

September 2020
Cerebral palsy, stillbirths and gene sequencing

Stillbirths and cerebral palsy are devastating events. Anyone who has experienced either will attest to the need for sympathetic reactions and, if possible an explanation to help parents cope. Both circumstances are associated with profound grief and causes are sought which usually include enquiry about genetic factors but can gene sequencing be helpful in these situations?

It is known that in miscarriages karyotyping will demonstrate abnormalities in 10% of cases but with genomic analysis, will more subtle anomalies be identified if the pregnancy ends with demise later on? In the case of stillbirths it is understood that very few syndromes are monogenic disorders so groups of candidate genes are selected and investigated ([Wojcik NEJM 2020;238:1182-3](#)). In theory this could refine searches but when applied to a series of more than 200 stillbirths only 6% had genetic changes that could be suspected to be responsible for fetal death ([Stanley et al NEJM 2020 doi. 10.1056/NEJMoa1908753](#)). Gene sequencing of a stillbirth to assist bereaved parents is, as yet, not a recommended pursuit.

However, with cerebral palsy (CP) the outcome of genetic investigations may be more productive, especially if parental and index case results are viewed together. Researchers from Australia looked at 250 examples and were able to “show a likely causative genetic variant in at least 30% of CP cases” (MacLennan – personal communication). Their published work ([Jin et al Nature Genetics 2020;52:1046-56](#)) radically alters present-held concepts on potential origins of CP and must be considered when legal matters arise. Advice for parents should be to have whole genome sequencing carried out prior to consulting with a lawyer.

Prevention is the first line of action and this applies to CP which is associated with preterm delivery. Previous work has shown reduction in the incidence of CP in preterm deliveries when MgSO₄ is given prior to delivery ([Rouse et al NEJM 2008;359:895-905](#)) and now collated results “provide conclusive evidence that antenatal MgSO₄ in women at imminent risk of preterm delivery decreases the risk of CP in the offspring without increasing the risk of perinatal mortality” ([Wolf et al BJOG 2020;127:1180-8](#)). Despite robust evidence, not all units administer MgSO₄ in situations where preterm delivery is anticipated or planned. As Grobman suggests ([BJOG 2020;127:1226](#)) MgSO₄ use in these circumstances should be standard practice: “If not now, when?”

CS wound drainage

There is no evidence that draining caesarean section (CS) incision sites decreases infection rates. But it may be that grossly obese patients present a different set of challenges at surgery than women with normal BMIs and possibly “negative pressure wound therapy” would offer advantages.

To test such a hypothesis, a trial was conducted in the US in which obese women having an elective or emergency CS were randomly allocated “negative pressure wound therapy” or routine wound closure ([Tuuli et al JAMA 2020;324:1180-9](#)). The mean BMI of all the recruits was 40 and the surgical-site infection rates were 3.6% and 3.4% respectively for the cohort of more than 1 500 women.

Editorial comment: Despite the BMI range being grossly or morbidly obese, a sepsis rate of below 4% is a remarkable achievement in a large series over 6 hospitals. The outcome demonstrating a lack of effect of these devices is consistent with other studies and should dissuade surgeons of incurring extra costs by using unproven methods.

Gynaecological surgery

Pain relief – It is difficult for non-Americans to perceive the human tragedy of opioid abuse in the United States. The country comprises 4% of the world's population but consumes 80% of its opioids (Bryson "The Body" *Transworld Publications* 2019 p366). Opioid use and abuse costs Americans more than \$500 billion annually and much of that is from prescription medication.

In general the Covid pandemic appears to be exacerbating the opioid epidemic although other illicit substances are increasing faster in popularity such as fentanyl, methamphetamine, cocaine and heroin ([Haley & Saitz JAMA](#) 2020 doi:10.1001/jama.2020.18543). Some of the opioid abuse can be traced back to persistent post-operative analgesia use.

Researchers checking the records of gynaecological procedures, such as dilatation and curettage, myomectomy, hysterectomy, endometrial ablation, tubal ligation and ectopic pregnancy operations found that each had opioids prescribed post-operatively in some but not all cases, and 7% of these patients persisted with their use which has made a substantial contribution to the addiction problem ([Wright et al *Obstet Gynecol*](#) 2019;134:250-60, [Huang et al *Obstet Gynecol*](#) 2020;136:565-75 and [Wall-Wieler et al *Obstet Gynecol*](#) 2020;136:548-55).

