VIRUS DISEASES IN OBSTETRICS

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In the beginning, when life started, mitosis was presumably the method of propagation. With the movement from unicellular to multicellular structures came the development of sex. A new variation of cell division — meiosis — became necessary so that one cell of each sex could unite, becoming a single cell which in turn would split and multiply by mitotic fission in order to become a multicellular recognizable entity. With the passage of aeons came gradual and, possibly, sporadic or explosive development with tremendous cellular technical improvement and specialization. The more intricate the system the greater is the care and attention demanded by all its manifold components. In the highest species the new living being, after conception, requires nurturing within its mother. A neatly planned structure which allows filtration of gases and articles of nutrition from host to parasite and products of excretion from foetus to mother, in addition to secreting substances which ensure the safekeeping of the developing ovum within the womb, is the link between the two. The placenta also acts as a barrier, preventing noxious substances from entering the foetus from the maternal side.

Certain small molecules, however, be they chemical or 'living', cross this placental barrier with great ease. For example, coumarin administered to the mother may produce foetal intracranial haemorrhage, whereas heparin (of large molecular size) apparently does not get through to the foetus.[19,47] Innumerable other drugs, when administered maternally, have deleterious effects on the foetus (e.g.

thalidomide,[25,26,43] thiouracil,[23] etc.). 'Living' or actively multiplying structures may also cross the placenta. Thus a few infants delivered of mothers with malignant disease may be born with manifestations of the disease.[4]

It must ever be borne in mind that materno-foetal circulatory communications often exist; foetal blood may be found in the maternal bloodstream and *vice versa*.[6,14]

Certain viruses find the placenta no barrier at all. They manifest their well-tabulated clinical and pathological findings in the foetus, e.g. vaccinia[36] and poliomyelitis.[50] Were they only to cross from mother to foetus and transmit their disease to the foetus, the problem would possibly not be so great. What, however, has become a major stumbling block in obstetrics, as is evidenced by innumerable papers and annotations in leading journals[7,8,28-32] and a Ministry of Health Report[35] is that certain viruses — rubella foremost among them — when attacking the embryo at its most formative stages before the 12th to 14th week of intra-uterine existence may:

(*a*) kill it, resulting in abortion,

(*b*) maim it, causing a host of congenital abnormalities resulting in intra-uterine death during the latter weeks of pregnancy,

(*c*) not maim it sufficiently to cause death, but leave the infant with various degrees of deafness, blindness, congenital cardiac lesions, mental deficiency, anencephaly, microcephaly, and so forth, or

(*d*) not affect the infant at all.

Tondury,[44] doing routine dissections of foetuses obtained from mothers who had suffered from rubella, found necrotic areas in the cardiac muscle. Necrotic foci of disengaged cardiac muscle were found obstructing arteries at a distance. He also found that maternal poliomyelitis caused serious injuries to the foetal brain and spinal cord. In a more major work this author[20] demonstrated that, no matter which virus was involved, the lesions were the same. He received specimens from many clinics in Europe and found that all the foetuses appeared normal on macroscopic examination. Serial sections of foetuses of 49 mothers with rubella, 2 with mumps, 6 with influenza, 4 with infective hepatitis and 11 with poliomyelitis demonstrated microscopic abnormalities in the heart, optic lens, inner ear, skeletal muscle and brain in 75% of cases. 'The infection begins by attacking the endothelium of the foetal blood vessels in the chorionic villi. The shed endothelium is carried as emboli of infective cells into the foetal circulation where they cause fresh infection and disturb the development of the organs affected.' Dr. Golda Selzer[41] will soon be reporting a case in which the rubella virus was found not only in the decidua but also in the foetus. As far as I am aware, it will be the first time this finding has been recorded. It has supplied the knowledge that was lacking when Warkany[47] stated that the virus has never been observed in action.

Experimental work corroborates these findings. According to Rhodes,[38] pregnant animals, when given virus infections, usually abort. Several viruses, when injected into 48-hour chick embryos, produce malformations ranging from microcephaly to microplasia of the lens. Hog cholera, given to sows, produces foetal deformities of the nose, leg, kidney, testis and gallbladder. Blue tongue virus of sheep is responsible for hypoplasia of the offspring's brain.

