DERMATOSCOPY SKIN CANCER

A HANDBOOK FOR HUNTERS

OF SKIN CANCER AND

MELANOMA CLIFF ROSENDAHL

and AKSANA MAROZAVA

A HANDBOOK FOR HUNTERS OF SKIN CANCER AND MELANOMA

CLIFF ROSENDAHL

Professor, Faculty of Medicine, The University of Queensland, Australia

AKSANA MAROZAVA

MD, Dermatology Resident at Vitebsk State Medical University, Belarus

ISBN 9781914961205

Updated edition published 2023
First edition published 2019

A CIP catalogue record for this book is available from the British Library.

Scion Publishing Limited

The Old Hayloft, Vantage Business Park, Bloxham Road, Banbury OX16 9UX, UK www.scionpublishing.com

Important Note from the Publisher

The information contained within this book was obtained by Scion Publishing Ltd from sources believed by us to be reliable. However, while every effort has been made to ensure its accuracy, no responsibility for loss or injury whatsoever occasioned to any person acting or refraining from action as a result of information contained herein can be accepted by the authors or publishers.

Readers are reminded that medicine is a constantly evolving science and while the authors and publishers have ensured that all dosages, applications and practices are based on current indications, there may be specific practices which differ between communities. You should always follow the guidelines laid down by the manufacturers of specific products and the relevant authorities in the country in which you are practising.

Although every effort has been made to ensure that all owners of copyright material have been acknowledged in this publication, we would be pleased to acknowledge in subsequent reprints or editions any omissions brought to our attention.

Registered names, trademarks, etc. used in this book, even when not marked as such, are not to be considered unprotected by law.

Cover photograph kindly provided by Brian Mallon, University of Queensland, Australia

Typeset by Evolution Design & Digital Ltd, Kent, UK
Printed in the UK

Last digit is the print number: 10 9 8 7 6 5 4 3 2 1

Contents

CHAPTER 5
The skin examination

CHAPTER 6
'Chaos and Clues' (Chaos, Clues and Exceptions): a decision algorithm for pigmented skin lesions

Dermatoscopic features of common and significant lesions: pigmented and non-pigmented

Preface

Fifty years ago when I entered my first year of medical studies in 1969, the same year that Neil Armstrong stepped onto the moon, dermatoscopy as we know it was science fiction. Much has changed. Dermatoscopy is now standard of care in the management of skin cancer and melanoma.

My interest in this novel science became focused after a family member, Graham, developed metastatic melanoma. Graham did not blame the GP who dismissed a lesion of concern on his thigh a couple of years earlier, and he made the point to me that GPs were not prepared for this challenge in their training, a challenge that was thrust on them due to a rising incidence of melanoma and an inexplicable shortage of dermatologists in Australia. Graham's GP looked after him well. Right up to the moment of his death, a death which was predictably terrible, aggra vated by multi-organ metastases and finally necrotising fasciitis.

My journey since then, commencing with a PhD expertly supervised by David Wilkinson and Peter Soyer and focused on improving skin cancer management in Australia, has been a very steep learning curve. I have been mentored by men of undoubted genius: Harald Kittler and David Weedon, men whose genius was only matched by their generosity. I have been assisted by excep tional colleagues: Ian McColl, Iris Zalaudek, Alan Cameron, Jeff Keir, Greg Canning, Phil Tschandl, Agata Bulinska, Simon Clark and Nisa Akay. I am particularly grateful to Harald

Kittler, Stephen Hayes and Jeff Keir for their critical review of the book and to Simon Clark for reviewing and correcting the dermato pathology chapter.

This book would never have been possible without my co-author Aksana Marozava. Aksana worked with me for two years, taught me how to do a skin examination and dispelled any delusions of grandeur by repeatedly discovering significant lesions I had passed over. Her diligence and skill in collating my image collection for the book and preparing all of the graphics has hopefully made this book the masterpiece we wanted to produce.

The hunting metaphor is no accident. Hunting and gathering (Aksana insists that she is a gatherer) are as natural to ***Homo sapiens*** as is falling in love. The romance and thrill of the hunt elevates what we do to more than the drudgery of repetitive work, and the satisfaction of every success motivates further effort.

Finally, I am indebted to my wife Debbie for putting up with me through this journey and for effectively managing our practice and business affairs so I could focus on hunting, research, teaching and writing.

To conclude, I quote Vice Admiral Horatio Nelson, hunter extraordinaire, speaking at the battle of Copenhagen in 1801:

"It is warm work; and this day may be the last to any of us at a moment. But mark you! I would not be elsewhere for thousands".

Cliff Rosendahl
Brisbane March 2019

Foreword

This new book is an important step forward in the developing art and science of dermatos copy for skin lesion recognition. The debate as to whether the technique is any good is surely over, but more help as to how to best do it, and (vitally) to best teach it, is most welcome.

Over the last decade or so, Cliff Rosendahl, and more recently Aksana Marozava, have documented some 19,000 excised skin lesions in Cliff's clinic in Capalaba, Brisbane, and fed the data into the SCARD online database which he set up with Tobias Wilson. This book summarises the knowledge gained from the analysis of that histopathological data and the lesion images, plain and dermatoscopic. The sheer scale of the data behind this book gives it an authority that can't be ignored.

The book is built around two algorithms, 'Chaos and Clues' and 'Prediction without Pigment' which, as explained, may not always lead to a diagnosis, but to a safe decision as to whether excision is required. The selected colour images illustrate well the dermato scopic features and terms set out in the text.

Cliff is fully committed to revised pattern analysis and the use of what he calls objective geometric terminology to describe derma toscopic structures, building on the 'descrip tive' terminology often associated with co-worker Harald Kittler of Vienna. There are no 'arborising' vessels here (if vessels are 'tree like', then what sort of tree?) but branched serpentine (admittedly, 'serpentine', i.e. snake like, is still a metaphor, but a much more consistent one than tree-like). And it is further explained that the apparent sharp focus of such vessels in BCC is due to the superficial

cutaneous vascular plexus being clarified by the translucent BCC stroma, rather than that vessel morphology being unique to BCC.

There is more basic science here than is usual in a book aimed at beginners, but the extra effort put into appreciating the embry ology, anatomy and histopathology pays rewards, particularly with regard to dermato scopic–pathological correlation. Recognising structures like blue clods and polarising-spe cific white lines is good, but understanding what they mean at the microanatomical level gives insight into the modus operandi of the target of the hunt: malignant tissue.