Bowel preparation. Is there a place for bowel preparation prior to any gynaecological surgery – and if so what form should it take? To investigate existing practice more than 200 000 hysterectomies were identified and any post-operative infections recorded and correlated with any bowel preparations ([Kalogera et al *Am Obstet Gynecol*](#) 2020;223:231.e1-231.e12).

The vast majority of operations, irrespective of whether they were billed as benign (94%) or malignant (87%), had no bowel preparation and when it was used, there was no decrease in rates of surgical site infections, anastomotic leaks or major morbidity. The authors concluded that bowel preparation prior to hysterectomy is redundant and "may be safely omitted."

When planning surgery the approach may influence risk and this applies to hysterectomies for benign indications ([Zhu et al *Obstet Gynecol*](#) 2020;136:803-10). Surgeons in the US found an "Increased risk of bowel injury associated with endometriosis and the abdominal surgical approach" including laparoscopically assisted hysterectomy.

Surgery & Lithotomy positioning

In vaginal surgery and laparoscopic procedures some degree of the lithotomy position is used. Depending on the access required, full or semi-lithotomy posturing is necessary but it can result in post-operative discomfort or more serious neurological sequelae or physical consequences which are fortunately, rare occurrences. However, according to researchers, one third of women complain of lower back pain following lithotomy-positioned surgery.

The commonest types of leg supports are strap or boot stirrups, with boot stirrup use resulting in a significantly better physical function at 6 weeks post-procedure than conventional (or candy cane) stirrup use ([Gupta et al *Obstet Gynecol*](#) 2020;136:333-47). See also "Low back pain" page 60.

Urinary incontinence in older women

About a third of post-menopausal women suffer from urinary incontinence in some form or another but most do not seek professional assistance. This failure to engage with medically trained personnel precludes them from the benefits of pelvic floor muscle training which should be the first line of treatment, either on a one-to-one or group basis. Individual therapy is held up as the ideal approach because of it is responsive to personal needs but does group-based training have an equal or non-inferior set of outcomes?

Canadian researchers compared the results of 3 month courses of individual or group therapy for stress or mixed urinary incontinence and found clearly-defined end-points to be similar in both sets of women ([Domoulin et al JAMA Int Med](#) 2020.doi.10.1001/jamainternmed.2020.2993). There was excellent adherence to protocols and a greater than two thirds improvement recorded across the board in episodes of incontinence at the end of the trial and up to one year thereafter.

As observed by [Huang \(JAMA Int Med](#) 2020.doi.10.1001/jamaintmed.2020.2983) there “never will be enough trained pelvic floor therapists” to provide one-to-one care and there may well be advantages in group involvement. De-stigmatisation of the condition by a common acceptance of the problem is possible with an encouraging if not competitive attitude and group support.

Editorial comment - It is not inconceivable that this initiative on a targeted therapy could be expanded to include other symptoms or even general physical well-being. Yoga is a parallel example of single or group-practiced exercises that combines postures, muscle control with mental conditioning. The resultant development of strength, balance and flexibility has clear benefits in reducing the risks of falls ([Tew et al BMJ](#) 2020;370:m3246). These are known as “mind-motor” activities and promote socialising, raise self-esteem and improve cognitive performance ([Mattle et al JAMA Netw Open](#) 2020;3(9):e2017688).

The science of exercise in older people shows beneficial effects in terms of cerebral function that has evidence from animal research and is being extrapolated to elderly humans ([Horowitz et al Science](#) 2020;369:167-73). It was found that certain liver enzymes reached higher levels after exercise and when harvested from plasma and given to non-exercising people, “ameliorated age-related regenerative and cognitive impairments”.

Uncovering of the underpinning metabolic pathways whereby muscular activity expands well-being both physically and mentally, is exciting and encouraging. Will it attract the attention of entrepreneurs who see a gap in the rejuvenation market by reproducing “exercise generated” biochemically similar products? Benefits without the effort? Why do I feel a moral squirm at the notion?

Threatened miscarriage management

JASS has previously reported on the management of threatened miscarriages using progesterone:

A trial of over 4 000 pregnancies where bleeding occurred in the first trimester was conducted in the UK to test the efficacy of progesterone treatment ([Coomarasamy et al NEJM](#) 2019;380:1815-24). Half were given 400mg of micronised progesterone as vaginal suppositories twice a day until 16 weeks gestation and half given placebo. There was no significant difference (20% and 22%) in the number of pregnancies that did not result in a livebirth beyond 34 weeks gestation so the authors believe that “expectant management” is all that can be offered at present.

