'To everything there is a season, and a time to every purpose under the heaven' from the Book of Ecclesiastes in the Bible (3:1 King James Version) was echoed by the American folk rock band The Byrds on their second album ‘Turn! Turn! Turn!’ from 1965. It took The Byrds 5 days (78 takes!) to record the song, but the end result finally convinced their record company Columbia to commit it to vinyl. And it became their all-time biggest selling hit single.

It took Peter Humaidan and his group a little longer to try and convince the world that GnRHa triggering of final oocyte maturation and low-dose luteal phase support in GnRH-antagonist cycles is the way forward towards an ovarian hyperstimulation syndrome (OHSS)-free IVF clinic. They encountered fierce opposition as well as enthusiastic support in their attempts to convince us that theirs is the way to go in developing a safer IVF procedure. In this issue, we publish several papers on this subject from both sides, the evangelists and the sceptics. Arthur Schopenhauer is often credited (probably falsely) with the observation that truth passes through three stages. First (turn), it is ridiculed. Secondly (turn), it is violently opposed. Thirdly (turn), it is accepted as self-evident (Shalit, 2005). According to the work published in this edition of our journal, we have arrived somewhere between phases 2 and 3. However, the findings in favour of the new treatment regimen are gradually gaining robustness. In this issue, we publish an randomized controlled trial (RCT), or better two RCTs (Humaidan et al., 2013), that show that a GnRHa trigger followed by a single 1500 IU hCG bolus appeared to reduce OHSS in patients at risk, but that in a low-risk group a second bolus induced two cases of late-onset OHSS. Regrettably, the first RCT was stopped prematurely (after inclusion of only 118 patients), before the predefined target sample size (of 168 patients at risk) was reached. It is fortunate, for patients and clinicians, that severe OHSS is not a frequent complication. For investigators, however, it means that not encountering a single case of OHSS in 60 patients at risk (as in this Humaidan study) may be due to chance. It still has a wide 95% confidence interval, which ranges from zero to as high as 7.5%. So the findings need to be regarded with some caution: a real-world OHSS-risk of up to 7.5% cannot be excluded on the basis of this study alone. Also in this issue, we publish a seemingly contradictory finding, by Seyhan et al. (2013), who report a combined retrospective case series from two centres in Turkey and Canada. They encountered six severe OHSS cases among 23 women (26%) at risk in whom the Humaidan protocol was followed. The authors conclude that severe OHSS could not be prevented by this protocol in high-risk patients [with a mean estradiol of $18 \pm 8$ nmol/l, and a mean follicle ($>12$ mm) number of $20 \pm 6$]. Daniel Bodri, one of our Associate Editors comments on these studies in an accompanying Editorial (Bodri, 2013). And, in turn, the authors (as expected) sent Letters-to-the-Editor, three of which we publish as well (Ata, 2013a; Ata, 2013b; Humaidan, 2013). Meanwhile we received another paper, by Iliodromiti et al. (2013), reporting the results of yet another retrospective cohort study from five renowned centres, three in the UK, one in Belgium and one in Australia. Their study included 275 women at high risk of OHSS. Only two cases of severe OHSS were found (0.7%). These authors conclude that, in GnRH-antagonist suppressed women who develop an excessive ovarian response, the use of a GnRHa-agonist trigger combined with modified luteal support may still offer the option of proceeding to embryo transfer (Iliodromiti et al., 2013). This, however, will not prevent the occurrence of severe OHSS completely.

With increasing success rates of freezing, a ‘freeze-all’ policy with segmentation of IVF procedures has been proposed by Devroey et al. (2011) earlier in Human Reproduction (2011). These authors suggest uncoupling the oocyte collection cycle from the embryo transfer cycle. This becomes more and more attractive: ‘a time to build up, a time to break down; a time to plant, a time to reap that which is planted’. As an Editor of this journal, I would whole-heartedly welcome a manuscript on the first sufficiently powered RCT of GnRHa triggering in one arm, and traditional hCG triggering in the other; with subsequent secondary randomization to a ‘freeze-all’ strategy or a ‘fresh transfer’ strategy in either of the two arms. We will publish it straightaway.

References

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human reproduction

EDITORIAL

Turn, turn, turn

J.L.H. (Hans) Evers
Editor-in-Chief