More recently described signs such as white circles in early invasive SCC and angulated lines and polygons in melanoma ***in situ*** are detailed. I have witnessed Cliff working in his clinic and I can say that the author has a zero tolerance approach to such lesions, with approximately 80% of the melanomas diagnosed in his clinic being pre-invasive.

Dermatoscopy and skin cancer is a more challenging read than some earlier textbooks on this subject, but builds on hard-won, audit-backed knowledge to take us to the next level of advanced pattern analysis. It can be commended to the beginner/improver and indeed expert, who is willing to put in some work to embrace the latest evidence-based approach and terminology, which seems likely to supersede the earlier algorithms based on metaphorical language. This may mean some effort for those of us who learned dermoscopy/dermatoscopy with terms like maple leaf, arborising, comedo-like, ovoid nests, etc., but the new approach makes sense

if for no other reasons than the need for trans lation and utility for international research, for dermatoscopy is now highly globalised.

Dr Stephen Hayes
Independent dermatoscopy educator
Associate Specialist in Dermatology, University Hospital Southampton UK board member, International Dermoscopy Society

Abbreviations

AK actinic keratosis
BCC basal cell carcinoma
DF dermatofibroma
DOPA dihydroxyphenylalanine
EFG elevated, firm and continuously growing
H&E haematoxylin and eosin
KA keratoacanthoma
LN lymph nodes

LPLK lichen planus-like keratosis
MHC major histocompatibility complex
Naevus melanocytic naevus
NMSC non-melanoma skin cancer
PAM primary acquired melanosis pBCC
pigmented basal cell carcinoma pIEC
pigmented intraepidermal carcinoma pSCC
pigmented squamous cell carcinoma RPA
revised pattern analysis
RPE retinal pigmented epithelial
RR relative risk
SCARD skin cancer audit research
database SCC squamous cell carcinoma
UV ultraviolet

CHAPTER 2

Skin – the organ

Skin as an organ

Skin was the fi rst organ to evolve in multi cellular organisms and, weighing approxi mately 4kg over a surface area of 2m^2, it is the largest organ in the human body[1]. Because skin covers the external surface it is vulner able to injury from many sources, including incident radiation, and so unsurprisingly it is the most common site of malignancy. For the same reason those malignancies are more accessible to direct visual inspection, making the development of tools to assist such inspection highly relevant. Knowl edge of the microanatomy and physiology

Embryology of skin

After fertilisation of the ova by a spermato zoon, a single pluripotent cell,

the zygote, carries the genetic blueprint for a unique integrated individual which commences life as a developing embryo. This genetic material will launch a cascade of events where each stage in the sequence leads to subsequent ones throughout the development, growth, maturation, reproduction and decline of that individual, until terminated by death. The resulting progression will include the diff eren tiation of multiple cell types and their organi
sation into organs, including the fi rst organ to evolve in multicellular organisms, the skin[1].

Immune system

Development of the embryo includes the diff erentiation and integration of the compo nents of an immune system. Invertebrates develop an innate immune system which responds to an immune attack in a generic manner, but vertebrates also develop an adaptive immune system which allows them to tailor an immune response to specifi c antigens[2]. Both responses are employed in the vertebrate's response to tumours, including skin tumours. Sexual reproduction is relevant because it provides a virtually infi nite number of potential combinations of genetic material relevant to the innate and adaptive immune systems, for forces of natural selection to sort and select or reject. This gives the species the greatest chance of surviving in a hostile and changing environment.

of skin is fundamental to an understanding of dermatoscopic correlation in relation to pigmented, collagen and keratin structures, as well as with respect to vascular structures and patterns.

The signifi cance of certain patterns and clues vary according to anatomical site and this is particularly relevant on the head and neck, in the nail apparatus and on volar skin.

Finally, skin type as defi ned in the Fitzpat rick phototype classifi cation, infl uences both patterns of disease prevalence and the inter pretation of dermatoscopic clues.

Formation of the skin precursors: the ectoderm, neural crest and mesoderm

After fertilisation and formation of the zygote, the process of cell division forms a hollow ball or 'blastula' and then it undergoes 'gastrula tion' (***Figure 2.1***)[1]. A pouch forms at one end of the blastula and bulges into its centre so that a 3-layered structure or 'gastrula' is formed. The outer layer of cells is the ectoderm and the inner layer of cells formed by the pouch is the endoderm. The pouch will eventu ally form the gut, with the opening of the pouch, the blastopore, being its excretory orifice. The mesoderm will develop between the ectoderm and endoderm in the space labelled blastocoele in the image on the far right of ***Figure 2.1***.

During the fourth week of embryo devel opment, the single cell thick ectoderm and underlying mesoderm begin to proliferate and differentiate. The neural crest develops from the ectoderm as do specialised struc tures formed from skin elements, including sebaceous glands, sweat glands, apocrine glands, mammary glands, fingernails and toenails. The teeth and hair follicles formed from both the ectoderm and the mesoderm also begin to appear during this period.

Melanocytes

The neural crest develops from the ectoderm and melanocytes are derived from neural crest cells produced at the dorsal neural tube, from where they migrate to the basal layer of the epidermis to populate all parts of the skin[3]. Also, growing nerves projecting throughout the body as a stem/progenitor niche, contain Schwann

cell precursors, from which some skin melanocytes also originate[4,5].

The migration of melanocytes proceeds in a cephalad-to-caudal and axial-to-peripheral sequence. By week 8 melanocytes are present both in the dermis and in the basal layer of the epidermis, as well as in the hair bulbs, choroid, inner ear and pia arachnoid[6]. This melano cyte migration may lead to 'rests' of naevus precursor melanocytes within the dermis, explaining the appearance of congenital naevi later in life as well as possibly explaining the occurrence of primary dermal (nodular) melanomas. This distribution of melanocytes also accounts for melanocytosis and the risk of developing melanoma in the eye (e.g. choroid). It also explains melanoma developing in the leptomeninges that is seen in some patients with naevus of Ota, as well as the occur rence of neurocutaneous melanocytosis in patients with large and/or multiple congenital melanocytic naevi[6]. Dermal melanocytes first appear in the head and neck region, and they begin to produce pigment at a gestational age of approximately 10 weeks. However, by the time of birth, active dermal melanocytes have disappeared, with the exception of three anatomical sites – the head and neck, the dorsal aspects of the distal extremities, and the pre-sacral area. Of note, the three locations of persistent dermal melanocytes

