines being recommended for use in practice. Guideline developers should focus on improving CPG applicability and rigour in the development and reporting processes. Critical appraisal of guidelines should become a standard practice prior to implementation into clinical settings.

## Database

Wiley Online Library

**Title:** [Effect of Intravenous Alfentanil on Nonpainful Thermally Induced Hyperalgesia in Healthy Volunteers](#)  
**Author:** Carolyn Schiffner, Gery Schulteis and Mark S. Wallace  
**Journal:** The Journal of Clinical Pharmacology  
**Volume:** Version of Record online: 2 MAY 2017  
**Doi:** 10.1002/jcph.911

### Abstract

Experimental interventions that activate specific components of clinical pain are necessary for characterization of underlying mechanisms and pharmacology. Cutaneous hyperalgesia has been described that uses nonpainful heat to induce secondary hyperalgesia. This study evaluated the effect of intravenous alfentanil on experimental cutaneous hyperalgesia created using this method. Eighteen subjects participated in a randomized, double-blinded, placebo-controlled crossover study consisting of 2 sessions, 1 with alfentanil and 1 with placebo. Using a computer-controlled infusion pump, alfentanil or matching placebo was maintained at a constant plasma level of 75 ng/mL for 1 hour followed by the application of a 40°C heat stimulus to the right thenar eminence for 15 minutes. The temperature was raised by 1°C every 15 minutes until the subject reported pain or 45°C was reached. After the end point was reached, the temperature was maintained, and repeat testing was performed. The nonpainful heat created an area of secondary cutaneous hyperalgesia and significant decrease in mechanical pain threshold on heat-treated right vs untreated left during placebo administration. Alfentanil prevented the hypersensitivity when compared to placebo ( $P < .05$ ) but failed to reduce the area of secondary hyperalgesia created by nonpainful heat when compared to placebo ( $P = .06$ ). Neither alfentanil nor the heat lamp treatment showed any significant effect on other neurosensory measures. This study demonstrated a reliable production of cutaneous hyperalgesia using a nonpainful stimulus that is affected by the systemic delivery of alfentanil. This model for human cutaneous experimental pain may be a useful method for scientific characterization of analgesics.

### Database

Wiley Online Library

**Title:** [Fasting inhibits hepatic stellate cells activation and potentiates anti-cancer activity of Sorafenib in hepatocellular cancer cells](#)

**Author:** Oriana Lo Re, Concetta Panebianco, Stefania Porto, Carlo Cervi, Francesca Rappa, Stefano Di Biase, Michele Caraglia, Valerio Paziienza and Manlio Vinciguerra

**Journal:** Journal of Cellular Physiology

**Volume:** Accepted manuscript online: 4 MAY 2017

**Doi:** 10.1002/jcp.25987

### Abstract

**BACKGROUND:** Hepatocellular carcinoma (HCC) has a poor outcome. Most HCCs develop in the context of liver fibrosis and cirrhosis caused by chronic inflammation. Short-term fasting approaches enhance the activity of chemotherapy in preclinical cancer models, other than HCC. Multi-tyrosine kinase inhibitor Sorafenib is the mainstay of treatment in HCC. However, its benefit is frequently short-lived. Whether fasting can alleviate liver fibrosis and whether combining fasting with Sorafenib is beneficial remains unknown.

**METHODS:** 24 hour fasting (2% serum, 0.1% glucose)-induced changes on human hepatic stellate cells (HSC) LX-2 proliferation/viability/cell cycle were assessed by MTT and flow cytometry. Expression of lipopolysaccharide (LPS)-induced activation markers (vimentin,  $\alpha$ SMA) was evaluated by qPCR and immunoblotting. Liver fibrosis and inflammation were evaluated in a mouse model of steatohepatitis exposed to cycles of fasting, by histological and biochemical analyses. 24 hours fasting-induced changes were also analyzed on the proliferation/viability/glucose uptake of human HCC cells exposed to Sorafenib. An expression panel of genes involved in survival, inflammation and metabolism was examined by qPCR in HCC cells exposed to fasting and/or Sorafenib.

