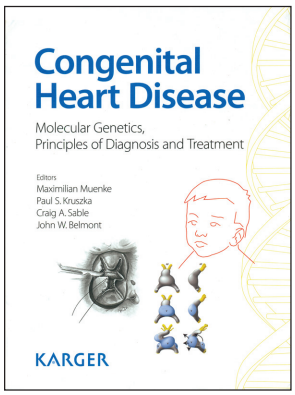
Book Reviews

Congenital Heart Disease—Molecular Genetics, Principles of Diagnosis and Treatment. Max Muenke, Paul S. Kruszka, Craig A. Sable, John W. Belmont (eds). Karger, Basel, Switzerland, 2015. *326 pp, price not mentioned*. ISBN 978–3–318–03003–7.



Congenital heart defects (CHDs) are a leading cause of mortality in infants. Despite early recognition of cardiac malformations, William Osler in his book *The principles and practice of medicine*, commenced his chapter on congenital heart disease thus: 'These [congenital affections of the heart] have only limited clinical interest, as in a large proportion of the cases, the anomaly is not compatible with life and in others nothing can be done to remedy the defect or even to relieve the symptoms.' Angiocardiography, cardiac catheterization and cardiac surgery rapidly changed this sense of futility. Surgical pioneers such as Robert Gross, Alfred Blalock, William Rashkind and Aldo Casteneda and paediatric cardiologists such as Helen Taussig paved the way for successful therapy in congenital heart disease as well as the growth of interest of researchers in elucidating the causes and morphogenesis of cardiac anomalies.

During the past six decades the care of patients with congenital heart diseases has been revolutionized. The combination of human genetics and biochemical analysis has provided tools for recognizing disease genes causing CHDs.

This new book is a collection of 27 comprehensive reviews encompassing the latest advances in embryology, genetics, imaging, and interventional and surgical treatment of congenital heart diseases. The essays also include epidemiological and preventive aspects as well as ethical issues related to the diagnosis and management of CHDs and the role of stem cells, gene editing technologies and tissue engineering in the development of future therapies. Several chapters provide insight into the diverse approaches of investigators in elucidating the causes and morphogenesis of cardiac anomalies and the current knowledge about the genetic basis and molecular mechanisms in the pathogenesis of CHDs. Each chapter is authored by international leaders in the respective domains. The first chapter of the book is a stimulating historical overview of congenital cardiovascular anomalies.

Jacqueline Noonan, a pioneer in integrating genetics to paediatric cardiology and well known for characterizing the genetic syndrome caused by the mutation in *PTPN11* gene, has written the foreword for the book. She highlights why publication of this book is well-timed. Making specific genetic diagnosis, identifying heritable syndromes, providing genetic counselling and repair of complex heart malformations are no more a fantasy, but a reality thanks to the tremendous progress in our understanding of the molecular basis of normal heart development and the invention of both genetic and imaging tools for diagnosis.

The advent of molecular genetic techniques such as composition of fate maps have unveiled the origin of cells which build the different components of the heart from Carnegie stage (CS) 8 to (CS) 23 and their molecular determinants. These new insights permit a paediatric cardiologist to understand the morphogenesis of structural CHDs and potential substrates for associated arrhythmias. M. Sylva and A.F.M. Moorman in their chapter on normal development of the heart explain the importance of copy number variations, somatic mutations and variations in regulatory sequences of genes and their implications in the pathogenesis of CHDs.

In a thought-provoking chapter, Lorenzo Botto review the not well-characterized gene–environment interactions in the causation of CHDs. What proportion of heart defects can be prevented? The CHDs which have a strong genetic background cannot be corrected and the rest can be prevented by measures such as multi-vitamin supplementation to pregnant women and monitoring maternal chronic illnesses. Indian paediatric cardiologists would find useful the experience of E.N. Ekure and A.A. Adeyemo on management of CHDs in Nigeria. They discuss both the challenges and opportunities in the management and prevention of CHDs in developing countries.

Knowledge on various risk factors for CHD helps for better pre-pregnancy planning and minimize the chance of CHD in the newborns. T.J. Riehle-Colarusso and Sonali Patel based on evidences gathered during the past 25 years describe how to measure non-genetic maternal risk factors for CHDs. Practising clinicians and clinical geneticists would find the instructions valuable.