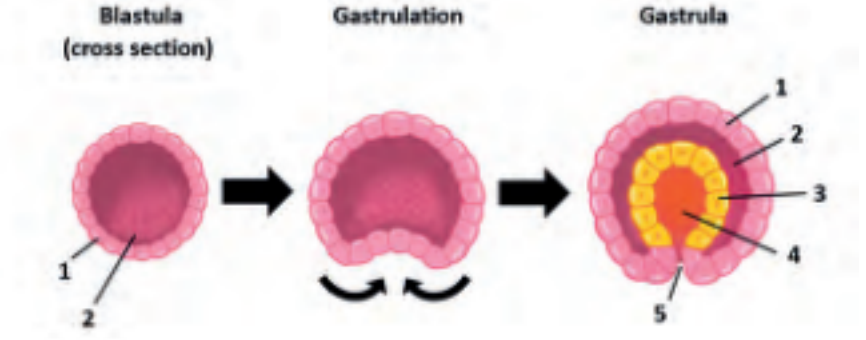

Figure 2.1: ***Early stages of embryo development. 1 – ectoderm; 2 – blastocoele; 3 – endoderm; 4 – archenteron; 5 – blastopore.***

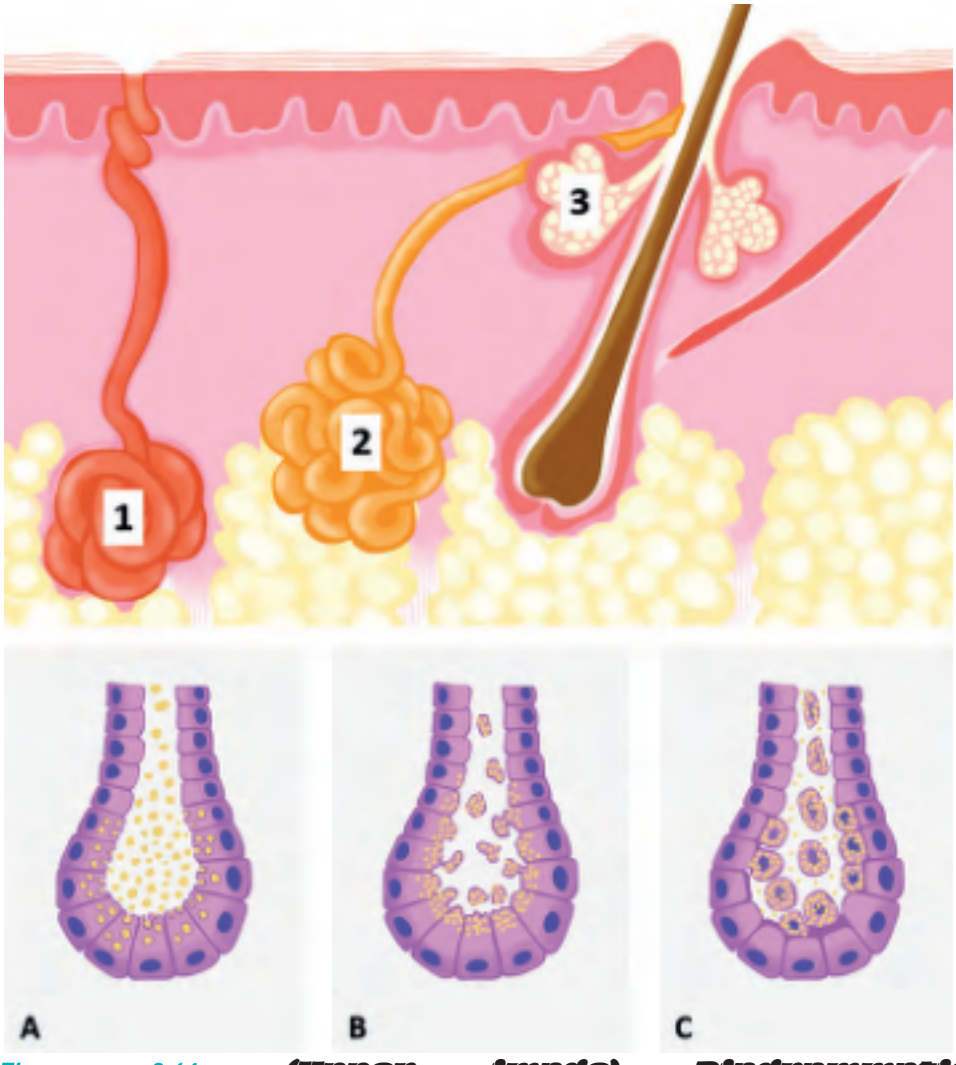

Figure 2.14: ***(Upper image) Diagrammatic representation of skin demonstrating eccrine (1), apocrine (2) and sebaceous gland (3). (Lower image) Schematic diagram of exocrine glands of the skin. (A) Cuboidal cells lining eccrine glands secrete sweat into the lumen (merocrine secretion), this reaches the skin surface via the eccrine duct. (B) Apocrine glands secrete by pinching off vesicles which are secreted into hair follicles close to the skin surface where they mix with sebaceous secretions. (C) Holocrine glands (e.g. sebaceous glands) secrete by discharging the entire cytoplasm of their cuboidal cells into the lumen of the gland. Lower panel adapted from*** Anatomy and Physiology Learning System ***4e by E. Applegate, 2010, with permission from Elsevier.***

2.3.7 The basement membrane

The basement membrane which separates the epidermis from the dermis is an important structure both for the anatomy of normal skin and as a potential barrier for malignant cells between the epidermis and the dermis where their metastatic potential can be facilitated by blood and lymphatic vessels[20].

Basal cells of the stratum basale are connected to each other and to the layer of cells above them by desmosomes (see

