Apgar Score and Postnatal Outcomes

Doris SY Chong, BSocSci(Stat), MPhil(Stat); Paul SF Yip, PhD; Johan Karlberg, MD, PhD

Controversy exists about the continued usefulness of the Apgar scoring system to predict early infant mortality and morbidity. This review examines published evidence of its clinical reliability, together with the validity of postnatal outcomes that were 'predictable' by the score. No one can deny that an encouraging Apgar score value in the first few minutes of life is desirable for a newborn. This review focuses on the risk factors associated with low Apgar scores.

The Apgar score is named after the American anaesthesiologist Virginia Apgar (1909-1974) who in 1952[1] invented the practical method of evaluating the general physical condition of a newborn infant shortly after delivery. It is a composite of a number of objective parameters to assess the general condition of the baby at birth. By scoring the heart rate, respiratory effort, muscle tone, skin colour and reflex irritability 0, 1 or 2 points, a score of 7 to 10 is considered normal, 4 to 6 might require some resuscitative measures, and 3 or less requires immediate resuscitation.[2] Values for each indicator are listed in the Table. The Apgar score is measured routinely 1 minute after birth and commonly repeated 5 minutes after birth. Additional assessments at 5-minute intervals may be warranted depending on the newborn's status. It is noteworthy that a Hong Kong study (unpublished) showed no clear cut-off point for the scoring system in terms of the absolute or relative risk of neonatal mortality. The scoring system is, in terms of mortality risk estimation, more or less a continuous scale.

Poor 10-minute or 15-minute Apgar scores together with poor

Table. The Original 1953 Apgar Scoring System

Component	Score		
	0	1	2
Heart Rate	Absent	<100 beats/min	>100 beats/min
Respiratory Effort	Absent	Weak cry; irregular	Breathe and cry lustily
Reflex Irritability	No response	Facial grimace	Sneeze or cough
Muscle Tone	Flaccid	Some reflexion	Active motion
Colour	Blue or pale	Body pink, extremities blue	Completely pink

Adapted from reference 1.

1-minute and 5-minute Apgar scores reflect an ineffective resuscitative measure or a worsening status of the newborn. Moreover, the negative correlation of Apgar score with postnatal outcome reflects the impact of the baby's condition at birth on subsequent outcome. Intuitively, 10-minute Apgar score or 15-minute Apgar score should have a better predictive power for later morbidity or mortality. A cursory inspection of the Swedish Birth Medical Registry, which covers virtually all births (99%) in Sweden,[3] showed that not more than 50% of newborns have a valid record of the 10-minute Apgar score. Moreover, only a few publications can be found in the literature that studied the association of the 10-minute Apgar score with infant mortality or morbidity. For these reasons, research usually focuses on either the 1-minute or 5-minute Apgar score, or both.

The 5-minute score is considered to be the most accurate and widely accepted predictor of morbidity and mortality.[4] However, controversy continues over its ability to predict neonatal (≤4 weeks) or infant (≤1 year) morbidity and mortality, or the neurological development of the infant. It was never intended for the latter.[5] Nonetheless, some clinicians have speculated that improvements in perinatal and neonatal care over the past few decades might have diminished the predictive power of the Apgar score.[6]

A critical appraisal of the Apgar system concluded that it is not especially sensitive, but fairly specific for predicting later death or handicap.[7] It also stressed that it is important to consider changes in the Apgar score from the first minute to 5-minutes and/or 10-minutes. Recent studies have, however, demonstrated that the Apgar system remains as relevant for the prediction of neonatal survival today as it was almost 50 years ago,[4] although other researchers report its limited helpfulness in pre-term infants.[8]

POSTNATAL OUTCOMES

Mortality

Using either the 1- and/or 5-minute Apgar score to predict infant survival is probably the easiest way to validate the predictive power of the scoring system. Most studies over the last 45 years that tested the significance of the mortality predictive power of the Apgar score divided newborns into subgroups for analysis.[5-17] They were classified as either term or preterm, low birth weight or normal birth weight, small for gestational age or normal for gestational age, twin or singleton, born naturally or by Caesarean section. Early neonatal mortality, neonatal mortality or infant mortality were considered as outcomes.