As a result of improvements in surgical care, more survivors of CHDs reach their adulthood. They however later develop a host of complications which many adult cardiologists find challenging to recognize and treat. Considerable progress made in exploring the unique issues associated with this special CHD population is succinctly summarized by Koichiro Niwa.

A large section of the book deals with cardiovascular complications in chromosomal disorders. Epidemiological aspects, genetics, embryogenesis, clinical manifestations and treatment strategies are well elucidated. Prospects of gene therapy for Down syndrome by silencing the HAS21 with XIST RN molecule are explained. A chapter on congenital cardiovascular malformations that result from sub-microscopic genomic deletions and/or duplications that cause disorders such as Williams–Beuren syndrome, Kleefstra syndrome, Wolf–Hirschhorn syndrome, etc. is also included in the book. Separate chapters discuss RAS/MAPK pathway syndromes, transcription factor-related heart diseases and single gene disorders. Key features of the inherited primary arrhythmia syndromes and channelopathies, their diagnosis through genetic testing and management are also incorporated in the text. The section titled 'The genetic workup for congenital structural heart disease: from clinical to genetic evaluation' provides a genetic testing algorithm advantageous for physicians to choose appropriate genetic tests for CHD. Interventional techniques ranging from stent and valve implantation to hybrid palliation for hypoplastic left heart disease are lucidly spelt out in the book.

Insights gained from fundamental research, together with the results of clinical trials are now being used to develop novel strategies for treating CHDs. Discoveries in tissue engineering,

regeneration triggering factors and gene editing technologies are expected to provide avenues to reconstitute a healthy heart *in vivo* or *de novo*. These strategies may revolutionize cardiovascular therapies. Exciting possibilities are suggested by recent techniques such as parabiosis developed by Lee and Wager and identification of GDF11 for reversing cardiac hypertrophy. The final chapter on future therapeutics discuss these seductive treatment opportunities.

Excellent illustrations and a description on novel research tools such as gene reporter assays that are useful in evaluating clinical importance of mutations are attractive attributes of this book. The quality of production is excellent.

In summary, the book surveys the state-of-the-art concerning causation and management of CHDs. Given that the contents are enlightening, inspiring and utilitarian, it is a valuable reference for both cardiologists and researchers engaged in cardiac biology. They would certainly profit from studying this volume. The text is also relevant for cardiac surgeons and imageologists.

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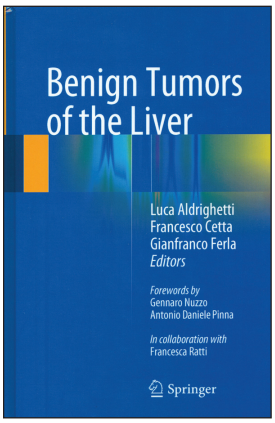
Benign Tumors of the Liver. Luca Aldrighetti, Francesco Cetta Gianfranco Ferla (eds). Springer, Switzerland, 2015. *337 pp, prince not mentioned*. ISBN 978–3–319–12984–6.



The ever-expanding horizon in the field of medicine has led to the accumulation of increasing amount of information about diseases that up to a few decades ago were either considered medical mysteries or not important enough to merit more than a few paragraphs in medical texts. An interesting outcome of this development has been the publication of new texts dedicated solely to such entities; this book is a part of that trend. The editors and contributors are experienced hepatobiliary surgeons.

Benign tumours of the liver have traditionally been considered to be of lesser clinical importance than the more ominous malignant conditions of the liver. However, proliferation of screening ultrasound and improvement in the quality of imaging tools such as CT and MRI have led to increased rates of detection of benign tumours of the liver; the important ones being haemangiomas, focal nodular hyperplasia (FNH), hepatic adenomas (HA), cystic lesions and infectious conditions. The incidental discovery of such asymptomatic lesions during imaging causes anxiety, both to the patient and the treating clinician. In such situations, the clinicians are often unable to provide convincing prognostic information and management plans to patients. This book should help clinicians in resolving many questions for patients. The authors should be commended for their meticulous literature search and the efforts made to include the latest information on hepatology.

The natural history, morphology and imaging characteristics of benign tumours of the liver have been described well in previous texts on liver pathology and, in those aspects, this book does not add much. What is new and really interesting is the detailed discussion on the molecular biology and genetics of benign tumours. Hepatic adenomas have been sub-classified on the basis of the underlying mutations (Bordeaux classification). Now we have HNF 1A mutated adenomas, beta-Catenin activated adenomas and inflammatory adenomas. Beta-Catenin-activated adenomas are associated with the highest risk of malignant transformation and, therefore, should be subjected to surgical excision.