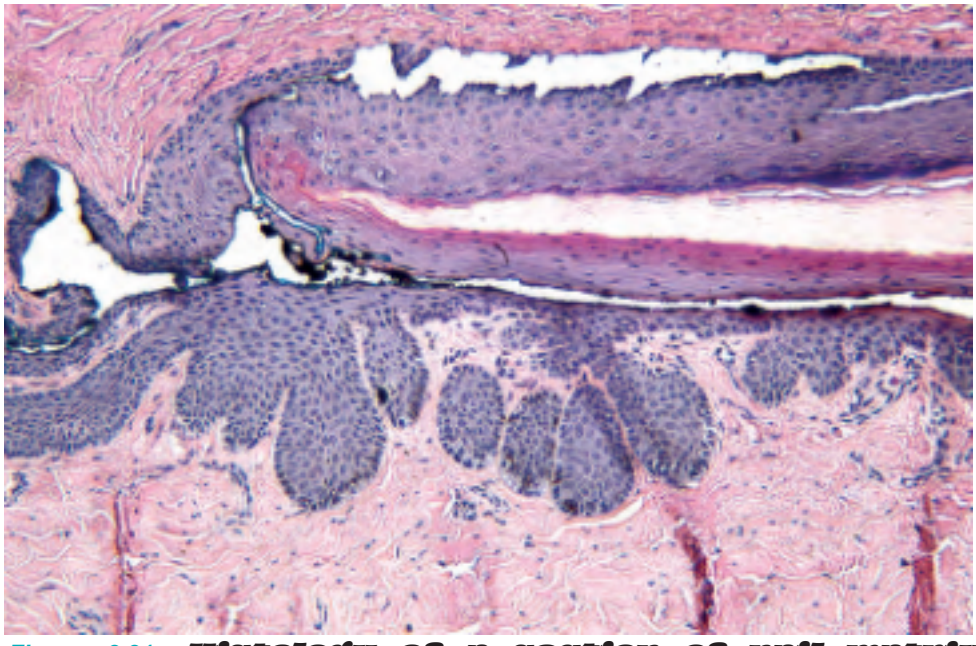

Figure 2.21: **Histology of a section of nail matrix showing the normal epidermal–dermal appearance with rete ridges. Note that the epidermis of the nail matrix wraps around the proximal extremity of the nail plate, being inverted above it. It is only the germinative matrix beneath the nail plate from which melanoma is expected to arise.**

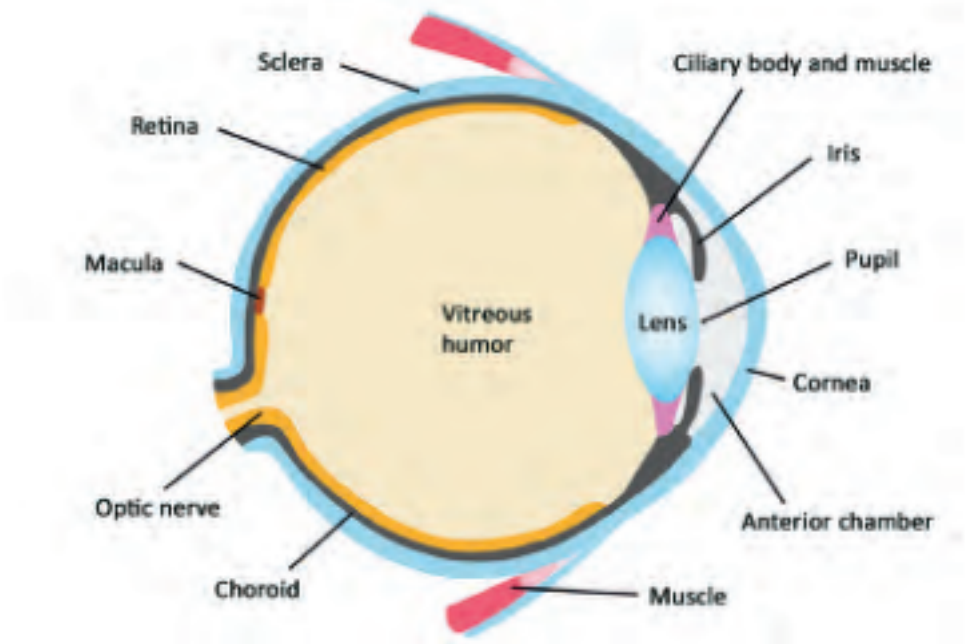

Figure 2.22: ***Diagrammatic cross-section of the eye: the uveal tract comprises the iris, ciliary body and choroid and is the vascular, pigmented middle layer of the three concentric layers that make up the eye.***

CHAPTER 3

Dermatopathology for dermatoscopists

The dermatoscope is a low powered micro scope which permits visualisation of the epidermis and dermis in the horizontal plane compared to the view in the vertical plane provided by a conventional microscope using vertically sectioned specimens. It is there fore not surprising that there are histological features which correlate with what is seen through the dermatoscope and an under standing of this correlation is critical both to the dermatoscopist and the dermatopathol ogist.

The dermatopathologist can only report based on the pathology slides presented by laboratory technicians; with standard processing, as little as 2% of the whole specimen is assessed[1]. As a result, structures seen by the dermatoscopist are not always displayed to the dermatopathologist, a situa tion which may result in an incorrect dermato pathological diagnosis being rendered. It is a responsibility of the dermatosco pist to convey relevant information to the dermatopathologist, documented in writing

and, ideally, by providing clinical and derma toscopic images. This enables the pathologist to know what to search for and provides the opportunity of requesting additional material ('levels') from the technician if the expected features are not discovered. The dermatos copist also has the opportunity to communi cate directly with the dermatopathologist if the report does not correlate with the derma toscopic fi ndings, causing the rendered diagnosis to be in doubt. The corollary is that it is also an advantage if the dermatopatholo gist has an in-depth knowledge of dermatos copy as it correlates with histology. This chapter will provide an account of the fundamentals of dermatopathology including:

- specimen processing
- the histology of normal skin
- dermatopathological terminology
- basic dermatopathology of melanoma, BCC, benign keratinocytic lesions and SCC, along with important dermatoscopic–histological correlations.

From the scalpel to the microscope

The processing of an excised specimen to produce microscope slides suitable for diagnostic assessment by a dermatopatholo gist is both elaborate and critical. Not only is correct processing important for an accurate outcome, but so is expert examination and interpretation of the fi ndings.

An example of typical specimen processing workfl ow is presented here.

3.1.1 Specimen processing workfl ow

1. **Integrity of specimen identifi cation.** Specimen mix-up can occur anywhere in the chain of specimen handling, starting with the operating room, and steps are necessary to avert that eventu ality[2]. Protocols should be set in place; one example is for the clinician to be confronted with the specimen label at the time of placing the specimen in the formalin container, in response to which he or she vocalises the name and body site written on that label for verification by both the patient and surgical support staff.
2. **Transport to the laboratory.** Following the procedure, the specimen jar is placed into a plastic bag along with the pathology request form, and a courier, employed by the pathology provider, picks this up along with any other pathology specimens. The courier ideally also checks that the specimen container is labelled with patient and body site details and that there is actually a specimen in the container. They then sign for the specimen in a book filled out in advance by practice staff. This effectively ensures a chain of possession which has now passed to the pathology provider.
3. **Specimen transferred to the labora tory.** The courier delivers the speci mens to the laboratory where the specimen containers are checked again for contents, labelling and correctly matching paperwork.
4. **Measuring, cutting up (specimen grossing) and inking.** A labelled plastic cassette is prepared for each specimen. The specimen is now ready to be removed from the formalin and this is done on a cutting-up table on which the respective labelled plastic cassette has been placed ready to receive the cut-up tissue (***Figure 3.1***). It is important that no material

remains on this surface from previous specimens.