**RESULTS:** Fasting decreased the proliferation and the activation of HSC. Repeated cycles of short-term starvation were safe in mice but did not improve fibrosis. Fasting synergized with Sorafenib in hampering HCC cell growth and glucose uptake. Finally, fasting normalized the expression levels of genes which are commonly altered by Sorafenib in HCC cells.

**CONCLUSIONS:** Fasting or fasting-mimicking diet diets should be evaluated in preclinical studies as a mean to potentiate the activity of Sorafenib in clinical use. This article is protected by copyright. All rights reserved

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Wiley Online Library

**Title:** [Women who drank while pregnant: The importance of social context in the lives of South African pregnant women](#)  
**Author:** Jane F. Kelly & Catherine L. Ward  
**Journal:** Drugs: Education, Prevention and Policy  
**Volume:** Published online: 27 Apr 2017  
**Doi:** 10.1080/09687637.2017.1316703

### Abstract

**Aims:** This study aimed to explore how women who drank alcohol while pregnant understand and make sense of alcohol use. **Methods:** Using social representation theory and elements of Foucauldian discourse analysis, 14 narrative episodic interviews were conducted in a Western Cape, South African community with women who drank alcohol while pregnant, and two focus group discussions with 13 members of the pregnant women's community. The interview and focus group data were analysed using thematic decomposition analysis.

**Findings:** Drinking alcohol was represented by participants as a social activity, a way of coping with domestic problems, and also as connected to their experiences of motherhood. Access to social support through their partners and a desire to protect the fetus and care for their children helped some participants to cease drinking during their pregnancies. These representations highlight that alcohol use is not simply an individual decision but is embedded in a particular social context and also framed by particular discourses.

**Conclusion:** Interventions should prioritise the social context of drinking, include a component that works with both pregnant women and their partners, use a supportive and non-judgemental approach that capitalises on pregnancy and motherhood, and focus on empowering pregnant women to manage problems effectively.

### Database

Taylor & Francis

**Title:** [Golimumab for the treatment of ulcerative colitis](#)  
**Author:** Mathurin Flamant, Stephane Paul & Xavier Roblin  
**Journal:** Expert Opinion on Biological Therapy  
**Volume:** Accepted author version posted online: 04 May 2017  
**Doi:** 10.1080/14712598.2017.1327576

### Abstract

**Introduction:** Tumor necrosis factor antagonists have revolutionized the therapeutic management of inflammatory bowel disease. Infliximab and adalimumab were the first biological agents used to induce and maintain remission in ulcerative colitis. More recently, a third tumor necrosis factor antagonist, golimumab, was approved, extending the therapeutic approach for moderate-to-severe ulcerative colitis.

**Areas covered:** In this review, the authors review the literature on the efficacy and safety of golimumab in the context of other anti-TNF agents used in the treatment of this disease. The role of therapeutic drug monitoring in the case of loss of response to an anti-TNF agent is also discussed.

**Expert opinion:** Golimumab is currently effective to induce and maintain remission in patients with ulcerative colitis, especially those patients who are naive for an anti-TNF agent. No large studies have evaluated the efficacy of golimumab after failure of a first-line TNF antagonist therapy. In the case of loss of response to a first anti-TNF agent, therapeutic drug monitoring is essential to determine the most suitable therapeutic option.

### Database

Taylor & Francis

**Title:** [Understanding barriers and facilitators to healthy eating and physical activity from patients either before and after knee arthroplasty](#)

**Author:** Christine A. Pellegrini, Gwendolyn Ledford, Rowland W. Chang & Kenzie A. Cameron

**Journal:** Disability and Rehabilitation

**Volume:** Published online: 05 May 2017

**Doi:** 10.1080/09638288.2017.1323026

### Abstract

**Purpose:** We sought to identify patient-reported barriers and facilitators to healthy eating and physical activity among patients before or after knee arthroplasty.

**Materials and methods:** Twenty patients with knee osteoarthritis aged 40–79 years who had knee arthroplasty surgery scheduled or completed within 3 months were interviewed. Interview topics included perceived barriers and facilitators to healthy eating and activity before or after surgery. Interviews were coded and analyzed using constant comparative analysis.

