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Paediatric pathology: a work in progress

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What is in fact the importance of Paediatric Pathology in developing countries? Why are there so few dedicated paediatric pathologists? The answers to these questions are not straightforward as there are probably many different reasons. What is perfectly understandable is the need for Paediatric Pathology to be practiced as a specialty and this can be demonstrated by some figures provided by the Instituto Brasileiro de Geografia e Estatística (IBGE).¹

Brazil has seen a dramatic change in demographics and vital statistics in recent decades and especially in the past 14 years, according to IBGE data. Population increased by 12.3% from 2000 to 2014 and general mortality decreased 9.15% in the same period. However, infant mortality rate per 1,000 live births plummeted 51.6% in the same period. The fall in infant mortality was far greater than the general mortality, reflecting socio-economic trends rather than medical intervention. Birth rate also dropped dramatically in the same period, from 20.9 per 1,000 people in the year 2000 to 14.5 per 1,000 in 2014, a decrease of 30.6%. Of course, this is coupled with fecundity rate, which presented a 27.2% fall in the same period. As a direct result of all these changes, population distribution according to age groups demonstrate the decrease in the number of children 0-14 years with a consequent increase in people aged 15-64 and 65 and above.¹

With a striking decrease in infant mortality it is reasonable to think that this would negatively affect paediatric pathology, but it is not that simple. The change in birth and fecundity rates indicate that the importance of any pregnancy is in fact greater, because

it reflects better pregnancy planning. Childbearing age is changing towards older women, who tend to be better educated, dedicating more time for their professional career and imposing more challenges to the health system. This trend has been seen in developed countries in past decades and there is no reason it will be different in developing nations. In this setting, the loss of a fetus or baby is more likely to make parents willing to know what happened and therefore the demand for high quality investigation is necessary. As a sub-specialty, with its own body of knowledge and techniques, Paediatric Pathology would be ever more in demand.

Paediatric Pathology involves a vast and complex developmental period ranging from embryos to teenagers, encompassing not only autopsy but paediatric surgical pathology and the special pathology of the placenta. In the UK, Paediatric Pathology is subdivided into Perinatal Pathology, dealing with post-mortem examinations and placenta pathology, and Paediatric Histopathology, dealing with surgical pathology. Some professionals can do both activities, usually in dedicated Children's Hospitals, but others will do one or another. In Brazil there is no clear definition of the role of paediatric pathology. Most of the time, the occasional full time paediatric pathologist works in an academic institution rather than in a general hospital. The general histopathologist, especially those in private practice, however, may deal with placentas and products of conception rather than a proper autopsy. In any situation, the examination of a fetus without a placenta is usually pointless, since

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the cause of fetal demise or miscarriage may lie in the placenta in many cases. It is the latter that should always be examined by a trained pathologist to find or rule out abnormalities. But what is the kind of training most general pathologists have in terms of placenta examination?

Except for the obvious implications of acute chorioamnionitis and infectious villitis, some relevant lesions will rarely be adequately evaluated by a general pathologist. These are usually those that may recur in subsequent pregnancies, such as the so called chronic villitis of unknown aetiology (VUE), placental floor infarction/massive perivillous fibrin deposition, fetal thrombotic vasculopathy (FTV), extensive subchorionic thrombosis (Breu's mole) and Chronic Histiocytic Intervillositis. Another common problem is the apparently macro and microscopically normal looking placenta in a case of fetal demise, especially perinatal, due to its small size compared with that of the fetus. The placental disc weight without the membranes and umbilical cord must be compared with appropriate tables and so should be the fetoplacental weight ratio. When the fetus is large, the relative weight of the placenta to the fetus may be small, indicating that any lesion that decreases the availability of areas for fetomaternal transfer, such as placental infarct or fetal thrombotic vasculopathy, can tip the delicate balance and induce intrauterine hypoxia which can eventually lead to fetal demise. This is only a small sample of the need for adequate training in paediatric and placenta pathology seen in daily practice. There are excellent textbooks that bring up to date relevant information in placenta pathology which are really helpful for both paediatric and general pathologists, with special emphasis to Kraus et al.²