The specimen, having been removed from the formalin, is measured, as is any visible lesion, and the dimensions are recorded. The location of any orientating suture or other marker is also noted and recorded. The specimen then has ink

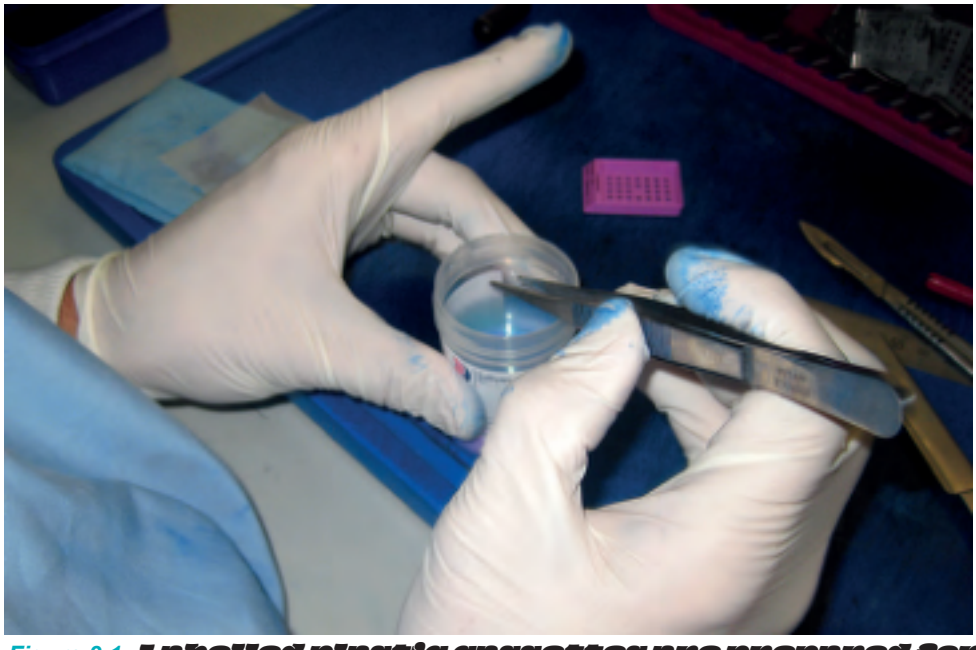

Figure 3.1: **Labelled plastic cassettes are prepared for each specimen jar. The specimen is removed from the jar on a bench on which sits its unique plastic cassette.**

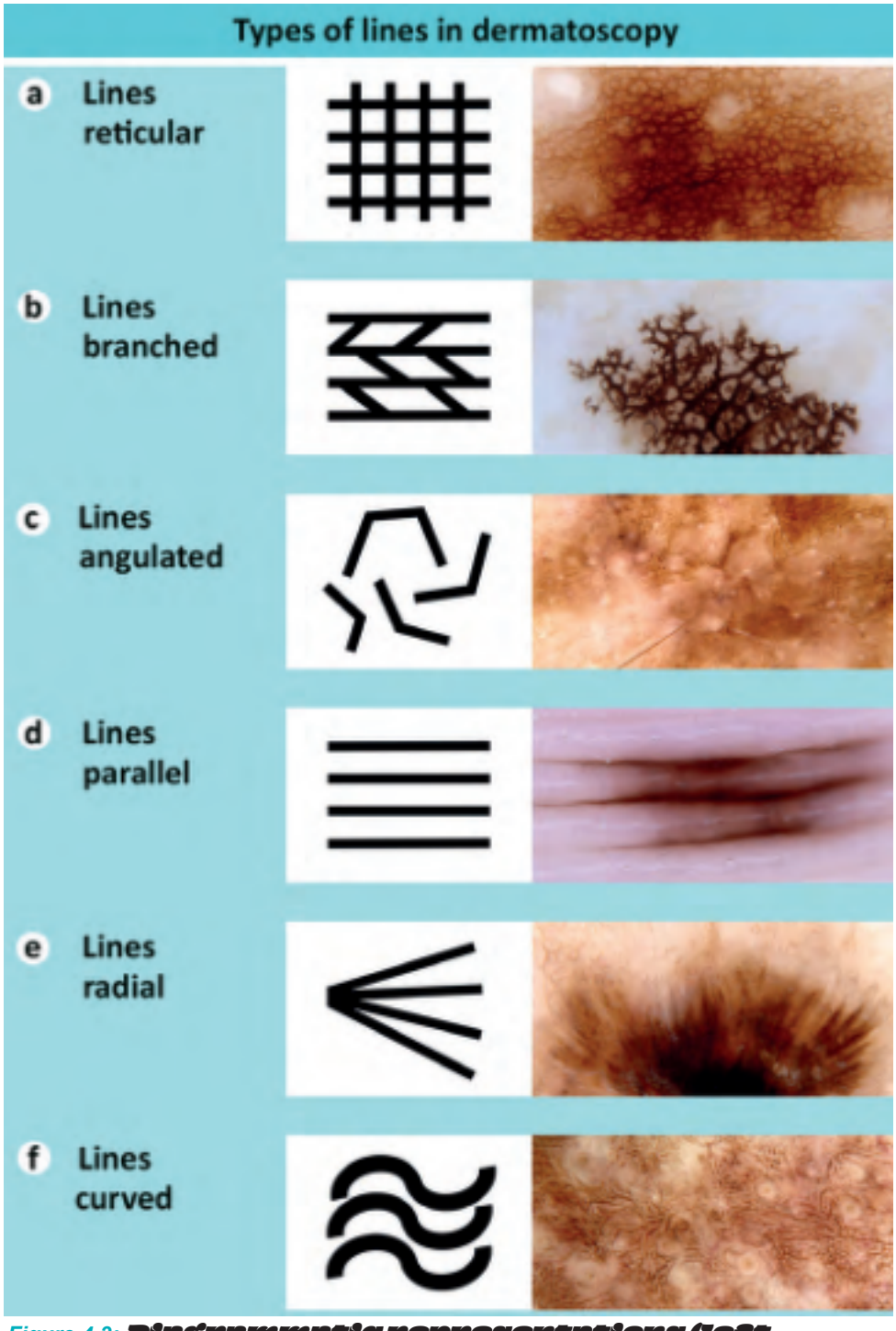

Figure 4.3: ***Diagrammatic representations (left column) and representative images (right column) of the various dermatoscopic lines as defined in revised pattern analysis.***