Since the inception of the Apgar system, there has been a general consensus that it is a useful predictor of neonatal/infant mortality for newborns who are full-term with normal birth weight, or normal birth weight for gestational age.[4,9,10,18] Any criticism centred on the possibility of miscalculating the Apgar score,[6] or that new technology that dramatically reduces neonatal mortality may have outdated the usefulness of the system. However, numerous studies have shown that the scoring system remains as relevant for the prediction of infant survival today as it did almost 50 years ago.[5,11-13,19]

A recent study of about 0.13 million US live-born full-term singleton infants without malformation showed that the relative risks of neonatal mortality were 1460 (95% CI: 835-2555) and 53 (95% CI: 20-140) for those with a 5-minute Apgar score 0 to 3 and 4 to 7, respectively, with reference to a 5-minute Apgar score of 7 to 10.[5] Another study in Norway of about 0.24 million live-births without congenital malformation, except congenital dislocation of the hips, and with birth weights of at least 2500 g showed the corresponding relative risks were 386 (95% CI: 270-552) and 45 (95% CI: 30-68).[13] The results of these studies were reinforced by an unpublished study of the Swedish Medical Birth Registry that analysed almost two million live-born full-term single-

ton infants without malformations. The relative risks of neonatal mortality for those with 5-minute Apgar score 0 to 3 and 4 to 7 were 464 (95% CI: 409-529) and 33 (95% CI: 29-38), respectively.

Most neonatal deaths occur in the first week of life. It is thus to be expected that the risk of mortality with a low Apgar score will drastically diminish thereafter. The 5-minute Apgar score is regarded as a better predictor of mortality than its 1-minute counterpart.[4,16] This more powerful prognostic value is not only observed in term or normal birth weight infants, but also in premature or low birth weight infants.[15,19]

The final conclusion in another critical appraisal[7] noted that a change in the Apgar score from 1 to 5 to 8 in the first few minutes of life substantially reduced the probability of neonatal death. This demonstrated the importance of considering both the 1- and 5-minute Apgar scores together. The Norwegian study meanwhile demonstrated that the accuracy of the Apgar score was even stronger when scores at 1 and 5 minutes were combined.[12] If both scores were 3 or lower, the risk of neonatal death was 642-times higher than if they were 7 to 10.

Using the Apgar score to predict mortality in premature, small for gestational age or low birth weight infants is still controversial. In very low or low birth weight infants, a low Apgar score partly correlates with mortality, although the weak correlation emphasizes the limitations of the score in predicting mortality.[7,8] When 1-minute and 5-minute Apgar scores were assessed in 748 low weight infants, a significant relationship was found with survival in the univariate analysis; however, neither of them accounted for more than 32% variance in the outcome.[16] In a cohort of 852 preterm newborns, low Apgar scores were associated with increased neonatal mortality.[17]

Neurodevelopment

It is generally accepted that the Apgar score is not a useful predictor of neurodevelopment in term or preterm, or even normal birth weight or low birth weight infants.[19-24] Some researchers have reported a significant correlation between the Apgar score and developmental outcome later in life.[19,20,23] However, when important confounding variables, such as birth weight and gestational age were controlled for in the statistical analyses, Apgar scores provided only a very limited prognostic indicator of developmental outcome.[20,23,24] In an investigation of 256 infants weighing less than 1800 g at birth, it was demonstrated that after controlling for birth weight and gestational age, the Apgar scores did not predict developmental outcome (ie. using the Bayley Mental and Psychomotor Developmental Indices as proxy), while a significant bivariate correlation existed between the Apgar scores and the indices.[20]

In the analysis of collaborative perinatal project data, 80% of infants who had an Apgar score between 0 and 3 at 10 minutes or later and survived were free of major handicap at early school age.[21] In addition, the predictive value of a low Apgar score for neonatal neurological morbidity was confirmed to be poor in 805 appropriate-for-date term infants who were delivered vaginally.[22]

A prospective study of 111 term infants with a 5-minute Apgar score of less than 7 showed that a low Apgar score warranted developmental surveillance during the early years of life.[23] However, in order to predict subtle developmental dysfunction evident at school entry age, it concluded that neonatal seizures must be considered.