Another notable development has been the emergence of MRI as the imaging modality of choice for investigating an incidentally discovered asymptomatic space-occupying lesion (SOL) of the liver. Most of these lesions can be convincingly diagnosed on the basis of their MR characteristics and needling the lesions is rarely required. Since the majority of benign tumours of the liver are haemangiomas or FNH and do not usually require an intervention, a convincing diagnosis at MRI is extremely important. The snapshots of ultrasound, CT and MRI included in this book help in understanding the imaging characteristics of these lesions. In fact, hepatobiliary surgeons should make themselves adept at reading liver MRI scans.

The editors have done well by conducting a systematic review of each benign tumour, covering its epidemiology, natural history, genetics and management. There are specific indications for surgical intervention in benign conditions of the liver and clear guidelines are given in the chapters on these topics.

Liver transplantation for benign conditions of the liver might seem odd to a casual reader but the chapter on liver transplantation will clear doubts that many physicians and surgeons may harbour. According to the European Liver Transplant Registry (ELTR) approximately 1.5% of all liver transplants in Europe from 1988 to 2012 were done for benign conditions of the liver such as polycystic disease, giant cavernous haemangiomas with Kasabach–Merritt syndrome, epithelioid haemangioendothelioma, liver cell adenomatosis and alveolar echinococcosis.

Intraoperative ultrasound (IOUS) is an indispensable tool for advanced hepatobiliary surgery and a chapter on this topic has been aptly included. However, it must be said that the chapter gives only a broad overview of IOUS and a more interested reader will have to refer to a separate text on this topic. The chapters on laparoscopic liver surgery and robotic liver resections should also be of special interest for hepatobiliary surgeons. Both limited and extensive anatomical liver resections are being performed laparoscopically at dedicated hepatobiliary centres and the editors have done well to devote a chapter to this aspect of liver surgery. Although the general steps of laparoscopic liver surgery have been described the paucity of illustrations makes this chapter inadequate for a surgeon. The same can be said for the chapter on robotic surgery. Moreover, the operative photographs lack details and are unsatisfactory.

Tubercular lesions of the liver are not uncommon, especially in developing nations such as India. Many times, caseating granulomas are an incidental finding on explant histology. The authors could have devoted more space to this entity for the benefit of readers from these parts of the world.

A flaw that would be evident to the reader is the repetition of information on epidemiology, morphology and imaging characteristics of benign lesions of the liver. In particular, there was no need for the chapter on differential diagnosis.

Overall, this lucid and readable book provides comprehensive and up-to-date information on a subject that deserves greater attention from clinicians. Both students and practitioners of hepatology and hepatobiliary surgery would find this book useful.

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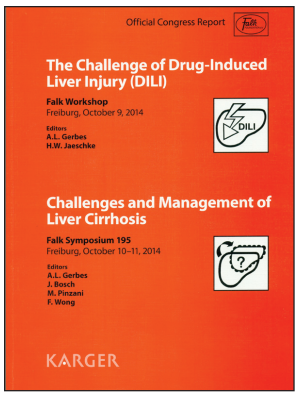
The Challenge of Drug Induced Liver Injury (Falk Workshop) and **Challenges and Management of Liver Cirrhosis (Falk Symposium 195).** A.L. Gerbes, H.W. Jaeschke, A.L. Gerbes, J. Bosch, M. Pinzani, F. Wong (eds). Karger, Basel, 2015. *457* and *628 pp, price not mentioned*. ISBN 978–3–318–05448–4.



The Falk Foundation, established in 1978 by Dr Herbert Falk in Freiburg, Germany, is a non-profit organization offering a wide range of altruistic services to the medical fraternity working in the field of gastroenterology and hepatology. High-quality scientific workshops and symposia organized by the foundation provide an excellent platform for learning and exchanging expertise among clinicians and researchers around the world.

As of now, over 200 such Falk symposia have been organized. The foundation organized a one-day workshop in October 2014 on a relatively orphan topic of hepatology—drug-induced liver injury (DILI), followed by a two-day symposium on a common topic—the challenges and management of liver cirrhosis. The proceedings from both these academic events are published in this book. The book itself is a reprint of the journal *Digestive Disease* (2015, Volume 33, No 4). The two very diverse topics, covered in 24 articles written by stalwarts in the respective fields, are organized into two sections in the book.