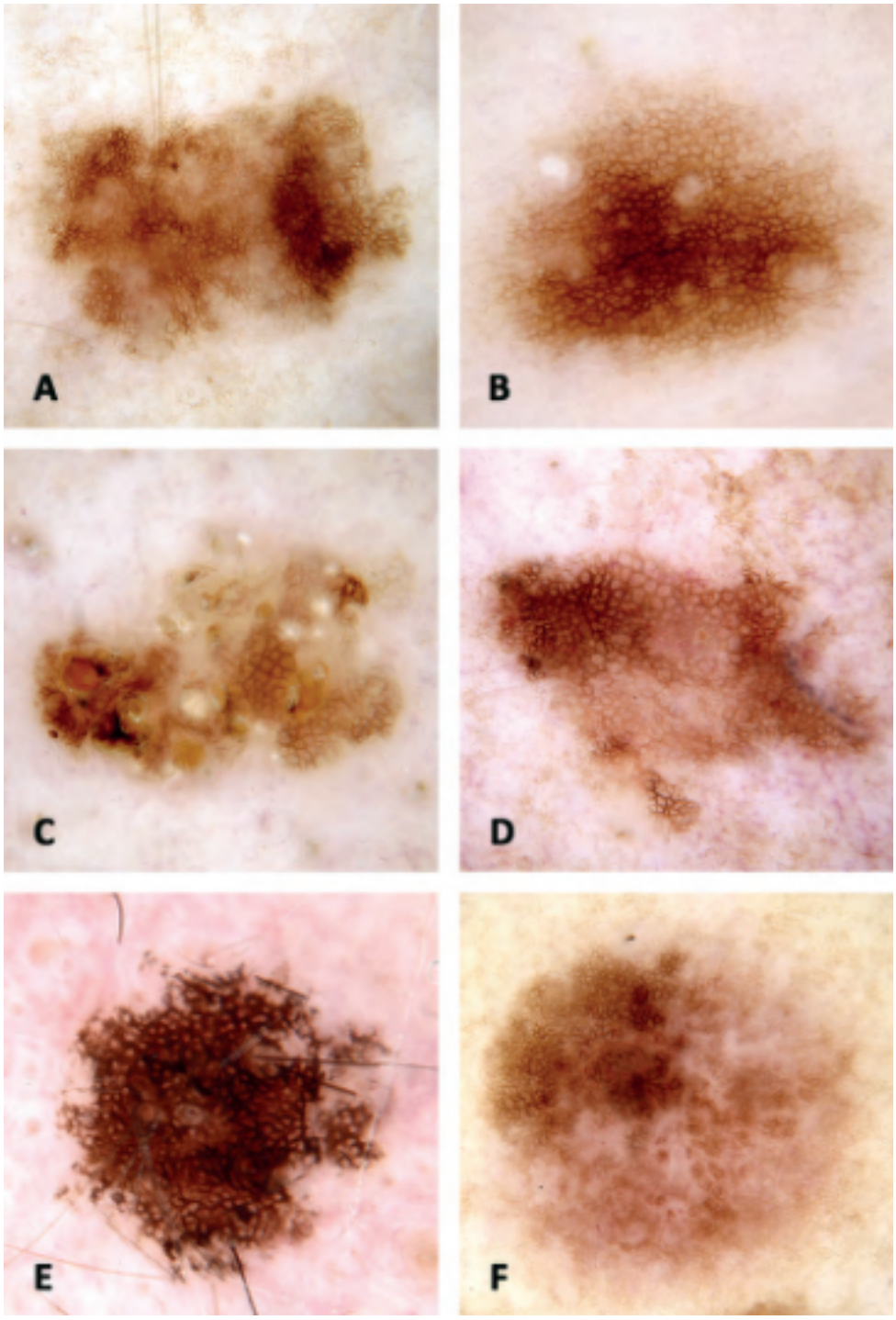

Figure 4.4: ***Six lesions each exhibiting a pattern of reticular lines: (A) melanoma*** in situ***; (B) naevus; (C) seborrhoeic keratosis; (D) solar lentigo; (E) ink spot lentigo; (F) dermatofibroma.***

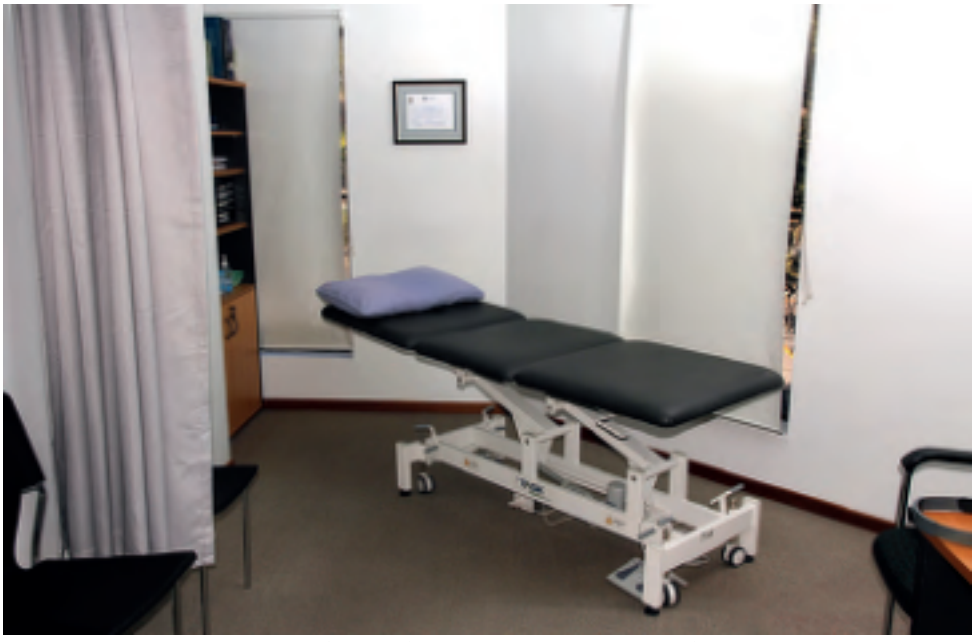

Figure 5.5: **The examination room contains an adjustable couch, set out from the wall, and which is brightly illuminated with fluorescent lights.**