The post-mortem examination in the paediatric setting involves mostly fetuses, with about 10% being 15 weeks gestation or lower in my Institution, and perinatal cases. Infant autopsies are usually coronial (for the investigation of the cause of death, basically), or forensic, and most cases are either Sudden Unexpected Death in Infancy (SUDI)/Sudden Infant Death Syndrome (SIDS) or non-accidental deaths. Childhood and teenager death is usually investigated by forensic pathologists as they are usually non natural. A recent textbook on Paediatric Autopsy may be a useful tool for both the general and paediatric pathologist.³

No matter how small a fetus is, if it is the product of a planned and wanted pregnancy, parents are usually eager to know what went wrong; therefore obtaining consent for a full post-mortem is less difficult than for adult patients. Our duty as pathologists is to provide meaningful information for the affected families and health system and this can only be achieved by a proper investigation. Fetal and perinatal autopsy require a different approach compared to adult ones since it is necessary to evaluate the developmental state of tissues and organs and the need to appropriately look for and record negative findings. Ratios between organ weights are particularly relevant, such as brain/liver and brain/thymus weight ratios for the identification of intrauterine growth restriction, lung/body weight ratio, for the evaluation of lung hypoplasia and fetoplacental weight ratio, to identify the adequacy of placental ability to support fetal life and development. In case of congenital anomalies, the correct identification of malformations is fundamental for reproductive counselling, which is the ultimate goal and disclosing minor congenital anomalies, the ones that may not have a physiological or surgical implication, may be difficult for non trained pathologists. These features are important for the correct diagnosis and determination of the recurrence risk. The obvious multiple malformation associated with the common trisomies 13, 18, 21 and monosomy X, neural tube defects, congenital heart defect and kidney agenesis seen in a third trimester fetus is more a medical catastrophe due to the failure of early diagnosis and adequate management rather than a challenge for the pathologist performing the autopsy. The need for a specialist paediatric pathologist can be illustrated by the unexpected intrauterine demise of a second or third trimester normally formed fetus. Was death the result of a fetal, placental or maternal cause? Unless a thorough investigation of the fetus and placenta is performed, preferentially supported by genetic, metabolic, microbiological and virological investigation, the answer may not be found. Group B *Streptococcus*, for example, can induce such a rapid and catastrophic sepsis that there is no time to properly mount an inflammatory response in the placenta or the fetus. Without microbiological cultures this may never be disclosed and the possible cause of death may be wrongfully assigned to other causes.

Demands of the society are more powerful than regulations, and it will become very clear in the coming years that this pressure will be felt by the health sector in terms of providing better diagnosis in cases of infant or fetal death. The bereaved families need appropriate answers to move forward and closure is not achieved without them. We must also be prepared for the inevitable call of the society that will surely demand adequate response from us and this will happen sooner or later. Insurance companies are expected to play an important role since the inability to provide high quality reports will negatively impact in claims by the families and will put more pressure on the doctors involved in those cases. Was the case appropriately diagnosed? Was there a timely intervention? Are the professionals sufficiently trained to perform their activities? The burden of a dead fetus or baby lies in the souls of the bereaved families, but the legal costs will be felt by the professionals involved and this will in the end reflect in more cases being sent for post-mortem or placenta examination. In the end, it is the society that determines what the professionals should do, not them.

As a final remark, I recollect something that happened a long time ago. A resident was about to start a post-mortem examination on a severely

macerated fetus on a Monday morning. He looked at the small body and asked: *"What can we find in such a small and macerated fetus?"* I could have said many things, but at that moment I replied: *"Look, people find a mineralised fragment of the middle phalanx of an animal that died millions of years ago and are able to say what animal it was, how big it was and even what it used to feed on. You have the whole body in front of you and it is not possible we cannot find what happened to this fetus!"* We both laughed, but days later. At that moment we were deeply involved in the case, looking for clues to why that baby died.

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