Another follow-up study was carried out in 1,942 subjects.[24] After controlling for possible confounding influences such as perinatal factors and demographic characteristics, the sensitivity of a low 1-minute and a low 5-minute Apgar score for predicting a low intelligence test score at age 17 was 8% and 1.5%, respectively. In other words, low Apgar scores correlate very poorly with long-term intellectual outcome.

However, contradicting the

studies quoted above, a recent Swedish study showed that the odds ratio was 9.5 (95% CI: 7.2-12.5) for mental retardation for term babies with an Apgar score below 7, even after controlling for birth year, maternal age, parity and smoking.[19]

Cerebral Palsy

Using Apgar score to predict or to determine which infants are at high risk for cerebral palsy is still a matter for debate. A low Apgar score at 1 minute has been reported to be significantly associated with cerebral palsy in preterm infants.[25] However, when delivery mode (Caesarean section or not) and parity were included in the statistical analysis, the Apgar score at 1 minute was no longer significant. The predictive value of the Apgar score was very limited in preterm infants.

For term infants, although a low Apgar score was a risk factor for the development of cerebral palsy, 55% of children who later developed cerebral palsy had Apgar scores of 7 to 10 at one minute, and 73% of them scored 7 to 10 at five minutes.[21] A full-term infant with an initial Apgar score of 0 to 3 whose 10-minute score improved to 4 or higher had a 99% chance of not having cerebral palsy at the age of 7.

In Norway, a study of babies with a birth weight of at least 2500 g showed that the Apgar score remained important for the early identification of infants facing an increased risk for the development of cerebral palsy at the age of 8 to 12.[13] Compared with children with a 5-minute Apgar score of 7 to 10, those who scored 0 to 3 had an 81-fold (95% CI: 48-138) higher risk for cerebral palsy. The study found the risk increased further to 642-fold (95% CI: 442-934) if both 1- and 5-minute Apgar scores were 0 to 3.

A recent Swedish study of over one million term births revealed that after controlling for birth year, maternal age, parity and smoking, infants with a 5-minute Apgar score under 7 had a 31-fold (95% CI: 27-36) increased risk for developing cerebral palsy.[19]

Asphyxia

A low Apgar score has often been misinterpreted as proof of birth asphyxia. This prompted the American Academy of Pediatrics (AAP) to express concern about 'abuse' of the score in 1986,[26] with a revised statement published in 1996.[27] They reiterated that Apgar scores alone should not be used as evidence that neurological damage was caused by hypoxia, a more appropriate term than asphyxia. According to the AAP, four criteria should be met to substantiate the diagnosis of birth asphyxia:

- profound metabolic or mixed acidaemia (pH <7.00) on an umbilical arterial blood sample, if obtained;
- an Apgar score of 0 to 3 for longer than 5 minutes;
- neurological manifestations, eg. seizure, coma or hypotonia;
- evidence of multiorgan dysfunction.

It is now quite clear that a low Apgar score is not synonymous with birth asphyxia, and few people still make this mistake.

OTHER OUTCOMES

Apgar scores have also been tested for their ability to predict immediate neonatal morbidity. Data from a prospective Scandinavian study suggested that both the 1- and 5-minute scores of infants born after 23 weeks' gestation and delivered vaginally were powerful risk indicators for respiratory distress.[28] Analysis of 270 intrapartum patients revealed that, when assessed independently, a 5-minute score of less than 7 was associated with both the need for admission to a neonatal intensive care unit and neonatal sepsis.[29] The significance of the score did not alter, even after controlling for cord pH or the presence of meconium.