Figure 5.6: **Tools of trade for the clinician include a dermatoscope (A) with both polarised and non-polarised options, as well as an LED torch (B) and varieties of immersion fluid to facilitate fluid-immersion contact dermatoscopy (C).**

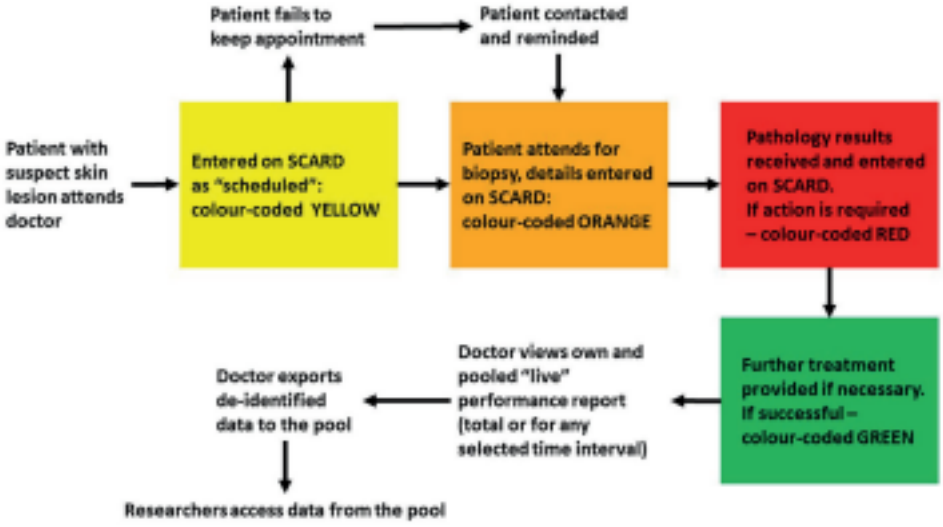

Figure 5.26: ***Flowchart demonstrating lesion tracking for the purpose of ensuring patient safety on the SCARD system.***

awaiting histology, red when requiring action and green when completed, thus facilitating tracking for satisfactory completion of treat

trained before dermatoscopy had been studied and validated, may still regard it as

ment (***Figure 5.26***). To fi nd out more about SCARD, including how to register, go to https://scard.co.

The lives of lesions

Being a relatively new science, dermatoscopy has only become accessible to clinicians in the last 30 years. It is not surprising that dermatologists and primary care doctors,

an optional tool which at best can confi rm a clinical impression or diagnosis. The idea that dermatoscopy can be used to diagnose lesions which are not clinically suspicious at all is a novel concept to many, and that belief can be reinforced by experience, due to the

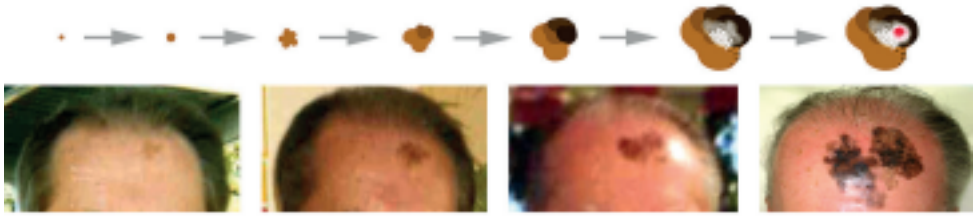

Figure 5.27: ***(Upper panel) The melanoma timeline: diagrammatic representation of the development of a melanoma from the juvenile stage, when it can only be detected by monitored change, to the childhood stage which can be diagnosed by dermatoscopy, to the mature stage of its life when it can be recognised clinically. (Lower panel) This large invasive melanoma (image far right), represents a lesion on the far right of the melanoma timeline, which can be diagnosed***

clinically, without dermatoscopy. By examining earlier opportunistic photographs it is possible to verify that this lesion has steadily grown and matured over at least 16 years, comparable to an infant growing and maturing into an adult. Lower images courtesy of Dr Ian McColl.

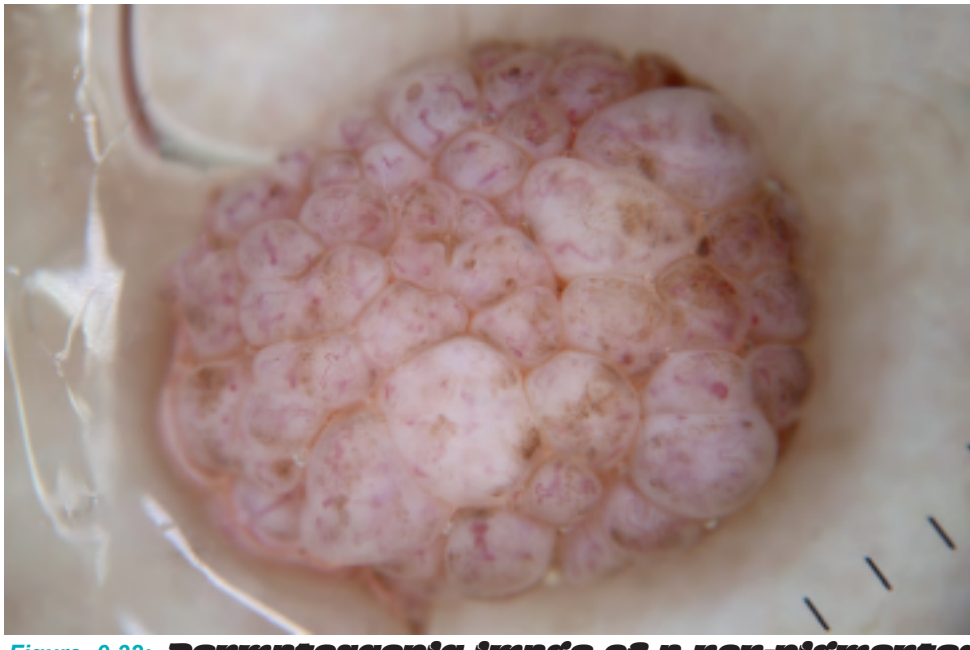

Figure 9.32: Dermatoscopic image of a non-pigmented dermal (congenital) naevus with a centred vessel pattern, vessels of varying types being centred in skin-coloured clods. The histological correlate of this pattern is papillomatosis.

