The Banff classification revisited

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From small beginnings in 1991, the Banff working classification of renal allograft pathology has grown to be a major force for setting standards in renal transplant pathology, and is widely used in international clinical trials of new antirejection agents. The meeting, classification, and consensus process have unique history, and look poised to continue for another several decades as the embodiment of the process for setting global standards in pathology. The Banff meetings have expanded from renal allograft pathology to most other areas of solid organ transplantation, and increasingly incorporate international working groups, so that productive collaborative activity is ongoing, creating an important dynamic process enhancing clinical success in transplantation. On the other hand, despite the successes of the working classifications and ongoing collaborative efforts, there are limitations in this and other pathological classifications, related to potential for sampling error, issues of reproducibility when implemented globally, and lack of formal incorporation of morphometry and molecular and genomics approaches. Some of these problems cannot be overcome within the realm of traditional histopathology, and will only be solved when the classification is able to confidently embrace genomics and molecular medicine parameters for all common diagnoses. The smooth integration of these newer technologies with traditional histopathology is one of the great challenges for the future.

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The Banff Classification of Kidney Allograft Pathology had its origin in a meeting in Banff, Canada, held on 2–4 August 1991.[1] This original Banff meeting in 1991 was part of the activities of the International Society of Nephrology Commission on Acute Renal Failure, which also included international disaster relief. The initiative was inspired by the then recent development of a consensus grading system for diagnosis of rejection in cardiac allografts[2] led by Dr Margaret Billingham, a key participant at the first Banff meeting. Looking back now 21 years later at that meeting and the working classification developed there, it is clear that the classification,[3] as it has evolved since then, has made a critical contribution to many advances in the field of transplantation (Figure 1). That success is a testament to the efforts of an ever-growing number of people who continued to meet every 2 years and refine and expand the classification. Beginning in the kidney, the Banff Allograft Pathology consensus process ultimately not only led to revisions and expansion in the schema for kidney allograft pathology but also extended to development of classifications of allograft pathology in the liver, pancreas, and composite tissue grafts,[4–6] as well as contributing to advances in the existing classifications of the heart and lung allograft pathology.

Counterbalancing the successes of the classification are its limitations—limitations that apply to any biopsy- and histopathology-based classification system. These include inherent potential for sampling error, suboptimal reproducibility when implemented globally, lack of widespread application of morphometry with true quantification, and lack of formal integration of molecular and genomics data into the classification. These are issues to be addressed in the ongoing international Banff conferences and related activities, described below.

BACKGROUND

The need for a new classification was quite obvious in 1991 when the Banff Classification of Allograft Pathology began. Most people learning kidney transplant pathology had no direct mentor and were learning from outdated textbooks. Although a few individual classifications for renal allograft rejection had been developed, none were in general use. The new consensus classification for heart allograft rejection had just been published[2] and served as a model for the process. A group of individuals who had published in the field met to discuss the literature, cardinal histopathological findings, and

potential categories of rejection that would be clinically relevant for guiding therapy.

The new classification used lesion scoring and guidelines to provide rigor in the evaluation of renal allograft pathology and the assignment of biopsies into diagnostic categories. Nonrejection pathology in the allograft was also considered and described in some detail, and this continues to be a focus in ongoing Banff meetings.

THEMES OF THE BANFF MEETINGS

A previous article on the history of the Banff Classification focused on the participants.[1] Here, we will concentrate on the ideas espoused by the Banff meetings (Table 1) and the Banff consensus process. The flavor of the Banff meetings from the beginning was one of flexibility and openness to the ideas of others. At the original meeting of 20 people in 1991, the kidney transplant pathology classification that emerged was very different from any of the drafts that individuals had created before the consensus discussions began. It was a true creation of the meeting itself, based on international expertise, the existing literature, and facilitated discussions. The classification was designed as a dynamic working document that could be modified as the need for future changes was demonstrated.