Apgar scores of 0 to 4 at 1 minute and 0 to 6 at 5 minutes were also investigated for risk criteria in the Utah High Risk Hearing Screening Program.[30] Even when moderately depressed (5-minute Apgar score of value 4 to 6), scores were sensitive risk factors for sensorineural hearing loss.

There was also a significant influence of combined low 1-minute Apgar score and maternal cigarette smoking in predicting offending behaviour in 832 African-American youths, whereas the independent effects of the independent measures had no such effect.[31]

RISK FACTORS

Birth Weight

It is generally recognized that birth weight is significantly associated with the Apgar score, irrespective of whether the baby is born at term or preterm.

Low birth weight or an unusually large birth weight at term has been strongly associated with an increased risk of low Apgar score.[19] Stratified by year of birth, maternal age, parity and smoking, the odds ratio for having a low Apgar score compared with babies of average birth weight was 5.3 (95% CI: 3.8-7.3) for birth weight less than 1500 g and 7.4 (95% CI: 1.4-40.5) for birth weight greater than 5500 g. A corresponding pattern was observed over the entire range of birth weight values, ie. the risk of low Apgar score increased with increasing deviation from the mean birth weight, in either direction.

Babies weighing under 2500 g at birth, whether growth restricted, preterm or from a low-income population, also showed a significant correlation of low Apgar score with birth weight.[8,32,34]

Maternal Smoking

Maternal smoking is known to be related to a number of negative postnatal outcomes. Whether maternal smoking has a direct influence on Apgar score remains unclear. In a 1982 study, neither a univariate statistical analysis nor a stepwise multiple regression analysis identified a significant negative association between cigarette smoking and 1- or 5-minute Apgar scores.[35] Maternal smoking, however, was a risk factor for babies with a moderately depressed Apgar score (4 to 6), particularly in older multiparas.[19] Similar findings were obtained in a previous study.[36] However, neither study considered confounding factors such as social class or alcohol intake in the statistical analysis.

Gestational Age

The premature newborn looks completely different from the full-term newborn, simply because of the different stages of maturity. A 28-week, 1100 g newborn is usually a bluish-red, not pink, colour at birth, with markedly reduced muscle tone and sluggish reflex irritability.[37] A maximum of 1 point is assigned for each of these vital indicators when using the Apgar scoring system. Even if the newborn scores very well for respiratory effort and heart rate, the maximum score possible is 7. The 1- and 5-minute scores are thus not independent of gestational age.

A study of 73 pregnant women with normal newborn babies with a gestational age from 22 to 42 weeks revealed that the scoring of the skin colour of newborns was statistically indifferent to the varying gestational ages.[38] Among the other vital indicators of the Apgar system, heart rate appeared to be the indicator least affected by immaturity, while respiratory effort, muscle tone and reflex irritability increased with gestational age.

Studies have therefore shown that for both preterm and term newborn groups, the Apgar score is significantly associated with the length of gestation.[8,19] The minimum risk of a low Apgar score was observed at 38 to 40 gestational weeks. The risk became more obvious for babies born in week 41, and even more pronounced for babies born in week 43.[19]

Fetus Presentation and Mode of Delivery

Caesarean section, compared with vaginal delivery, increases the health risk for the mother and for the baby, while breech presentation at birth introduces complications during delivery and increases the risk of perinatal mortality.[39,40] Many researchers have observed that breech births mean a higher

risk of low Apgar score.[19,33,41-42] It is uncertain whether Caesarean section increases the risk of a low Apgar score.