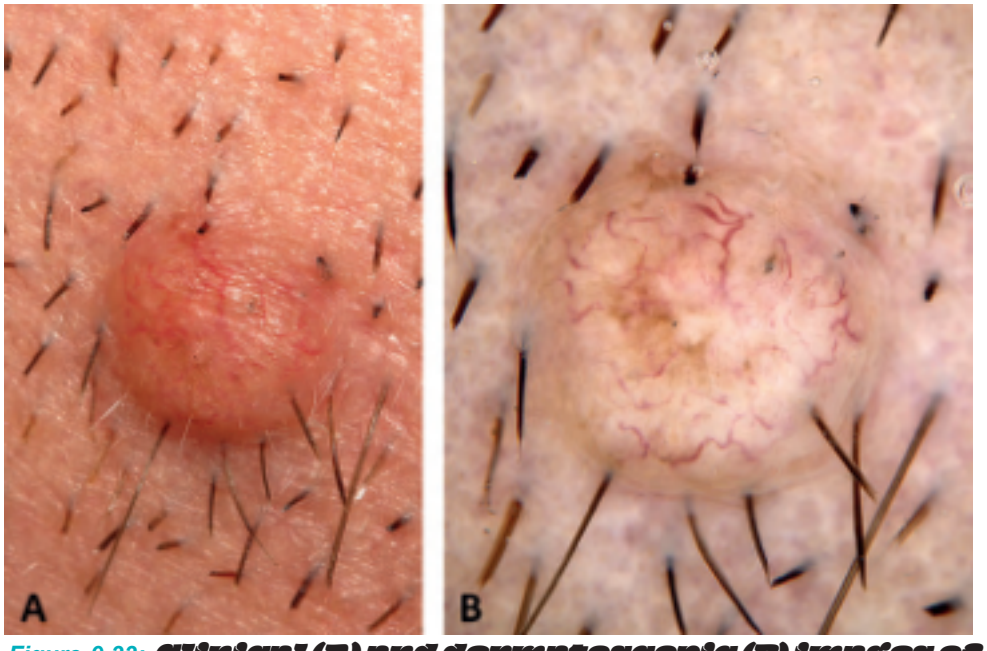

Figure 9.33: **Clinical (A) and dermatoscopic (B) images of a dermal naevus on the face (Miescher naevus). The lesion is only focally pigmented, and the 'curved' vessel pattern is, strictly speaking, serpentine, which is a common morphology for such naevi.**

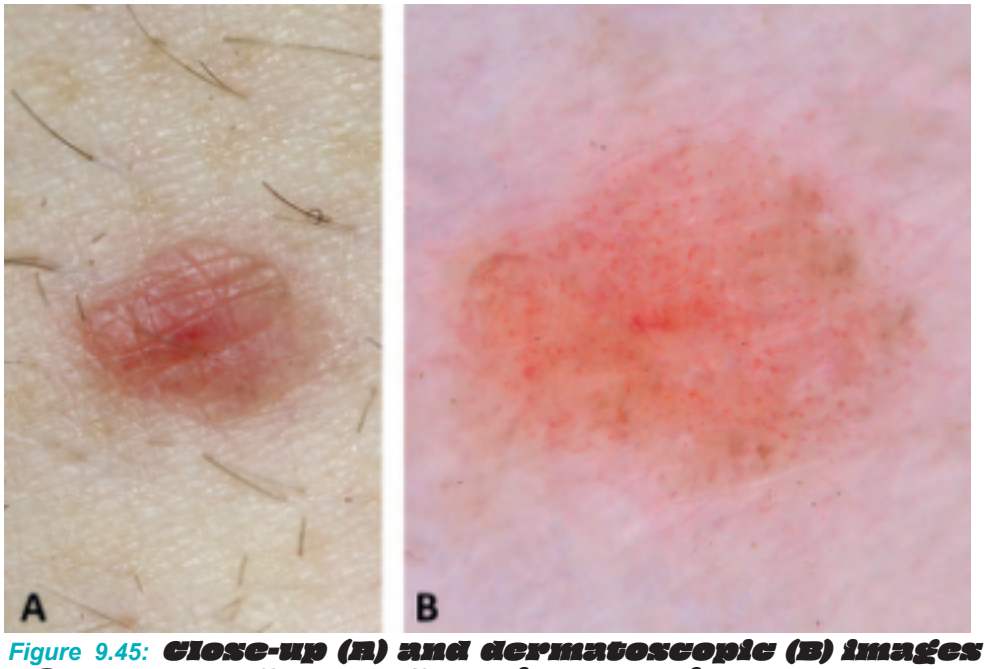

Figure 9.45: **Close-up (A) and dermatoscopic (B) images of a hypomelanotic Spitz naevus.**

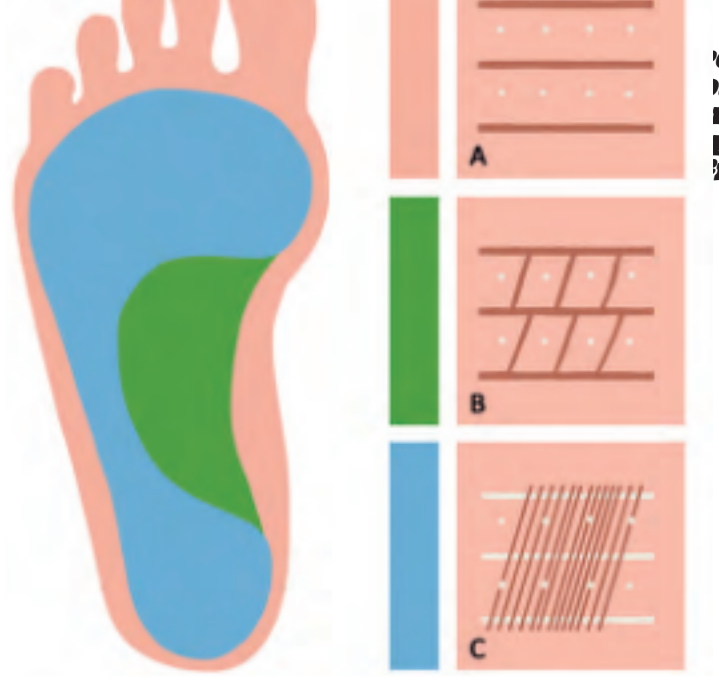

Figure 9.46: **Graphic representation of various benign pigmented patterns encountered on volar skin with a colour-coded representation of the plantar foot showing the expected distribution of each pattern: (A) parallel furrow, (B) crossing (also known as lattice), (C) fine crossing (also known as fibrillar). Adapted from** J Am Acad Dermatol, **2009;53:2301 and** Atlas of Dermoscopy, **2nd Edition, edited by Marghoob, Malvehy and Braun, 2012, Informa.**