ATLAS OF Fetal and Neonatal Brain MR Imaging

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It became obvious in the late 1990s that magnetic resonance (MR) imaging of the fetal central nervous system was going to be more than an intellectual curiosity wrapped around a technical challenge. There was (and remains in some circles) some resistance to accept that there is any need for supplementing ultrasonography with fetal MR in cases of suspected developmental brain abnormalities. Many recent studies have shown value of in utero MR of the fetus and there is also gathering interest in postmortem MR of the fetus as an adjunct or replacement to autopsy. The problem was how to start. Few radiologists have experience of the normal MR appearances of the brain at 20 to 40 weeks gestational age. Those who do have the experience have usually gained it from imaging premature babies in whom the predominant pathologies are the complications of prematurity, not malformations. It has taken us a long time to build up a base of normal fetal brain examinations; therefore our appreciation of age-related normality was slow to form. We hope, therefore, that this atlas will help others in this complex area of image interpretation. We must accept that fetal MR (particularly in utero MR) is still in its early stages of development. It is likely that in a few years I will look back in horror at the quality of the images that we were expected to interpret, very much like modern fetomaternal experts reviewing early obstetric ultrasonography. But you have to start somewhere.

When I was struggling to come to terms with mid-t trimester brain anatomy I was fortunate to be directed to the pathology atlas of Alison Fess-Higgins and Jeanne-Claudie Larroche. The book was out of print and proved difficult to find but once it was located it was invaluable. It occurred to me first of all that the book should be reprinted, but then considered an updated work including MR. I managed to contact Professor Larroche and was very pleased when she agreed to co-author this updated work with the Sheffield group. It has been a great privilege to work with her.

On a personal level, I have to mention my wife Jane, who is my inspiration, and on occasion, my refuge. Professionally, I would like to acknowledge a number of people who have influenced me over the years. Some have shaped my thinking by reading their papers, hearing them lecture, and subsequently coming to think of them as colleagues and I would include Jim Barkovich, Tom Naidich, Susan Blaser, and Erin Simon in that group. More fundamentally, however, I need to acknowledge the great burden of gratitude I owe to two people who shaped my career at different stages. First, Professor Ian Isherwood, Professor of Radiology at the University of Manchester, who persuaded me to become a neuroradiologist sometime in 1987, having known very little about the speciality previously. And then there was the late Derek Harwood-Nash! It was during my period at the Hospital for Sick Children, Toronto, as the Neuroradiology scholar in 1994-95 that Derek convinced me that pediatric neuroradiology was the only game in town, a decision I have not regretted since!

Paul D. Griffiths

When people listen to you don’t you know it means a lot? ’Cause you’ve got to work so hard for everything you’ve got Can’t rest on your laurels now not when you’ve got none You’ll find yourself in a gutter right back where you came from.

Novelty (I. Curtis)
INTRODUCTION

The development of the brain is an exceptionally complicated process, which makes interpretation of radiologic images of the fetal brain challenging. Imaging of the immature brain has become important in recent years for several reasons, with a corresponding increased requirement for clinicians with experience in fetal and neonatal brain imaging. One reason for this need is the desire to detect abnormalities of the brain during the second trimester of pregnancy in order to provide the best-quality information to parents about the likely clinical sequelae of the anomaly. Second is the need to investigate the increasing number of neonates surviving premature delivery who are at high risk for intracranial complications, both hemorrhagic and hypoxic/ischemic. The need for imaging and the manner in which it is delivered has influenced the techniques used. One of the overriding requirements is to not expose the fetus or child to ionizing radiation or at least to keep the exposure to the barest minimum because the potential risks are high in this population. A screening program of second-trimester fetuses cannot be built around an X-ray–based technique such as X-ray computed tomography (CT), hence the rapid rise and refinement of antenatal ultrasonography over the last few decades. It is also desirable to limit the amount of X-rays to which newborn babies are exposed, and ultrasonography has an important role here as well, although other factors are at play. Some ultrasound machines are relatively inexpensive and are portable, making them ideal for use in neonatal intensive care units given the risk management issues associated with moving a child from the neonatal intensive care unit to the radiology department.

Recent studies have shown the limitations of ultrasound for assessment of the fetal and neonatal brain that make the diagnosis of some types of pathology difficult or impossible. For example, the early stages of neonatal hypoxic/ischemic brain injury are difficult to show with transfontanelle ultrasonography; they are shown much better by X-ray CT or magnetic resonance (MR) imaging, particularly using diffusion-weighted imaging. It is becoming increasingly apparent that in utero detection of some developmental brain abnormalities is difficult with ultrasound; agenesis of the corpus callosum is a leading example. These factors have led many groups to explore alternative methods of fetal and neonatal neuroimaging, most of which involve MR imaging. Another use for MR imaging of the immature brain that has been explored by a small number of groups, including our own, is postmortem MR imaging as either an adjunct or an alternative to autopsy. The drive for this in the United Kingdom is the reduction in uptake of fetal/neonatal autopsy by parents concerned about the well-publicized retention of tissues and organs without consent at some British hospitals. It is possible to gain valuable information about brain abnormalities in the post 16-week fetus using postmortem MR imaging and to inform parents about the risk to future pregnancies based on the anatomic definition of the malformation.

The requirements for MR imaging of the brain in these three situations (in utero, postmortem, and postnatal) are fundamentally different, but all have been made possible by significant technologic advances in the field. They are also linked by another factor, namely, problems in interpretation for the reporter. A clinician who reports imaging studies from any specialty has two basic tenets for his/her work: knowledge of normality and knowledge of pathology. The purpose of this book is to assist clinical personnel involved in providing an imaging service to learn and understand normal MR appearances of the brain from the second half of pregnancy to 18 months postnatally.