That the foetus may therefore be severely affected and afflicted when the mother contracts a viral infection during the early weeks of gestation is an established fact. This finding has had an impact not only on medical thought but also upon all mankind. The initial observation, for which Gregg[18] deserves the highest praise, together with other work done in relation to non-hereditary causes of foetal abnormalities, has done much towards lightening the psychological burden of parents, since they can now be assured that non-genetic causes of abnormal babies are non-repetitive.

Problems facing the Clinician

The problems facing the clinician are mainly twofold: The first is rare. It was seen in the City of Cape Town in 1955 when an outbreak of smallpox was feared. Practically the whole population was vaccinated. Doctors and pregnant women repeatedly questioned the wisdom of vaccination during pregnancy. Immunization against the disease was deemed imperative. Pregnant patients who were vaccinated and attended the University of Cape Town teaching hospitals were studied, and the findings were reported by Abramowitz.[1] No increase in stillbirths, neonatal deaths or foetal abnormality rates was found. Naidoo and Hirsch[36] report foetal vaccinia following upon maternal vaccination. They advise that vaccination should be avoided during pregnancy. Tucker and Gibson,[45] as well as Entwhistle and his co-workers,[13] during a similar sweep of vaccinations in Britain, found that it was not 'prudent' to vaccinate during the first trimester of pregnancy, since the disease may be passed to the foetus. The same prudency might well be observed in administering live poliovirus, although, according to Lepine,[33] the Russians, who have the greatest experience with live poliovirus, have never reported harmful effects when it is administered in pregnancy. Sabin[40] states that pregnant women infected with poliovirus give birth to neither more nor different congenitally defective babies than do controls. There seems, however, to be an excess of foetal deaths during the first 6 months of pregnancy.

The other problem — the management of the patient who contracts viral disease during pregnancy — is the common, difficult and tricky one, since virus infections are not only ever present but, in many cases, almost impossible to diagnose accurately. Epidemics of influenza sweep the world at intervals. Asian influenza was the latest major global culprit. In a survey of its effect on pregnancy and infants taken in the maternity teaching hospitals of Cape Town, Abramowitz[2] made the observation that no untoward effects were found. Coffey and Jessop,[10,11] however, found twice as many congenital malformations in children of mothers who had had this illness as compared with a control group. Doll[12] states that Asian influenza doubles the risk of anencephaly. Record[38] deduces from Scottish figures that on present evidence it seems as if anencephaly is due to an infective agent. The difficulties encountered in analyses are pointed out by Hill and Galloway.[20] Mumps and measles rarely affect women during early pregnancy, but they also leave their scars on a percentage of the offspring.[39]

Rubella

Rubella has been the source of great trouble. Usually

a mild disease and certainly not always easily diagnosed, it may leave its indelible imprint on an individual who has not had it himself. An expectant mother contracting rubella during the first 12 weeks of pregnancy runs the risk of giving birth to a baby with deformities in the percentage ranges 87 (Abel and Dellen, reported by Abramowitz[1]), 30·7 (Brown and Nathan),[5] 30 - 70 (Campbell),[9] 34 (Liggins and Phillips),[34] 74 (Swan),[43] 50 (Rhodes),[39] and 80 (Lamay).[39] Bell[3] collected 712 cases from the literature and studied the histories. It was found that 149 developed cataracts, 263 were deaf, 210 had congenital heart lesions and 70 other children were reported to show further defects. 221 were believed to be normal. This is to quote but a few of the many authors who have done prospective and retrospective studies.

Clinicians deal with human beings and apply their knowledge to the best of their abilities to individuals who have done them the honour of seeking their advice and treatment. The mother who has just given birth to her baby invariably asks 'Is my baby alright, Doctor?' If she is not immediately reassured she will seek that information in her next question or series of questions. The possibility of an abnormal child lurks subconsciously and the thought is dispelled as soon as she receives the awaited answer. The aim of good obstetrics is to *deliver a live healthy mother of a live healthy infant.*

Medical and Legal Aspects

When confronted by a patient who has had proved rubella during the early weeks of pregnancy, the searing dilemma can be fully understood. Most women have read their journals and have full knowledge of the facts. The doctor responsible for the care during pregnancy, labour and the puerperium, is aware of the risk to which the foetus is submitted. The basic aim of obstetrics has, or should have, been ingrained into his very being. The law, according to Gordon, Turner and Price[17] reads '... abortion might be lawfully procured to save the life of the mother from certain death...'. How can these two opposing views be reconciled?