One study found term singleton babies with breech presentation had an odds ratio of 2.6 (95% CI: 2.2-3.0) for a low Apgar score (<7) at 5 minutes, compared with babies in vertex presentation.[19] Similar results were found in babies weighing less than 1000 g[42] (except for term babies): the risk further increased if the baby was delivered vaginally (OR 6.67, 95% CI 5.9-7.6). In addition, a Danish study showed a 15-fold increased risk of low Apgar score in vaginal breech delivery babies.[41]

In another study of growth-restricted infants born by vaginal breech delivery and Caesarean delivery, the odds ratios of low 5-minute Apgar scores[33] were 7.0 (95% CI: 1.8-28.3) and 0.2 (95% CI: 0.1-0.7), respectively. Breech delivery was therefore a risk factor for a low Apgar score, whilst Caesarean delivery was protective.

In contrast, the risk of having a low Apgar score for live born babies weighing less than 2500 g was independent of the mode of delivery as well as the presentation of the fetus at birth.[32] Another case-control study revealed that after controlling for birth weight, gestational age, maternal age and income, the relative risk was 1.29 (95% CI: 0.97-1.72).[43]

Meconium

The presence of meconium has been shown to be a significant predicting factor for a low 5-minute Apgar score among growth-restricted neonates.[32] Early passage of thick meconium correlated with a low 1- and 5-minute Apgar score, while thick meconium and no meconium at all appeared to have no association with the Apgar score.[44]

Anaesthesia

Maternal sedation and analgesia may decrease tone and responsiveness of the newborn, resulting in a lower Apgar score.[45] In vaginally delivered singleton infants born at term with a vertex presentation, epidural analgesia was associated with an increased risk of low Apgar score, giving an odds ratio of 2.1 (95% CI: 1.9-2.3).[15] Some anaesthetic methods may be more beneficial to the newborn than others. Among growth-restricted neonates, those exposed to general anaesthesia had a lower 1- and 5-minute Apgar score than those in all other anaesthetic groups.[33]

In a study of elective Caesarean section deliveries, epidural block was used in 139 mothers while 471 underwent general anaesthesia. No baby in the epidural group was severely affected (Apgar score less than 4), compared with 6.2% in the general anaesthesia group. Only 4.3% in the epidural group, against 15.4% in the general anaesthesia group, were moderately affected.[46]

In another study of 837 newborns weighing less than 1000 g, corticosteroid use was a strong predictor of a high Apgar score, aside from gestational age and birth weight.[42] This finding indicates that antenatal corticosteroids may benefit low birth weight newborns by preventing respiratory distress syndrome.

Other Risk Factors

In a Swedish study, the odds ratio for an Apgar score below 7 at 5 minutes increased moderately with maternal age and in neonates of primiparous mothers for term babies or for babies with birth weight over 2500 g.[14] The authors speculated that this risk increment was probably caused by multiple factors, since several complications of pregnancy increase with maternal age. A similar result was observed in another study.[11]

A larger proportion of low-Apgar-score-babies are also delivered during 'non-office hours' (5.00 pm to 6.59 am), as well as during holiday periods (June to August, December).[14] This may suggest that personnel resources are an important factor. Similar observations were noted in a recent study of the relationship between early neonatal mortality and birth hour – infants born during the night and around 9 am were at higher risk of early neonatal mortality.[47]

Male newborns are more frequently found to have an Apgar

score of less than 7, even after stratification for birth weight.[19] The risk of a low Apgar score has also been found to be higher in twins, and even more pronounced for the second twin;[19] a delay in the delivery of the second twin may introduce influences already in utero. For a similar reason, a prolonged second stage of labour for singletons was significantly associated with a low Apgar score.[12]

Maternal stress during pregnancy was also found to be an activator of physical illness processes in the mother which, when combined with other maternal risk factors such as past pregnancy complications, pregnancy symptoms during the first and third trimesters, and illness-proneness, relate to neonatal outcome measured by Apgar score at 5 minutes.[48] In another recent study however, maternal illness did not correlate with subsequent Apgar score.[17]

CONCLUSION

The Apgar score is as valid in clinical practice and medical research today as it was 50 years ago. Numerous studies have analysed its usefulness and limitations. More consideration of previous studies, together with future studies, will provide further insight into when and how the Apgar score should be used in clinical practice. But a clinical scoring system that has survived 50 years under the scrutiny of evidence-based medicine should, and must, be taken very seriously.

