incidence of toxicity would not be expected in such people since the incidence and severity of haematological toxicity seems related to the stage of HIV infection, being less in asymptomatic HIV positive individuals. Moreover, it is rare during the first 4 weeks of therapy. In another study, however, of 49 people receiving prophylactic zidovudine, some withdrawals were documented because of side-effects. We have not been able to assess more long-term side-effects such as carcinogenicity and this has not been reported in humans. In most instances seroconversion would have been expected to occur by 6–12 weeks and none of the five recipients seroconverted. It is impossible to conclude that zidovudine had been effective with such small numbers and a small risk of seroconversion. The Centres for Disease Control have reported 49 health care workers who were given zidovudine with no seroconversion, in a placebo-controlled study. However, the number of patients required to be enrolled in a study to demonstrate a significant effect would be extremely large and the study would take an inordinate length of time to complete.

There have been two reports of the failure of zidovudine as a prophylactic even when given as early as 45 minutes after exposure. Animal studies have suggested that there can be suppression of viraemia if zidovudine is given within hours of exposure. Far more disappointing was the finding that zidovudine given before or after Simian immunodeficiency virus was inoculated into macaques failed to prevent infection. However, these studies can be criticized on the grounds that they are indeed animal studies, not all the retroviruses studied are clearly related to HIV (Rausher murine leukaemia virus and feline leukaemia virus) and that the inoculation volumes used were relatively large compared with those one would have expected from a needlestick injury. Since zidovudine works only after HIV has been integrated within the human cell, it may be that it can only be virustatic and suppressive rather than virucidal. If this is the case, an affective chemoprophylactic effect would be dependent upon the ability of the host to mount neutralizing antibodies to HIV of which there is no evidence to date.

The absence, however, of data to support proven efficacy and long-term safety is not an argument against continuing to offer zidovudine prophylaxis to health care workers since established HIV infection is inevitably fatal and such individuals should be given the benefit of the doubt, however small.

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References

Multiple Pregnancy of High Fetal Order and Ovulation Induction

Sir,

Obstetricians and paediatricians are very much concerned about the recent increase in multiple pregnancies, particularly if it increases more than twins. This increase is mainly due to the use of gonadotrophins to stimulate ovulation and following in vitro fertilization and embryo transfer.

All complications of pregnancy are generally increased with multiple gestation. Moreover, delivery of more than two infants may present psychologic, social and economic problems.

During the period from January 1983 until October 1992, at the National Guard King Khalid Hospital in Jeddah, there were 12 deliveries of high order multiple fetal pregnancies—11 sets of triplets and one set of quintuplets. Ten of the 12 have occurred since 1988. Eleven of these cases were the result of ovulation induction therapy.

There were considerable neonatal complications in this series of multiple pregnancies of high fetal order. Anemia occurred in nine of the 12 cases (Hb<10 g/dl, MCV<76, MCHC<30%). Pregnancy induced hypertension occurred in three of the 12 cases and premature rupture of membranes occurred in six of the 12 cases. Preterm labour occurred in all cases. The gestational age at time of delivery varied between 24 and 36 weeks (mean of 31.9 weeks). All the 12 patients were admitted during pregnancy for bed rest and monitoring. They were given prophylactic tocolytic therapy. Cervical cerclage was inserted in eight of the 12 cases.
Nine patients were delivered by caesarean sections. One set of triplets delivered the first baby at 26 weeks, and the other two infants 8 days later. Another case of triplets started in labour at 36 weeks, all infants were in cephalic presentation and delivered vaginally. The other case of triplets went into preterm labour at 24 weeks and allowed to progress because of the expected poor outcome.

The perinatal mortality rate (PNMR) for this series of high fetal order multiple pregnancy was 81/1000 (5 times the total PNMR at the hospital for the same period).

This small series of high order multiple pregnancies highlights the fact that the liberal use of ovulation induction and assisted reproduction in the recent years are responsible for the majority of these cases (11 of 12 in our series). Ten sets have been delivered since 1988 while only two sets were delivered in the previous 7 years. It has been shown that 69% of all high order multiple pregnancies in Great Britain (triplets or more) were due to ovulation induction, GIFT and/or IVF.

In attempting to reduce the occurrence of the unwanted high order multiple pregnancies with our current practice of ovulation induction and assisted reproduction, it is recommended that no more than three oocytes should be transferred in any one cycle of GIFT and also not more than three embryos to be transferred at each IVF treatment cycle.

It would be very useful if we could predict which stimulated cycle would result in a multiple pregnancy in order to abandon it. However, there is at present no satisfactory method that could be used to predict which superovulated cycle would result in a multiple pregnancy.

Therefore, infertile patients and clinicians must be aware that 25–30% of superovulation treated patients will unavoidably have multiple pregnancy. Every effort should be made to avoid the occurrence of such high order multifetal pregnancies because of their dismal outcome. More research is required to identify parameters of hyperstimulated cycles that predict multiple pregnancy.

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Agenesis of the Gall Bladder

Sir,

I read, with interest, the recent article by Dr Hage and his colleagues on agenesis of the gall bladder (Saudi Med J 1992; 13(2): 117–119).

We came across a case in a 70-year-old female who presented with right upper quadrant pain, fever and jaundice. Ultrasound showed a stone measuring over 1 cm in the common bile duct (CBD) which was dilated together with the rest of the biliary tree. No gall bladder or cystic duct could be seen. Initial management comprised of antibiotics, vitamin K, lactulose, intravenous fluids, analgesia and insulin for her diabetes which was discovered on admission. A few days later she underwent surgery, meticulous dissection of the whole extra hepatic biliary tree including Kocherization of the duodenum and exploration of the CBD (after extraction of the stone) was carried out, but we failed to find the gall bladder or its duct. An arteriograph (AT) tube was inserted in the CBD and a cholangiogram was carried out 10 days later which confirmed the absence of the gall bladder and the cystic duct. The tube was removed 5 days later and the patient was followed up for 6 months with no problems.

Dr Hage and his colleagues, in their article, believe that repeated ultrasound and coeliac axis angiography can prove the diagnosis of agenesis without an operation. It was also noted that they did not perform cholangiography for their reported patient.

Arteriography seems a promising method, at least for some cases which were opened and found to have a normal CBD, closed without any intraabdominal procedure, and postoperatively were cured. But one cannot apply it to all cases, for in agenesis there are biliary and non-biliary causes for right upper quadrant pain. Of the biliary causes there are CBD stones, and biliary dyskinesia (overactivity of the ampulla). The non-biliary causes are many and include peptic ulcer disease, irritable bowel syndrome, pancreatitis, and many others.

Stones in the CBD occur in 25–50% of the cases of agenesis, and these patients will need either endoscopic procedure or open surgery, thus arteriography will not exclude surgery. Biliary dyskinesia (dilated CBD with no stones in it) is associated with agenesis. It is thought to be caused by overactivity of the ampulla of Vater which shows a significantly higher sphincter of Oddi resting pressure and increased retrograde propagation of phasic muscular contraction when compared with healthy volunteers. Exploration of the CBD with a sphincterotomy procedure such as sphincterotomy is needed in many of these cases.

The role of cholangiography, whether per- or postoperatively, for establishing the diagnosis of agenesis has been stressed and considered mandatory by the majority of reports. In one review in 1967, all reported cases were reviewed and based upon documented operative details and per- or post-operative cholangiography. Cases of agenesis were classified into 25 proven cases, 22 probable cases, 47 possible (insufficient data) cases and 16 questionable cases.

We therefore feel that arteriography has a limited role, and that cholangiography is an essential part of confirming the diagnosis of agenesis of the gall bladder.

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