**Results:** Interviews were completed with 11 pre-operative ( $67.1 \pm 7.6$  years, 45.5% female, BMI  $31.2 \pm 6.3$ ) and nine post-operative patients ( $61.7 \pm 11.7$  years, 44.4% female, BMI  $30.2 \pm 4.7$  kg/m<sup>2</sup>). The most commonly identified personal barriers to healthy eating identified were desire for high-fat/high-calorie foods, managing overconsumption and mood. Factors related to planning, portion control and motivation to improve health were identified as healthy eating facilitators. Identified personal barriers for activity included pain, physical limitations and lack of motivation, whereas facilitators included having motivation to improve knee symptoms/outcomes, personal commitment to activity and monitoring activity levels.

**Conclusion:** Identifying specific eating and activity barriers and facilitators, such as mood and motivation to improve outcomes, provides critical insight from the patient perspective, which will aid in developing weight management programs during rehabilitation for knee arthroplasty patients.

### Database

Taylor & Francis

**Title:** [Preparation of chondroitin sulfate-adipic acid dihydrazide-doxorubicin conjugate and its antitumor characteristics against LLC cells](#)

**Author:** Hiraku Onishi, Ai Fukasawa, Andang Miatmoko, Kumi Kawano, Yuri Ikeuchi & Yoshiyuki Hattori

**Journal:** Journal of Drug Targeting

**Volume:** Accepted author version posted online: 05 May 2017

**Doi:** 10.1080/1061186X.2017.1327593

### Abstract

Macromolecule–antitumor drug conjugates can reach tumor sites specifically via the enhanced permeability and retention (EPR) effect. It is desirable to release the drug efficiently from the conjugate at acidic pH in the tumor tissue or in the endosomes of cancer cells. In this study, we attempted to produce a carrier system with a labile chemical bond at acidic pH. Adipic acid dihydrazide (ADH)-chondroitin sulfate (CS) (termed CS-ACH) was synthesized by a two step method, with the introduction of formyl groups followed by reductive amination using ADH. Doxorubicin (DOX) was conjugated to CS-ACH by simple mixing at acidic pH. The conjugate, designated CS-ACH-DOX, showed gradual drug release pH dependently at 37°C; after incubation for 7 days, more than 60% of DOX was released at pH 4, whereas less than 20% was released at pH 7. CS-ACH-DOX showed in vitro cytotoxicity against Lewis lung carcinoma (LLC) cells, which was less effective than that of DOX itself. However, CS-ACH-DOX inhibited tumor growth more than DOX in LLC tumor-bearing mice. These results suggested that CS-ACH-DOX might accumulate in tumors via the EPR effect and release DOX effectively at acidic pH. CS-ACH-DOX was considered to act as a drug delivery system with tumor targeting.

### Database

Taylor & Francis

**Title:** [CNS Injuries in Abusive Head Trauma](#)  
**Author:** Jason N. Wright  
**Journal:** American Journal of Roentgenology  
**Volume:** 208      **Issue:** 5 May      **Page:** 991-1001  
**Doi:** 10.2214/AJR.16.17602

#### Abstract

**OBJECTIVE.** Abusive head trauma (AHT) is one of the most common subtypes of nonaccidental trauma and is a leading cause of traumatic brain injury in young children. Imaging plays a crucial role in the evaluation of children with suspected AHT and can aid in accurate diagnosis because clinical presentation may be nonspecific. In this article, the CNS injuries that are characteristic of AHT are reviewed with an emphasis on pathophysiology and imaging appearance.

**CONCLUSION.** AHT is a frequent cause of neurologic injury in children, particularly in infants in the first year of life. Imaging evaluation plays a vital role in determining the diagnosis and prognosis. A review of the intracranial injuries that are common in AHT cases has been provided. Understanding the common patterns of abusive head injury can help increase diagnostic accuracy both by increasing recognition of injuries with a high specificity for AHT and by avoiding unwarranted concern in patients with concordant injury patterns and clinical history.

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