REFERENCES

1. Apgar V. A proposal for a new method of evaluation of the newborn infant. Curr Res Anesth Analg 1953;32:260-267.
2. Apgar V, Holaday DA, James LS, et al. Evaluation of the newborn infant second report. JAMA 1958;168:1985-1988.
3. Cnattingius S, Ericson A, Gunnarskog J, Kallen B. A quality study of a medical birth registry. Scan J Social Med, 1990;18: 143-148.
4. Apgar V, James LS Further observations on the newborn scoring system. Am J Dis Child 1962;104:419-428.
5. Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. N Engl J Med 2001;344:467-471.
6. Anonymous. Is the Apgar score outmoded? Lancet 1989;1:591-592.
7. Schmidt B, Kirpalani H, Rosenbaum P, et al. Strengths and limitations of the Apgar score: a critical appraisal. J Clin Epidemiol 1988;41:843-850.
8. Hegyi T, Carbone T, Anwar M, et al. The Apgar score and its components in the preterm infant. Pediatrics 1998;101:77-81.
9. Drage JS, Kennedy C, Bernedes H, et al. The Apgar score as an index of infant morbidity. A report from the collaborative study of cerebral palsy. Dev Med Child Neurol 1966;8:141-148.
10 Naeye RL. Underlying disorders responsible for the neonatal deaths associated with low Apgar scores. Biol Neonate 1979;35:150-155.
11. Nathoo KJ, Chimbira TH, Mtimavalye LA. Mortality and immediate morbidity in term babies with low Apgar score (Zimbabwe). Ann Trop Paediatr 1990;10.239-244.
12. Jepson HA, Talashek ML, Tichy AM. The Apgar score: evolution, limitations, and scoring guidelines. Birth 1991;18:83-92.
13. Moster D, Lie RT, Irgens LM, et al. The association of Apgar score with subsequent death and cerebral palsy: A population-based study in term infants. J Pediatr 2001;138:798-803.
14. The Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke. In: Hardy JB, Drage JS, Jackson BC (eds). The First Year of Life. Baltimore: John Hopkins University Press: 1979:78-92.
15. Nelson KB, Ellenberg JH. Neonatal signs as predictors of cerebral palsy. Pediatrics 1979;64·225-232.
16. Behnke M, Carter RL, Hardt NS, et al. The relationship of Apgar scores, gestational age, and birthweight to survival of low-birthweight infants. Am J Perinatol 1987;4:121-124.
17. Weinberger B, Anwar M, Hegyi T, et al. Antecedents and neonatal consequences of low Apgar scores in preterm newborns: a population study. Arch Ped Adolesc Med 2000;154:294-300.
18. Ikonen RS. The Apgar scoring of newborn infants and its relation to neonatal mortality. Ann Paediatr Fenn 1967;13:111-114.
19. Thorngren-Jerneck K, Herbst A. Low 5-minute Apgar score: a population-based register study of 1 million term births. Obstet Gynecol 2001;98:65-70.
20. Behnke M, Eyler FD, Carter RL, et al. Predictive value of Apgar scores for developmental outcome in premature infants. Am J Perinatol 1989;6:18-21.
21. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic neurologic disability. Pediatrics 1981,68:36-44.
22. Dijxhoorn MJ, Visser GH, Fidler VJ, et al. Apgar score, meconium and acidaemia at birth in relation to neonatal neurological morbidity in term infants. Br J Obstet Gynaecol 1986;93:217-222.
23. Blackman JA. The value of Apgar scores in predicting developmental outcome at age five. J Perinatol 1988;8·206-210.
24. Seidman DS, Paz I, Laor A, et al. Apgar scores and cognitive performance at 17 years of age. Obstet Gynecol 1991;77:875-878.
25. Topp M, Langhoff-Roos J, Uldall P. Preterm birth and cerebral palsy. Predictive value of pregnancy complications, mode of delivery, and Apgar score. Acta Obstet Gynecol Scand 1997;76:843-848.
26. American Academy of Pediatrics. Committee on fetus and newborn: Use and abuse of the Apgar score. Pediatrics 1986;78:1148-1149.
27. American Academy of Pediatrics. Committee on fetus and newborn: Use and Abuse of the Apgar score. Pediatrics 1996;98:141-142.
28. Wennergen M, Krantz M, Hjalmarson O, et al. Low Apgar score as a risk factor for respiratory disturbances in the newborn infant. J Perinatol Med 1987;15:153-160.
29. Anyaegbunam A, Fleischer A, Whitty J, et al. Association between umbilical artery cord pH, five-minute Apgar scores and neonatal outcome. Gynecol Obstet Invest 1991;32:220-223.
30. Eichwald J, Mahoney T. Apgar scores in the identification of sensorineural hearing loss. J Am Acad Audiol 1993;4:133-138.
31. Gibson CL, Tibbetts SG. Interaction between maternal cigarette smoking and Apgar scores in predicting offending behavior. Psychol Rep 1998;83:579-586.
32. Ladehoff P, Pedersen GT, Sorensen T. Apgar scores in low birth weight infants delivered vaginally and by cesarean section. Acta Obstet Gynecol Scand 1986;65:3-5.
33. Levy BT, Dawson JD, Toth PP, et al. Predictors of neonatal resuscitation, low Apgar scores, and umbilical artery pH among growth-restricted neonates. Obstet Gynecol 1998;91:9-16.