In a subsequent analysis a subgroup of women were identified who had a previous miscarriage (one or more) and derived a statistical benefit from progesterone therapy with the advantage seemingly increasing with the number of preceding miscarriages ([Coomarasamy et al *Health Tech Assess* 2020;24\(33\)](#)). This raises the question of cost which in UK economic situation was calculated as being £7655 for progesterone included management and £7572 for placebo management. Eclectically this equates to £3305 per additional live birth attributable to progesterone use. The authors say the cost-effectiveness of this therapy “would depend on the amount that society is willing to pay to increase the chances of an additional live birth”.

Missed miscarriage management

A woman who has had a “non-ongoing” pregnancy diagnosed by pelvic ultrasound (with or without bleeding) is deemed to have a missed miscarriage. Although watchful expectancy is an option, most patients are offered medical or surgical resolution of the situation with the medical route becoming the more popular.

It has been shown that misoprostol alone is non-inferior to surgical evacuation but pre-treatment with mifepristone gives better results in terms of fewer repeat doses or prolonged treatments in small trials. A comprehensive study has been carried out in 28 UK hospitals using 200mg oral mifepristone or placebo followed by a single dose of vaginal, oral or sublingual misoprostol 800µg 2 days later ([Chu et al *Lancet* 2020 ;396:770-8](#)). They found that 17% of participants failed to pass the gestational sac within a week in the mifepristone group and 24% of the placebo group, with similar numbers requiring surgical intervention to complete the miscarriage. Most (90%) received vaginal misoprostol but other routes of administration gave comparable results.

Safe, effective, and acceptable treatment for missed miscarriages is now available and this practice should be standard worldwide ([Barnhart *Lancet* 2020 doi. 10.1016/S0140-6736\(20\)31789-X](#)).

Low back pain

Low back pain is one of the commonest and most debilitating symptoms for which patients consult the medical profession and their allies. Its costs in the US alone have reached \$100 billion annually and physical therapies are extensively use as adjuncts to medications but their relative efficacies are difficult to assess and recommend.

Two spinal therapeutic approaches enjoy wide application by those seeking relief from chronic low back pain but it is not known which is more effective and more fundamentally, is either better than placebo treatment. To address this question, a cohort of patients were allocated to the following actions twice weekly for 3 weeks:-

- Manipulation techniques using “high-velocity, low-amplitude force” to the spine as used by chiropractors which is often accompanied by audible joint sounds or “pop” known as cavitation
- Mobilisation techniques using “low-velocity, low force” techniques as used by physiotherapists that do not generally produce audible sounds
- Sham cold laser therapy – as the placebo or inert intervention.

All three groups were assessed for pain and disability at the completion of 6 sessions but no significant differences were apparent leading the authors to conclude that “neither spinal manipulation nor spinal mobilization appeared to be effective treatments for mild to moderate chronic low back pain” ([Thomas et al JAMA Netw Open](#) 2020;3:e2012589).

Editorial comment – Although the trial reported here is not specific to women (who were in a slight majority) it did demonstrate that physical therapies have little to offer in a situation analogous to pelvic pain in young women. The exclusion of defined pathology leaves the choice of referral for alternative therapies to shared decision-making with the knowledge that personal preference is as probably as important as evidence-based practices.

Vaccinology for non-vaccinologists – an editorial meander

Vaccines have saved more lives than any other medical discovery.

Vaccines have reduced or eliminated diseases responsible for major morbidity and mortality with the Global Alliance for Vaccine and Immunisation (GAVI) becoming one of the most important institutions world-wide for its role in promoting and distributing vaccines ([Berkley JAMA 2019](#) doi: 10.1001/jama.2019.13190). Under GAVI’s auspices an estimated 13 million deaths have been prevented over the last two decades and its success is about to expand exponentially because of advances in vaccine technology ([Pardi et al Curr Op Imm](#) 2020;65:14-20).

