Dr Annmarie Hedges—an appreciation
Elizabeth Whelan
DOI:10.1111/bcp.13572

In this issue we remember Annmarie Hedges, who died on 9 August 2017. She was one of the important pillars of the Journal in its first three decades, an accomplished clinical pharmacologist and a friend to many in the BPS. She will be missed.

A descriptive systematic review of salivary therapeutic drug monitoring in neonates and infants
Laura Hutchinson, Marlene Sinclair, Bernadette Reid, Kathryn Burnett and Bridgeen Callan
DOI:10.1111/bcp.13553

Most pharmacokineticists are used to plasma as the preferred medium for the measurement of drug concentrations. Although a venipuncture is not a big deal for most it is a serious objection for pharmacokinetic research in children. So, non-invasive collection of bodily fluids is of interest to this group. Saliva is the obvious fluid, but little is known about the distribution kinetics of medicines to saliva. Laura Hutchinson and colleagues from Londonderry have done a useful systematic review about what is known as a guide for further research into what is not known.

A review of the growing risk of vitamin D toxicity from inappropriate practice
Peter N. Taylor and J. Stephen Davies
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Vitamin D is considered to be good for everything and there is increasing fear of deficiencies. While a lot of that makes sense the idea that a substance is good for you (even though solid trial evidence is lacking) does not logically lead to the thought that more of that substance would be even better. So, whilst the guidance drives everyone to use this wonderful substance without any caveats, there will inevitably be toxicity. Peter Taylor and J Stephen Davies from Cardiff review the increasing number of cases of Vitamin D toxicity, which are not trivial.

The pharmacodynamic and clinical trial evidence for statin dose
Simon B. Dimmitt, Hans G. Stampfer and John B. Warren
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All statins are competitive antagonists of HMG CoA reductase. Basic pharmacology tells us that at a certain point increasing the dose will not produce any extra effect. However, adverse effects that are induced by non-specific drug-cell interactions may increase. Simon Dimmitt from Western Australia and colleagues revisit this idea based upon randomized trials and the notion of some clinicians that when a statin is good for you more must be better. Their conclusions are perhaps as expected but need to be restated. When you keep increasing the dose of a medicine the good old dose–response curve generates a diminishing return and an increase in side effects.

Exposure–response characterization of tofacitinib efficacy in moderate to severe ulcerative colitis: Results from a dose-ranging phase 2 trial
Arnab Mukherjee, Anasuya Hazra, Mike K. Smith, Steven W. Martin, Diane R. Mould, Chinyu Su and Wojciech Niezychowski
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Tofacitinib is a Janus Kinase (JAK) inhibitor used in chronic inflammatory diseases like ulcerative colitis. Arnab Mukherjee from Groton in the USA took data from a series of clinical trials and developed the concentration effect relationship for this new drug. He concluded that, as there was little difference between the dose response and the concentration response curves, this medicine can be dosed without monitoring of plasma concentrations. This is interesting as apparently the huge variability in response is caused by other factors.
Patterns and profiles of methylphenidate use both in children and adults
Vanessa Pauly, Elisabeth Frauger, Magalie Lepelley, Michel Mallaret, Quentin Boucherie and Joëlle Micallef
DOI:10.1111/bcp.13544

Vanessa Pauly and her group from France investigated the use of methylphenidate in different age groups. Their findings show that children used this medicine more or less as expected, which is a long period of treatment with little comedication. In the over 50 age group there was much more comedication and shorter treatment. This indicates that there is off label use of this drug and that was particularly interesting in the 18–24 age group. This group included a large proportion of students and the authors hypothesize that the French students use the drug to boost their academic performance, or just to feel good. The evidence for this is lacking, and France has (at least in the opinion of some of us at the BJCP) a large range of non-pharmacological features to make both its inhabitants and visitors feel good.

Adverse events linked with the use of chimeric and humanized anti-CD20 antibodies in children with idiopathic nephrotic syndrome
Alice Bonanni, Marta Calatroni, Matteo D’Alessandro, Sara Signa, Enrica Bertelli, Michela Cioni, Eddi Di Marco, Roberto Biassoni, Gianluca Cardi, Giulia Ingrasciotta, Roberta Bertelli, Armando Di Donato, Maurizio Bruschi, Alberto Canepa, Giorgio Piaggio, Pietro Ravani and Gian Marco Ghiggeri
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Nephrotic syndrome in children is often resolved by oral steroids taken for a short period of time, but if the pathology is more complex than minimal change disease often repeated courses of steroids or calcineurin inhibitors or even cyclophosphamide is used. More recently CD20 antibodies like rituximab are used, and Alice Bonanni from Genoa and 16 other nephrologists report that the adverse effects of this treatment in children are limited to some infusion reactions and that they are otherwise safe and a good alternative to the undoubtedly more toxic traditional treatments.

Prevalence of exceeding maximum daily dose of paracetamol, and seasonal variations in cold-flu season
Saul Shiffman, Deena R. Battista, Judith P. Kelly, Mary K. Malone, Rachel B. Weinstein and David W. Kaufman
DOI:10.1111/bcp.13551

Saul Shiffmann and his group looked at the reported use of paracetamol in about 20 000 consumers during and outside the cold and flu season, which they identified using the searches performed on Google (which can apparently identify when people have these symptoms!). Over-the-counter medications led to an overuse (more than 4-8 g per day) of about 6%. This happened more often during the Google determined flu season. We wonder if the 6% overuse is not related to the much higher incidence of being overweight in the US population and that therefore the users just required more, so an association with body weight would have been interesting. We can safely assume that Google also knows the body weight of all its users, so that should be no problem!

Large differences in neonatal drug use between NICUs are common practice: time for consensus?
Robert B. Flint, Floor van Beek, Peter Andriessen, Luc J. Zimmermann, Kian D. Liem, Irwin K.M. Reiss, Ronald de Groot, Dick Tibboel, David M. Burger, Sinno H.P. Simons and DINO Research group
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A team of Dutch pediatricians spearheaded by Robert Flint investigated the use of medicines in the neonatal intensive care unit. About one fifth of medicines were used off label, and there were big differences in prescriptions between the four different units involved in their study. There could be many reasons for these differences but this underscores the need for more consensus and more evidence in this vulnerable population.