34. Roger JE, Graves WL. Risk factors associated with low Apgar scores in a low-income population. Paediatr Perinatol Epidemiol 1993;7:205-216.
35. Hingson R, Gould JB, Morelock S, et al. Maternal cigarette smoking, psychoactive substance use and infant Apgar scores. Am J Obstet Gynecol 1982,144:959-966.
36. Garn SM, Johnston M, Ridella SA, et al. Effect of maternal cigarette smoking on Apgar score. Am J Dis Child 1981;135:503-506.
37. Druzin M. Neonatal depression and birth asphyxia in the low birthweight neonate. Am J Perinatol 1988;5:186.
38. Catlin EA, Carpenter MW, Brann BS, et al. The Apgar score revisited: Influence of gestational age. J Pediatr 1986;109.865-868.
39. Leung GM, Lam TH, Thach TQ, et al. Rates of cesarean births in Hong Kong: 1987-1999. BMJ 2001;28:166-172.
40. Gifford DS, Morton SC, Fiske M, et al. A meta-analysis of infant outcomes after breech delivery. Obstet Gynecol 1995;85:1047-1054.
41. Krebs L, Langhoff-Roos J. Breech delivery at term in Denmark, 1982-92: A population-based case-control study. Paediatr Perinatol Epidemiol 1999;13:431-441.
42. Gardner MO, Goldenberg RL, Gaudier FL, et al. Predicting low Apgar scores of infants weighing less than 1000 grams, the effect of corticosteroids Obstet Gynecol 1995;85:170-174.
43. Burt RD, Vaughan TL, Daling JR. Evaluating the risks of cesarean section: low Apgar score in repeat C-section and vaginal deliveries. Am J Publ Health 1988;78.1312-1314.
44. Starks GC Correlation of meconium-stained amniotic fluid, early intrapartum fetal pH, and Apgar scores as predictors of perinatal outcome Obstet Gynecol 1980;56:604-609.
45. Giacoia GP. Low Apgar scores and birth asphyxia. Postgraduate Medicine 1988;84.77-82.
46. Evans CM, Murphy JF, Gray OP, et al Epidural versus general anaesthesia for elective caesarean section. Effect on Apgar score and acid-base status of the newborn. Anaesthesia 1989;44:778-782.
47. Luo ZC, Karlberg J. Timing of birth and infant and early neonatal mortality in Sweden 1973-95: longitudinal birth register study. BMJ 2001;323:1-5
48. Kirgis CA, Woolsey DB, Sullivan JJ. Predicting infant Apgar scores. Nurs Res 1977;26:439-442.