Vaccine technology

Modern antiviral vaccine technology can be described as falling into 2 camps

- Protein-based or
- Gene-based

Protein-based vaccines use whole but inactivated (killed or attenuated) virus material to elicit the immune reaction – the technique used in polio or flu vaccines. Other similar approaches use subunit vaccines and virus-like particles – for example in human papillomavirus and hepatitis B vaccines. The principle is to convey the protein antigen to the cell which will then produce the antibody.

Gene based vaccines work differently using a more indirect approach. These vaccines carry the genetic instructions from the virus to the host’s cell which then makes the protein antigen itself. In effect the vaccine brings the virus’s “genetic recipe” to the cell that recognises a foreign substance/protein it has made and this triggers an immune response. These genetic instructions are DNA or messenger RNA (mRNA). Since it is now possible to sequence these genetic strands and reproduce them, scientists can find the code of pathogens (such as Covid 19) and create a gene-based vaccine.

In the gene-based technique this viral genetic code can be carried into the cell by various mechanisms. These are naked nucleic acid transfer or using vectors such as carrier nanoparticles or piggy-backed onto less harmful viruses such as a common cold adenovirus. This is the viral vector technique.

Advantages of these new vaccine production platforms are:

- Neither protein- nor gene-based technology relies on cell cultures to grow the antigen. They are made in laboratory tanks by catalysing chemicals so they are cheaper and quicker to make and “up-scalable” for mass- production.
- It may be possible for a single inoculation to “simultaneously target multiple antigens and pathogens” reducing the number of vaccinations required ([Maruggi et al *Mol Therapy* 2019;27:757-72](#)).
- One vector could carry 50 antigens (or the code for them) and usher in a new era of “single-shot” immunology. This would have major effects on costs and inoculation programmes.
- The vaccines can be made thermostable meaning they do not require a cold-chain network for distribution
- These techniques are being used to develop vaccines against influenza, rabies, Ebola and Zika with the promise of a broad-spectrum vaccine for all (known) corona viruses.

HPV vaccine

Human Papillomavirus vaccination is unusual in that it is given to children aged 11 or 12 years old initially or as catch-up vaccination to those up to the age of 26 years ([Marks et al *JAMA Dermatol* 2020 doi.10.1001/jamadermatol.2020.2927](#)). Although there is no evidence of links to the incidence of autonomic dysfunction in women some parents hesitate to have their children vaccinated ([Hviid et al *BMJ* 2020;370:m2930](#)). Governments, schools and paediatricians have taken stances against children whose parents do not abide by regulations concerning HPV vaccination ([Ko et al *JAMA Pediatr* 2020;147:861-7](#) and [O’Leary et al *JAMA* 2020;324:1105-7](#)).

The latest Swedish data show the incidence of invasive cervical cancer up to the age of 31 years is substantially reduced following **early** vaccination. The rate ratio was 0.12 (CI 0.00 - 0.34) meaning an 88% reduction in the disease ([Lei et al *NEJM* 2020.383:1340-8](#)).

Influenza vaccines

In February of each year, WHO and the US Centers for Disease Control (CDC) decide on the composition of the “Flu vaccine” for the year. It is based on the strains circulating in Eastern Asia that are likely to reach Europe and the Americas at the start of the northern hemisphere’s autumn and winter seasons. There are 2 types of protein on the flu virus’s surface – haemagglutinin and neuraminidase – and each has 5 strains – hence the H and N plus a digit used to define the strain. The H5N1 strain is particularly virulent one also known as “bird flu”.

Not everyone who catches the flu virus is infected by the same strain so each year’s current flu vaccine offers limited coverage – in the order of 30-40% but this is sufficient to reduce morbidity and hospital admissions. The present circumstances demand that hospital resources be conserved to deal with the Covid pandemic making valuable any reduction in the use of facilities.

There are concerted efforts to reach as many people as possible this year with special appeals to health-care workers, the elderly, children, those with asthma, diabetes and pulmonary diseases ([Kuehn *JAMA* 2020;324:1025](#) and [Jaklevic *JAMA* 2020;324:926-7](#)). There is an opportunity prevent the complications of cardiovascular disease as any viral illness exacerbates the possibility acute cardiac syndromes, stroke, thromboembolic events and heart failure ([Sperling et al *JAMA Cardiol* 2020 doi.10.1001/jama.2020.16968](#)).