1. By encouraging all young girls to contract German measles and all the minor viral infections during their school-going ages. Although the same individual may have more than one attack of rubella[16] the chances are, in any individual case, slight that this will happen. This sane concept runs somewhat contrary to public health regulations.

2. Virologists should develop techniques so that women contemplating pregnancy or those who have recently become pregnant may be safeguarded against infections. Isaacs[22] has demonstrated that interferon, a substance produced by cells, has a broad antiviral action. It is non-toxic and does not stimulate antibody reaction. It can therefore be administered frequently. However, as yet it cannot be manufactured in commercial volume.

3. Patients who have been exposed to rubella should be treated with convalescent gamma globulin. Of 251 women so exposed and treated, the disease was contracted in 6.[29] Adequate supplies should therefore be made available.

4. Should rubella be contracted during the early weeks of pregnancy or during the month preceding pregnancy,[49] and if the diagnosis is firmly established, the problem is indeed most difficult because the medical decision is relatively straightforward, but its implementation does not fit in with legal considerations.

Pregnant women who become infected by the rubella virus immediately seek medical advice and are psychologically deeply disturbed; usually they cannot be placated, no matter what form attempts at reassurance take.

Changing the Laws

The time has therefore come for the medical profession to take the necessary steps to arrange a round table conference with colleagues in the legal profession to set about changing the laws — laws which have a strong moral and ethical background, but which have possibly become outdated by changing concepts. We know that the mental strain laid upon a patient who knows that she runs a great risk of giving birth to an abnormal baby — when her whole soul hankers after a child — may drive her to great depths of despair. She seeks help from her doctor, who views her subjection to the probable disasters with 'pity and horror'.[15] If he finds that the pregnancy cannot be terminated, she may carry on grimly, becoming ever increasingly a psychological wreck with severe adverse effects on husband, home and friends, and she may eventually give birth to an abnormal child. She may be told at birth that the child is normal, but knows full well that this little mite will have to be watched for years, since it takes time for some abnormalities to rear their ugly heads. The effect of an abnormal child in a family is both psychological and material. An abnormal child receives greater love and attention from the mother — at the expense of the normal members of the family. Abnormal children are often deeply hurt because of hidden taunts made by the cruellest of individuals — healthy young children.

Remedial medical treatment is often extremely costly. The abnormal child usually receives other luxuries, thereby greatly diminishing what should have been spent on home and family.

On the other hand, the mother may become utterly dejected and by devious ways find herself in the hands of an abortionist. This endangers her life since inferior people do inferior work. If she survives this issue her chances of pelvic inflammation with subsequent chronic ill-health and infertility are increased. It would be so much better for all concerned (if the diagnosis is established) if pregnancy could be terminated by an experienced individual under ideal conditions. Further pregnancy should be advised since termination leads to psychological scarring which can be greatly overcome by another wanted baby.

It has been said[46] that, once therapeutic abortion for this condition is legalized, the diagnosis of rubella may be falsely made in order to rid an expectant mother of an unwanted pregnancy. There is nothing in this life that is not open to perjury. Should a doctor be guilty of this misdemeanour, he or she has no right to be a citizen held in esteem, and, surely, there is a law dealing with that particular crime. Serious consideration should be taken of Parkes'[37] statement that 'a man and a woman thrust life on a new individual without his consent and for reasons which are mainly egotistical. Surely there is a most urgent need to forget ancient shibboleths and evolve ethics and policies which reconcile humanitarianism and medical

science.' It is the duty of the medical profession to the individual and to the nation to ensure that a baby is 'well born'.

CONCLUSION

It is most stimulating to realize that vast inroads are made into the unknown by men who think clearly. How pleasant it must be to have a great truth revealed although in an unrelated subject. Gregg[18] has opened up vast fields of research. The repercussion of his observations will yet yield much fruit. So many questions remain unanswered. Why are some babies not affected? Do molecules and 'living' particles actually cross the placental barrier or do they pass through materno-foetal fistulae? Why is foetal deformity not dependent upon the severity of maternal disease? Why do foetal abnormalities apparently vary from one epidemic to another? Are the foetuses that get through unscathed the carriers of rubella, as the wildebeest is of malignant catarrh in cattle?

Time will reveal the answers provided research work is constantly done. An important maxim is yet again highlighted in medicine: There is no known condition that has not a special bearing on pregnancy. Obstetrics has gradually changed from being a purely mechanical and manipulative subject to taking its rightful place in scientific and clinical medicine.

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