The first part of the book deals with DILI, a phenomenon commonly encountered but rarely discussed in most academic fora. Though the liver is the most common organ involved in drug-induced injury, apart from a few drugs, DILI has not been studied well. We have large voids in our understanding about DILI such as risk factor, mechanism of injury, diagnostic criteria, management and natural history, etc. We have limited opportunity to discuss, learn and read about DILI. The Falk workshop was such an opportunity to learn and discuss about DILI. As DILI is encountered not only by hepatologists or gastroenterologists but by all in the medical fraternity at various levels, it may help the book to seek a widespread readership among medical students, internists, gastroenterologists, hepatologists and those involved in drug development and marketing industry. The information is summarized in only five chapters, which discuss various aspects of DILI in a superficial manner and would be of little value particularly to a novice in the field of hepatology.

The second and the major portion of the book is on liver cirrhosis which retains its indisputable cardinal position in the majority of academic gastroenterology and hepatology. It is partially attributed to its higher disease burden, life-threatening complications and ever-changing field of management. The entire section is organized in 19 well-written chapters. The book has a special focus on assessment of liver fibrosis, renal dysfunction and bacterial infections in cirrhosis. The updated and concise information on various aspects of cirrhosis and its complications are included in this section. This gives the flavour of an abridged version of a current edition of any standard textbook of hepatology. The content is flawless from pathophysiology to management and recent advances. Addition of portions on epidemiology and ascites might have made the book even better.

The chapters are written in a simple language with the information flowing in a regulated manner that is easy to understand. Overall, the book is a useful, brief overview on the subject.

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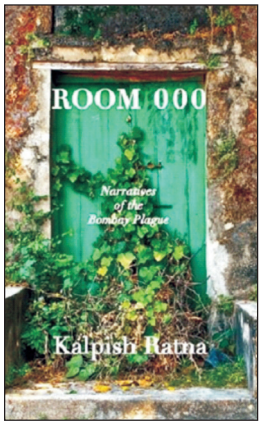
Room 000: Narratives of the Bombay Plague. Kalpish Ratna. Macmillan, New Delhi, 2015. *495 pp, ₹599 (HB).* ISBN 978–93–82616–35–1.



In a *Letter from Mumbai* in an earlier issue of this *Journal*, I have introduced you to the duo who go under the single pen name Kalpish Ratna.[1] This book is their latest offering. All the photographs included in it are by Ishrat Syed.

The prologue sets the stage in contemporary Grant Medical College, Mumbai and introduces us at once to the turreted Gothic building that was, in 1845, the college and the younger building to its left, the Petit Laboratory. Ratna (our duo use the first person singular throughout their books) shows us the plaque to the right of the entrance of the laboratory from which the book derives its title. The inscription in lead on the marble tells us that it marks the site where Waldemar Haffkine (1860–1930) created the first successful vaccine against the bubonic plague. It specifies the actual room (No. 000) where Haffkine worked. Ratna points out an error when the plaque was sculpted. 'Mankind' was spelt 'mainkind' by the sculptor. As a last minute correction, the lead was scraped out of the first 'i'. We

now see 'ma nkind'. Although I have passed by this plaque many times, this remained unobserved by me. In passing let me add that the plaque followed the efforts of a determined acolyte of Dr Haffkine. Ms Edythe Lutzker (1904–1987), a historian from New York who went to college at the age of 46, after her family was well-settled, collected the funds for the plaque, got the various permissions for its installations and even arranged for President V.V. Giri to unveil it!

Ratna rightly bemoans the dilapidated state of the crumbling historic college building—the only structure on the campus that dates back to 1845—and the fact that generations of medical students were taught pharmacology in the Petit Laboratory without being told of Room 000 and the historic work done in it. If there is an explanation for the unusual number given to the room in the book, I have missed it. I wonder if the general convention of using 000 for emergency services was applied here when Surveyor started his work in it. And this is where this tale takes off.

Ratna uses flashbacks throughout the book, positing the author at the site of action from time to time, giving us a feel of that period as events unfolded. The identification of the first patient with bubonic plague in Bombay on 18 September 1896 by Dr Acacio Gabriel Veigas is described in considerable detail, giving ample credit to Dr Veigas for making the diagnosis without ever having seen a patient with plague earlier and for his persistence in getting the authorities to accept it when business interests called for turning a blind eye to it. It was only on 29 September that Lord Sandhurst. Governor of Bombay, announced to Lord Elgin, Governor-General in Calcutta, that there was an outbreak of the plague in Bombay.