Pregnant women should be especially encouraged to receive flu vaccinations as both they and their fetus are afforded protection. Any fears that vaccination could be associated with autism disorders in offspring have been reassuringly dealt with – at least concerning the H1N1 “swine flu” vaccine that affected large numbers of people 10 years ago. Research by Swedish workers found no link between vaccination at any stage of pregnancy and autism spectrum disorders ([Ludvigsson et al *Ann Int Med* 2020 doi. 10.7326/M20-0167](#)).

The data on respiratory syncytial virus vaccination in pregnancy is less convincing. Although it is the commonest cause of respiratory infections in infants, maternal vaccination in late pregnancy reduced infections from 2.5% to 1.5% which did not reach significance ([Madhi et al *NEJM* 2020; 383:426-39](#)).

Anti-vaxxers

Those who refuse to be vaccinated or hesitate to have their children vaccinated are known as anti-vaxxers. Their views are contrary to medical science and they steadfastly deny the balance of benefit and harms of vaccination for them or the communities in which they live. Although emotionally it is tempting to confront and ridicule their stand-point, this approach is likely to be counter-productive and entrench their ideas ([Ritchie *The Post* 2020](#) and [Rosenthal et al *JAMA Pediatr* 2020;174:916](#)).

Covid vaccines

On 10th January 2020 Chinese researchers released the genetic sequence of the newly identified Covid 19. Being a corona virus it had a specific spike protein on its surface so immediately vaccinologists set about creating vaccines, some using protein-based and others gene-based platforms. Experience with the acute respiratory syndrome and the Middle East outbreaks gave developers a head start and phase 1 and 2 trials on efficacy and safety followed rapidly. It took 66 days for the first mRNA phase 3 (clinical trials in humans) to begin.

As of September 2020 there are 140 vaccines in pre-clinical development and 30 vaccines in clinical trials. For robust data to be collected the placebo controlled trials have to attract 40 000 to 60 000 participants and achieve an efficacy of (ideally) more than 70% although 50% would probably be acceptable according to [Fauci](#) and the [FDA](#). One factor that limits effectiveness is host immunity to the viral vector which means the person’s immune system may eliminate the – say – adenovirus carrying its Covid mRNA load thus rendering the process unsuccessful. To circumvent this, scientists are using non-replicating adenoviruses that infect chimpanzees, and not humans, as the carrier ([Folegatti et al *Lancet* 2020;396:467-78](#)). This is the route being followed by the AstraZeneca and Oxford University group but a battery of other candidate vaccines use protein- or gene-based techniques and various vectors and delivery mechanisms so there is no single “right” road to a successful anti-Covid vaccine.

It is hoped that several vaccines will be efficacious as well as safe and that some may prove better for specific groups such as children, the elderly and those with co-morbidities. Quantities of the strongest candidate vaccines are being stock-piled in anticipation of clinical success, regulatory ratification and then distribution. Distribution will be an ethical minefield beyond the remit of this meander ([Persad et al *JAMA* 2020 doi. 10.1001/jama.2020.18513](#)).

The most optimistic estimate for the launch of the first legitimate Covid vaccine – accepted by the medical community – is towards the end of November or early December 2020 although this is purely speculative as no other vaccine manufactured by these methods has ever been clinically tested in large trials so there is no precedent on which to base guesswork. Let us hope that new technology will supply a defence against a new pathogen and provide faster answers in the future.

Snippets

Vestibulodynia revisited

Vestibulodynia is the sensation of pain when pressure is applied to the introital region. It is provoked by intercourse or tampon insertion and it is implicated as the most common cause of superficial dyspareunia. Its origins are obscure with a theory being peripheral receptor sensitisation leading to a “neurogenic inflammatory response” whereby mild or trivial touch is perceived as significant pain or allodynia.

With such a paucity of aetiological knowledge there are a wide range of psychological and pragmatic solutions offered with a recent trial using injections of botulinum toxin A into the bulbocavernosus muscles twice, 3 months apart ([Haraldson et al *Obstet Gynecol* 2020;136;524-32](#)). Compared with placebo the active injections showed a non-significant reduction in dyspareunia and tampon use but no change in sexual function or distress although “secondary outcomes suggested positive effects of the treatment.”

Do you like coffee?

Is there any evidence that coffee is good or bad for you?

Coffee is one of the most widely and regularly enjoyed beverages globally, but are there clear indications in the nutritional literature of its benefit or harm? There are some possibly unfair associations with smoking, alcohol and cancer but what is on the positive side?