ACKNOWLEDGMENTS

This study was supported by the Department of Paediatrics and the Clinical Trials Centre, Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China. We are indebted to the reviewer, Dr Barbara CC Lam, for her constructive comments on previous versions of the manuscript

About the Authors

Ms Chong is a PhD candidate in the Clinical Trials Centre and the Department of Paediatrics, Faculty of Medicine, The University of Hong Kong. Dr Yip is a Senior Lecturer in the Department of Statistics and Actuarial Science, Faculty of Social Sciences, The University of Hong Kong Professor Karlberg is Director of the Clinical Trials Centre, Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.

Competing interests: none declared.

• GYNAECOLOGY •

References to "Postmenopausal Osteoporosis".

19. Lindsay R, Hart DM, MacLean A, Clark AC, Kraszewski A, Garwood J. Bone response to termination of estrogen treatment. Lancet 1978;1:1325-1327.
20. Ettinger B, Grady D. Maximizing the benefits of estrogen therapy for prevention of osteoporosis. Menopause 1994;1:19-34.
21. Cauley JA, Seeley DG, Ensrud K, et al. Estrogen replacement therapy and fractures in older women. Study of Osteoporotic Fractures Research Group. Ann Intern Med 1995;122:17-23.
22. Quigley ME, Martin PL, Burnier AM, Brooks P. Estrogen therapy arrests bone loss in elderly women. Am J Obstet Gynecol 1987,156:1516-1523.
23. Ettinger B, Genant HK, Steiger P, Madrig P. Low dosage micronized 17beta-estradiol prevents bone loss in postmenopausal women. Am J Obstet Gynecol 1992;166:479-488.
24. Evans SF, Davie MW. Low and conventional dose transdermal estradiol are equally effective at preventing bone loss in spine and femur at all postmenopausal ages. Clin Endocrinol 1996;44:79-84.
25. Genant HK, Lucas J, Weiss M, et al. Low dose esterified estrogen therapy: effects on bone, plasma estradiol concentration, endometrium and lipid levels. Arch Intern Med 1997;157:2609-2615.
26. Recker RR, Davies KM, Dowd RM, Heaney RP. The effect of low dose continuous estrogen and progesterone therapy with calcium and vitamin D on bone in elderly women. Ann Intern Med 1999;130:897-904.
27. Naessen T, Berglund L, Ulmsten U. Bone loss in elderly women prevented by ultralow doses of parenteral 17beta-estradiol. Am J Obstet Gynecol 1997;177:115-119.
28. Genant HK, Cooper C, Poor G, et al. Interim report and recommendations of the World Health Organization Task-Force for Osteoporosis. Osteoporos Int 1999;10:259-264.
29. Practice Guidelines from the Osteoporosis Society (Singapore). Singapore: Osteoporosis Society, 1998.
30. Black DM, Cummings SR, Karpf DB, et al. Randomized trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Lancet 1996;348:1535-1541.
31. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures. JAMA 1998;280:2077-2082.
32. Peretz A, Body JJ, Durmon JC, et al. Cyclical pamidronate infusions in postmenopausal osteoporosis. Maturitas 1996;25·69-75.
33. Tiras MB, Noyan V, Yildiz A, Yildirim M, Daya S. Effects of alendronate and hormone replacement therapy, alone or in combination, on bone mass in postmenopausal women with osteoporosis: a prospective, randomized study. Hum Reprod 2000;15:2087-2092
34. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA 1999;282:637-645

References continued on page 48.