The histologic basis of this book is the Development of the Human Foetal Brain: An Anatomical Atlas by Feess-Higgins and Larroche, which was published in the 1980s but has been out of print for some time. It has been a great privilege for us to work with Professor Larroche on this project. We have used a large number of the line diagrams and histologic photographs from the original INSERM publication in the production of this atlas. The text of the original publication was in French and in English. The annotation of the line diagrams was in Latin, as was the classic approach. We have decided to use a more anglicized approach to the
anatomic descriptions, more often than not using the nomenclature provided by Carpenter's Core Text of Neuroanatomy.²

One of the primary goals of this atlas is to assist doctors who report brain imaging in interpreting in utero MR (iuMR) examinations, a procedure that is gaining in popularity as many centers begin to offer a fetal MR service. MR imaging of the fetus is not recommended before 19 weeks' gestational age (calculated from last menstrual period, as are all of the dates in this book); therefore we start our imaging at 19 to 20 weeks' gestational age. From that maturity to 37 weeks, we present iuMR and postmortem MR (pmMR) images to match the histologic sections and line diagrams as closely as possible. This atlas is illustrated with T2-weighted MR imaging only in fetuses for reasons that are outlined later in this book. Unlike the original Larroche atlas, we continue into the postnatal period, showing both T1- and T2-weighted images of normal infants up to 18 months.

**OVERALL LAYOUT OF THE ATLAS**

As explained previously, the core of this atlas is the histologic sections and line diagrams published by Professor Larroche more than 20 years ago. The first section of this atlas merely reproduces the images of surface views of the fetal brain, but we use only the gestational ages shown in cross-sectional detail in Section 2. We do not show fetuses ranging from 10 to 18 weeks' gestational age that were included in the original atlas because we do not perform iuMR imaging at those early ages. The images of the surface anatomy of the brains are included to highlight the huge changes occurring in the late second- and third-trimester brain, particularly with respect to sulcation of the cerebral hemispheres. We go into some detail about the timing of the appearance of the major sulci at the start of Section 1 and give an overview about the appearance of sulci in the "mature" brain.

Section 2 shows images from six sequential gestational age periods ranging from 19 to 37 weeks and shows pmMR and iuMR images matched as closely as possible to the tissue sections and line diagrams of the original atlas. One of the most important features of fetal brains during that period is the complicated appearance of transient structures within the developing cerebral wall. We provide a simplified overview of those structures with the aim of assisting interpretation of fetal MR images.

Section 3 shows images of the brain from infants after birth for whom iuMR imaging is not a consideration. Six ages (ranges) are illustrated: 0 to 1 month, 3 to 4 months, 6 months, 9 months, 12 months, and 18 months. For all of the cases we provide the appropriate line diagram of anatomic features from the 40-week fetus of the Larroche atlas. The primary purpose of doing so is to remind the reader of the importance not only of knowing the gross anatomy of the brain but of becoming familiar with the normal patterns of myelination.

**DESCRIPTIONS OF THE TECHNIQUES USED**

We use four different methods to show the neuroanatomy of the fetus and infant in this atlas: postmortem tissue sections, pmMR, iuMR, and postnatal MR imaging of live children. The techniques used for each of the methods are described here.

**Postmortem Fetal Tissue Sections**

Brains that appeared normal were chosen for the study. Cases were excluded if the pregnancy was complicated by maternal diabetes, toxemia, intrauterine growth restriction, viral or parasitic fetal infection, materno-fetal bacterial infection, or blood group incompatibility. Brains with malformations were excluded, as were cases with large hemorrhages that altered the appearance of the brain. Most of the cases were infants who were stillborn or who survived for only a few hours or days. Exceptionally, survival for 10 days and 2 weeks has been accepted and the corrected age calculated (gestational age plus survival time). The brains were weighed in the fresh state, but because fetal brain tissue is extremely fragile the brains were fixed in formalin before being measured and photographed. After dehydration the brains were embedded whole in celloidin and cut in serial sections at 30 μm. (Techniques for obtaining postmortem fetal tissue sections are modified from Feess-Higgins and Larroche.)³

The histologic stains used were hematoxylin-eosin, cresyl violet, and the myelin stains Loyez and Luxol fast blue.

**Postmortem MR Imaging of the Fetus**

The rationale behind our program of pmMR imaging of the fetal central nervous system was to explore the possibility of using imaging as either an adjunct or an alternative to autopsy. The interested reader is directed to some of our earlier publications.³⁻⁵ The majority of our cases resulted from either therapeutic abortions for known central nervous system abnormalities shown on antenatal sonography or from spontaneous abortions. All of the cases in this book were referred to the pediatric pathology department at Sheffield Children's Hospital, which is a regional referral center for fetal and pediatric autopsies. The parents were asked to consent to MR imaging as well as the formal autopsy. All of the pmMR cases shown in this atlas had no abnormality of any description shown on autopsy, pmMR imaging, or any chromosomal/genetic tests performed subsequently.

MR imaging is exquisitely sensitive to patient movement, which usually imposes limits on image acquisition time. This is not an issue when imaging postmortem, and long acquisitions with improved signal-to-noise ratios can be obtained. We took full advantage of this in our earlier cases, routinely acquiring four excitations for each imaging data set. That acquisition required more than 12 minutes for each T2-weighted sequence at 1.5 T, but we subsequently dropped to two excitations at 6 minutes with little noticeable reduction in image quality.