Coffee possesses “antioxidant, anti-inflammatory and insulin-sensitising effects” which may contribute to anti-cancer activity as there are data suggesting, in people with colorectal cancer at least, that the more coffee drunk the longer patients survive ([Mackintosh et al *JAMA Oncol* 2020 doi. 10.1001/jamaoncol.2020.3938](#)). This association held for up to 4 cups of coffee per day decaffeinated or regular. Taking the notion of health promotion and cancer reduction further, commentators point to lower risks of endometrial and liver cancer plus cardiovascular disease protection with coffee intake and suggest randomised trials to prove the point ([Loftfield et al *JAMA Oncol* 2020 doi. 10.1001/jamaoncol.2020.3313](#)). Any takers?

Cannabis & pregnancy revisited

Last month we meandered through the fields of cannabis consumption and touched on its increased use by pregnant women, possibly in the belief of its antiemetic properties. Its use has reached 7% of pregnant Americans but there are red lights flashing concerning its effects on childhood and adolescent brain development.

The Adolescent Brain Cognitive Development (ABCD) investigation is a long-term study looking into possible origins of young people’s psychopathology, particularly behavioural, social, cognitive issues and sleep problems while measuring any gray-matter reduction measurements ([Paul et al *JAMA Psychiatry* 2020 doi. 10.1001/jamapsychiatry.2020.2902](#)). There were associations with maternal cannabis use suggesting interference with normal endocannabinoid development which starts a 7 weeks gestation. If women quit cannabis use when they realise they are pregnant the effects may be mitigated so there is good reason to encourage disuse at first antenatal contact ([Fine et al *JAMA Psychiatry* 2019;76:762-4](#)).

 **JOURNAL ARTICLE
SUMMARY SERVICE**

September 2020

Dear Colleague

I have tried not to hone in on Covid information because I am sure you receive enough from other sources but I got caught up in the vaccination story. It seems the technology to create vaccines in new ways narrowly preceded the pandemic so we may all benefit from the immense progress in this sphere. Hence the "Vaccinology meander".

Imagine a "single shot" that carries mRNA for all the common pathogens that we currently inoculate children against! There is hope for a malaria vaccine and HIV is in many vaccinologists sights but not yet available.

The possibility of using the social media to our advantage interests me and although a few years behind those who use it constantly – I can't work out why there why are there not many more "self-help" or "Women to Women" groups for people with common symptoms to assist themselves and others?

- Maybe report such as the group therapy for urinary incontinence in older women will encourage such a trend.
- Will the next generation embrace these opportunities in pregnancy and gynaecology?
- Will national or international societies champion them?
- How can they be made viable – not forever" but just to kick-start them and let them run their courses?

Low back pain is probably a consequence of our up-right posture and we pay the price for upper limb freedom but it seems the physical techniques on which so many people rely are not that evidence- based. I have no doubt there is a major placebo effect – with which I have no quarrel – but let us accept that and not exploit one method in place of another for material gain.

Kind regards

Athol Kent

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JASS questions for September 2020

	True/False
1. Magnesium sulphate offers some protection against cerebral palsy in the offspring if given to their mothers prior to premature delivery	_____
2. In gynaecological surgery for malignancies, bowel preparation is a crucial factor in reducing sepsis	_____
3. In older people exercise has been shown to be of benefit against cognitive impairments	_____
4. In the medical management of missed miscarriages, the use of mifepristone improves outcomes in terms of fewer women requiring repeat misoprostol treatment and evacuation	_____
5. In gene-based vaccines DNA or messenger RNA are used to stimulate antigen production within the host cells	_____
6. Gene and protein-based vaccines are produced in egg-cell cultures	_____
7. Manipulation techniques are superior to mobilisation techniques in the treatment of chronic low back pain	_____
8. Gene-sequencing represents a major step forward in the diagnoses of stillbirths of unknown cause	_____
9. In grossly obese women undergoing caesarean delivery, the use of “negative pressure wound therapy” significantly reduces the risks of surgical site sepsis	_____
10. Cannabis use in pregnancy is associated with poorer cognitive and behavioural outcomes in the adolescent offspring	_____

Continuing Professional Development points information

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Please request the current CPD Annual Answer Sheet if you do not have a copy.

You are advised to fill in your answer sheets each month but to return the CPD Annual Answer Sheet (only) to JASS administration early in 2021.

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