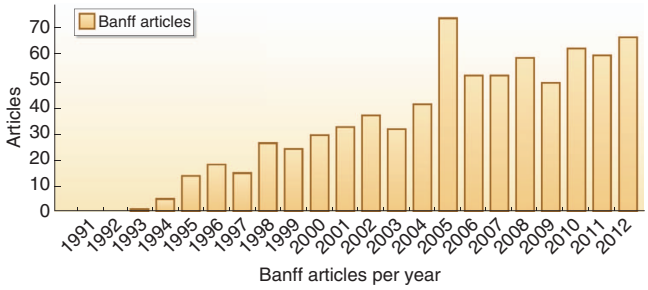

Figure 1 | Number of Banff articles in transplantation per year. The peak of 73 articles in 2005 was the combined effect of increasing interest in antibody-mediated rejection and viral disease, and the controversy surrounding the term 'chronic allograft nephropathy'. The distribution into categories was Kidney-Clinical (human) 611, Kidney-Experimental 40, Liver-Clinical (human) 48, Liver-Experimental 8, Pancreas-Clinical (human) 4, All Organs-Clinical (human) 2, Composite Tissue-Clinical (human) 3, and Heart-Clinical (human) 1. There are 38 articles thus far in 2012 to July 31, which extrapolate to 65 for the year making 2012 the second highest year for Banff articles.

At the second meeting in 1993, a similar effort was initiated to create a classification for liver transplant pathology, and this became a major focus of the Third Banff Conference held in July 1995.[4] The third conference had four times as many attendees as the first conference and was conducted with an air of positive expectation that could not have been anticipated in 1991. The 1995 meeting also brought Banff lesion scoring into line with the CADI scoring system,[7] so there was no difference between the two classifications.

By the time of the 1995 meeting, the original Banff Classification of Renal Allograft Pathology was in wide use, and there had been extensive studies showing its clinical validity and reproducibility.[8–12] Extrapolating from these studies, it seemed likely that the classification had already resulted in improvement in patient care. The Banff classification had been endorsed by the FDA and other regulatory agencies, and had enabled the use of objective histological endpoints for international clinical trials of new antirejection agents and other scientific studies, a process that continues to this day.

Table 1 | Banff Allograft Pathology Meetings since 1991 with key themes

	Location	Length (days)	Links	Key subjects debated
1991	Banff, Canada	1.5	ISN	Classification established, lesion scoring, diagnostic categories, physician-led consensus
1993	Banff, Canada	3	ISN, CAP	Liver classification, chronic rejection, first presentation on molecular pathology approaches
1995	Banff, Canada	4	ISN	Pancreas classification, glomerulitis, first international medical meeting on CD-ROM, first Banff conference with microscope sessions. Lesion scoring normalized with CADI.
1997	Banff, Canada	5	ISN	Merging of Banff and CCTT classifications, establishing basis for current Banff classification, post-transplant lymphoproliferative disorder, first Banff conference with posters
1999	Banff, Canada	5	ISN, NKF, NIH	Protocol biopsies, chronic rejection, and viral diseases, clinical practice guidelines. First conference supported by an NIH grant.
2001	Banff, Canada	5	ISN, NKF	AMR, donor biopsies, genomics, CAN, heart transplantation
2003	Aberdeen, Scotland	4	ISN, NKF	C4d, macrophages, tolerance, accommodation, immunodepletion
2005	Edmonton, Canada	6	NKF	Genomics and molecular markers, B cells, chronic allograft injury with elimination of CAN, establishment of criteria for chronic rejection
2007	La Coruna, Spain	6	UofA	Protocol biopsies, transcriptome, mechanisms of rejection, ptc grading, new total inflammation score; working groups for v-lesion, genomic integration, pancreas and composite tissue rejection schemas
2009	Banff, Canada	5	UofA	Viruses, quality assurance, AMR in kidney, heart, and pancreas, liver allograft accommodation, endothelial cells, surrogate markers. Working groups.
2011	Paris, France	5	UofA	Sensitized patient, C4d, isolated v-lesion, the future, genomics, glomerulitis, epithelial injury/epithelial mesenchymal transformation, operational tolerance monitoring in liver grafts

Abbreviations: AMR, antibody-mediated rejection; CAN, chronic allograft nephropathy; CAP, Canadian Association of Pathologists, and Future of Pathology/Laboratory Medicine in Canada Consortium; ISN, International Society of Nephrology; NKF, National Kidney Foundation (US); NIH, National Institutes of Health (US); ptc, peritubular capillary; UofA, University of Alberta.