‘The times they are a changin’

Shaun R. McCann¹

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Bob Dylan. American singer—songwriter. (1941 -) [Fig. 1] ‘What is time, really. When you are diagnosed with a terminal disease like cancer or leukaemia your perception of time changes’; said Craig Sager sports commentator who died of acute myeloid leukaemia (AML) in 2016. Although death from infectious diseases is uncommon in developed countries, malignant diseases and cardiovascular diseases still remain problematical.

Thomas et al. showed that bone marrow transplantation could cure leukaemia [1]. Subsequently mobilised peripheral blood cells were shown to be capable of regenerating human haematopoiesis [2]. So-called myeloablative conditioning has been replaced in some instances by reduced intensity conditioning (RIC). Haploidentical haematopoietic cell transplantation became a reality so that, in theory everybody has a donor. Umbilical cord cells have been shown to be an active source of haematopoietic cells and many successful transplants have been carried out since the first in 1989 [3] Recently genetically engineered T cells (CAR T-cells) have been administered to patients with refractory ALL and they may have a role in the treatment of AML and multiple myeloma. Some investigators and clinicians claim that CAR T-cell therapy might replace autologous haematopoietic cell therapy and even allogeneic haematopoietic cell therapy in certain circumstances. Although definitely showing promise in the treatment of haematopoietic malignancies so far the results of CAR T-cell therapy in the treatment of solid tumours has been disappointing

The acute toxicity of CAR T-cell therapy appears to be under control although long-term efficacy and toxicity remain to be investigated. Pre-emptive therapy and early recognition and treatment of acute toxicities have been

reported as being effective in abrogating or negating harmful toxicities [4].

In Haemophilia we have gone from cryoprecipitate (cryo) to factor concentrates, haematopoietic cell transplantation, extended factor life therapy gene therapy and monoclonal antibodies in a relatively short time. Vitamin K antagonists have been replaced by direct acting anticoagulants (DOACS), anti FXa and anti thrombins and perhaps soon we will have anticoagulants aimed at the ‘contact’ system. This list is not an exhaustive but does show that ‘the times they are a changin’.

Have changes occurred in the wine world? Of course they have. Although fermentation has taken place in concrete tanks since Roman times the introduction of stainless steel tanks in the 1960s [Fig. 2], screw top closure, mechanical grape picking and the introduction of ‘wine-in-a box’ have had a huge impact on wine making internationally. Stainless tanks do not allow any oxygen to get in so wine makers since the 1990s, use microoxygenation, slowly infusing O₂ throughout the wine.

The beautiful wine growing areas around Montalcino and the area of Chianti Classico, from San Casciano, south of Florence to Castel Nuovo Bereardenga just outside Siena were not always so well manicured. Andrew Jefford, writing in the weekend FT [5] points out that even in the mid 1970 these were very poor areas of Italy. A combination of phylloxera (an aphid infection), Prohibition (in the USA), two world wars and the devastating frost in 1956, all share the blame. The end of the Semi – Feudal system of share cropping in the 1970s helped to establish the world – wide reputation of Italian wine.

Climate change, whether you believe in it or not, is credited with late ripening of Pinot Noir grapes in Germany and some even believe that Germany produces the best Pinot Noir wines in the world! Of course oenologists from Burgundy, Oregon and New Zealand might not agree.

Château Lafite Rothschild, in Pauillac Bordeaux, is one of the most famous wines in the world and one of the four ‘premier cru’ or first growth wines in Bordeaux awarded in 1885. It is made from Cabernet Sauvignon with a little

✉ Shaun R. McCann
shaunrmccann@gmail.com

¹ Emeritus Haematology Trinity College Dublin, Dublin, Ireland

Fig. 1 Bob Dylan

Fig. 2 Stainless steel fermentation tank

Cabernet Franc and Merlot, although in some years exclusively from Cabernet Sauvignon. Like many vineyards, Château Lafite has had its difficult times. It was badly

affected by phylloxera and was occupied by the Germans during World War II who plundered its cellars. According to Jancis Robinson, writing in the weekend FT [6] Lafite has now extended its operation to China. The 2017 vintage, labelled as Long Dai (chiselled mountain), will be available in September 2019 at about €140 per bottle. According to Robinson, Long Dai will initially be aimed at the Chinese market and subsequently the Chinese expatriate communities in Canada and Australia.

Other countries such as Argentina, Chile, Hungary and New Zealand are producing top quality wines for export, a situation that was unimaginable 20–30 years ago. In the future we might see wine production in countries without a pedigree in oenology such as Ireland!

For those of you who don't like change, be mindful of the words spoken by Tancredi in Giuseppe Tomasi's novel 'Gattopardo' published posthumously in 1958 by Feltrinelli: '*For everything to stay the same, everything must change*' [7].

Saluti,

Compliance with ethical standards

Conflict of interest The author declares that they have no conflict of interest.

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