The following pain management protocol is tiered to ensure a global relevance, recognizing that not all analgesic modalities are available to veterinary practitioners and vary from region to region around the world. Its implementation will be guided by the various analgesic modalities available along with the needs of the individual patient requiring treatment. This protocol is reproduced from the WSAVA Global Pain Treatise, a succinct yet comprehensive review of pain assessment, various pain modalities, and the treatment of various clinically painful scenarios in both dogs and cats. The WSAVA GPC Pain Treatise published in the *Journal of Small Animal Practice* and is available for open access at the GPC pages of **www.wsava.org**.

Pregnant or lactating patients

Very little information is available about the pharmacology of analgesic drugs in dogs and cats during pregnancy and lactation; some information is presented from studies in humans and laboratory species.

Pregnancy

Physiological changes associated with the maternal-placental-foetal unit alter drug pharmacodynamics, pharmacokinetics and distribution to the foetus. The maternal factors that may alter drug absorption are decreased gastrointestinal motility, oesophageal reflux and vomiting; and an increased cutaneous blood flow, which may enhance absorption of transdermally administered drugs. Increased total body water, increased total body fat, reduced serum albumin, altered hepatic enzymatic activity and increased renal function are all factors that may alter the response of pregnant animals to analgesic drugs.

The placental barrier is considered to be a lipoprotein, therefore drugs with high lipid solubility are permeable. Drugs that are polar, ionized, protein-bound or water soluble are less likely to cross the placenta into the foetus.

Opioids: Currently, opioids are commonly used for analgesia in pregnant dogs and cats. Methadone, morphine and hydromorphone are used during pregnancy in humans. Fentanyl, pethidine (meperidine), butorphanol and nalbuphine are more lipid soluble, and therefore may reach higher concentrations in the foeti. Opioids are frequently used preoperatively for caesarian section, and most puppies and kittens are successfully delivered and are vigorous. If the puppies or kittens are depressed after delivery, alongside provision of warmth, stimulation, and oxygen and application of suction as required, a drop of naloxone placed sublingually should reverse these effects; however repeat dosing may be required. Buprenorphine resulted in lack of milk production in animal studies, which may be a problem following casesarian.

NSAIDs: Due to possible teratogenicity and development-interfering effects, it is advised that NSAIDs are not administered to pregnant animals.

Ketamine: Ketamine rapidly crosses the placenta; however, no foetal effects have been observed during organogenesis and near delivery in rats, mice, rabbits and dogs. Ketamine increases uterine tone and should be avoided during pregnancy. An in-depth review of caesarean section in dogs is available.

Alpha$_2$ adrenoceptor agonists: Reduce uterine blood flow. Xylazine should not be used during pregnancy. Evidence regarding the use of medetomidine and dexmedetomidine in dogs and cats during pregnancy is not available.

Local anaesthetics: Generally considered to be safe and non-teratogenic – they are highly recommended.

Herbal analgesic medications: Due to a lack of information, these should be avoided.

Lactation

Characteristics of a drug which would facilitate secretion into milk are high lipid solubility, low molecular weight and the non-ionized (charged) state. It is estimated that the neonate receives approximately 1% to 2% of the maternal dose of a drug. Where analgesia is essential and there are concerns for potential toxicity in the offspring, the milk should be pumped and discarded for 12 h before resuming suckling, and puppies and kittens should be bottle fed.

Opioids: The lipid solubility of the opioid influences its appearance in the milk; pethidine (meperidine) > sufentanil > fentanyl > morphine > hydromorphone, therefore a more hydrophilic opioid, such as morphine, may appear in smaller amounts than a more lipid-soluble opioid such as pethidine. It is recommended that suckling occurs after peak levels of the opioid have waned. Pethidine (meperidine), butorphanol, nalbuphine are not recommended. Where opioids are selected for analgesia, mothers and offspring should be carefully observed and monitored for signs of opioid adverse effects.

NSAIDs: Most NSAIDs are not lipid soluble, are highly protein bound to plasma proteins and may be present to a great degree in an ionised form in the plasma. It has been suggested that a single use of an NSAID is safe in nursing human mothers. Until studies are performed in lactating cats and dogs, NSAIDs should be administered with caution and as single doses only. Hemorrhage is a potential concern following the administration of non-COX selective, or COX-1 selective NSAIDs immediately after caesarian section, or even natural birth. In general, paracetamol is safe for use in dogs, but cannot be administered to cats.

Local anaesthetics: Lidocaine and its metabolites have low lipid solubility; at therapeutic doses the concentrations in milk are small and unlikely to be a risk. Incision line infiltration is highly recommended.

Ketamine: No reports on passage into breast milk were found, but it is expected to pass into breast milk.

Herbal analgesic medications: Due to a a lack of information, these should be avoided.

For additional pharmaceutical dosing information, see the dosing tables in the WSAVA GPC Treatise at www.wsava.org

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