In rapid succession, we are introduced to Dr Cowasji, Dr Blaney and, the unsung hero, Dr Nusserwanji Fakirji Surveyor. Ratna deserves full credit for highlighting his pioneering work, without which Haffkine could not have created his vaccine. It is sad that Dr Surveyor has been neglected by historians all these years. Search for details on this remarkable researcher on the internet and you will be inundated with references to the book under review, little else having been published on his life and work. Ratna has drawn extensively on the notes written by Dr Surveyor as he worked on the identification of the plague bacillus and on the letter he wrote to *The Times*.

As the narrative proceeds, we are also introduced to Drs Ernest Hanbury Hankin, Shibasaburo Kitasato, Alexandre-Emile-Jean Yersin, James Alfred Lawson, Ismail Jan Mohammad (commemorated at the Seth G.S. Medical College and K.E.M. Hospital, Mumbai), Bhalchandra Krishna Bhatawdekar, Nusserwanji Choksey (who treated over 4000 patients with plague and was eventually knighted) and others who, willy nilly, were involved in identification of patients, attempts at preventing spread of the disease and administrative decisions in the Municipal Corporation of Bombay and the Governments of Bombay and India.

The narrative is fast-paced, with real and some imagined events giving an almost palpable awareness of what happened throughout the period covered in the book.

The frustrations of those working at ground-level and of the patients are graphically described. Indian doctors were slighted by the administrators, while the pronouncements of British 'experts' with a fraction of their expertise and experiences were listened to gravely and acted upon.

The disasters following ill-advised measures to prevent spread of the disease included turning thousands of poor families out of their homes, destruction of their meagre possessions and fumigation that rendered their homes uninhabitable are described in detail. Destruction of rats was granted overarching importance as the British scientists and administrators ignored the observations by Paul-Louis Simond (who succeeded Yersin in Bombay) on how the actual transmission of *Pasteurella pestis* to man was through bites by fleas whose digestive systems were clogged by masses of these germs.

The treatment meted out to scientists not invited expressly by the British administrators was appalling and is exemplified in the manner in which Dr Yersin was dealt with (see the chapter titled *The solitary scientist*).

The introduction of Rao Saheb Tatoba, alias Tatya Lakshman, inspector with the Bombay Police—the local incarnation of Sherlock Holmes—provides welcome relief in the otherwise grim narration of events starting with the detection of the first patient to the eventual acceptance of the actual mode of transmission of the disease to man. Tatya makes his appearance in the chapter with an equally interesting title, *The strange events surrounding the Giant Rat of Bombay Province*.

Human nature being what it is, we are probably condemned to more mismanagement of epidemic diseases, willful ignorance of evident facts (as we continue to adhere to old and outdated beliefs) and steps taken not in the interest of the sick and the poor but to favour big business and those in the good books of powerful administrators. Ratna's statement at the end of the last chapter (*A study in scarlet*—a tribute to the creator of the original Sherlock Holmes?) is tragic and prophetic: 'Then, as today, in the thick of the event, nobody noticed the obvious.'

To fully understand the saga of the plague epidemic that hit the Indian citizens of Bombay Presidency (and then other parts of the country), a study of *Room 000* must be coupled with that of an earlier book by Ratna (*Uncertain life and sure death*). Plague in India forms an important part of that narrative and aspects discussed there are somewhat different from those in *Room 000*. In the earlier book, the historical review of bubonic and pneumonic plague is detailed with plenty of references to works that are not easily available. That book also provides much information on the development of Bombay, from the seven islands and the portion of the mainland immediately to their north that the Portuguese favoured on account of the harbours it offered. While *Uncertain life and sure death* is slanted towards maritime history, it is much the richer book to me as it provides invaluable references on pages 331–64.

The dedication of *Uncertain life and sure death* could well have served *Room 000* and all other books on epidemic diseases: 'for the hundreds of thousands who died in obscure villages, unknown and unheeded'.

Neither book carries an index—a major handicap for the reader wanting to go back to particular topics. *Room 000* lacks references collected together at the end but provides them as footnotes.

Both books are strongly recommended to students of the history of medicine in India, Bombay and the plague epidemics—especially that hitting Bombay in 1896.

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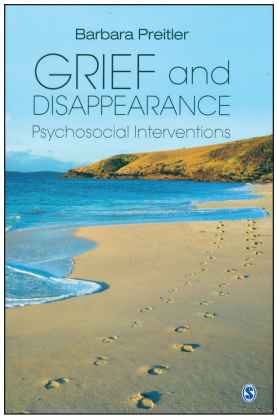
Grief and Disappearance: Psychosocial interventions. B. Preitler, Sage Publications, New Delhi, 2015. *228 pp, ₹895.* ISBN 978–93–5150242–5.



Sudden disappearance of people, without definite proof of death, is not uncommon and is periodically reported in the local, national and international media. However, these reports do not impinge on our consciousness as the majority of us live in much safer worlds. Consequently, these events are often treated as statistics rather than as individual and personal tragedies. Nevertheless, the 2004 Indian Ocean tsunami widely reported in the media brought to attention many such disappearances. Reports on recent overt and covert wars, genocide and internal emergencies in Vietnam, Cambodia, Chile, Argentina, South Africa, Rwanda, Sri Lanka and Russia and the 9/11 attacks on the USA have brought such disappearances into focus. Investigations into these disasters coupled with earlier work, done in the context of the world wars and the Holocaust, have re-engaged our attention. Political violence, police states, authoritarian dictatorships, structural violence, low-intensity wars, ethnic strife and cleansing, and forced internal migration and systematic abuse of human rights found in many parts of the world make it imperative to highlight these issues and bring them into public and international consciousness.

The field has seen a shift from anecdotal reports to systematic study of the problems of people affected by disappearance of their relatives in both natural and man-made disasters. It has seen a shift from theoretical approaches to practical strategies for helping people grieve their loss, resolve difficult conflicts, heal minds and rebuild lives despite uncertainties.

Barbara Prietler's book discusses theoretical models of normal and complicated grief, in general, and their application to sudden disappearances, in particular. It discusses Greek mythology and highlights the integration of therapy and solutions into historical, cultural and religious frameworks. It raises philosophical, ethical and legal concerns. The book highlights the social consequences of such trauma on individuals, families and society. It discusses therapeutic work with individuals, families and local communities.

The book, in addition to reviewing the literature, includes the author's own work. It highlights the loss, failure to bid farewell, absence of ritual goodbyes, lacunae in relationships, unfulfilled attachments, unresolvable conflicts, need for redefinition of social roles, absence of definite closure and also the faint, but ever present, hope of return. She reviews psychotherapeutic work involved, the provision of safe counselling relationships, handling individual reactions of grief, anger and aggression, managing transference and countertransference, and the use of interpreters. She graphically brings out how the relatives who survive are caught between search, despair and resignation. She emphasizes the processes of acceptance of the irreconcilables, achieving a sense of coherence and building resilience. The fear of further losses, the desire for justice, the arbitrariness of authorities and the fickleness of the media, which has moved on to other eye-catching stories, complicate issues.

She examines community responses to coping. She mentions attempts at comprehending and giving meaning to such events and the provision of support networks. She discusses the role of 'truth and reconciliation commissions' used in South Africa and also in El Salvador, Peru, Guatemala, Chile, East Timor, Sri Lanka and Rwanda. She highlights movements that were able to transform grief and traumatization into political action. She talks of different ways communities commemorate individuals who have disappeared and their role in acceptance of irreconcilability. She also describes specific steps involved in such efforts at helping individuals, families and communities.

The book dedicates a chapter to the issues raised when the occasional individual actually returns. She discusses renewed injury due to reliving of past trauma, the stress of re-engagement, changed roles and relationships, acceptance of time apart and new beginnings.

Stress among health professionals, who manage psychological problems of people whose relatives have disappeared, is also examined. It recognizes the challenge of keeping a balance between empathy and emotional involvement, between intellectual comprehension of issues and an emotional understanding of the person. It highlights possible countertransference, stress and fatigue among counsellors over time. She describes methods to prevent burnout.

Some chapters ramble while others are focused and make one wonder if there was loss in translation from the original German. Nevertheless, many chapters discuss practical issues and highlight concerns with case-based examples. The book will captivate academics trying to understand the issues concerning this complex field. It will be useful for counsellors facing similar dilemmas, when faced with people who are confronted with such trauma. The elaboration of principles, discussion of perspectives and the detailed examples increase its usefulness.

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