DECISION ANALYSIS IN

CANINE HEARTWORM (*Dirofilaria immitis*) TESTING

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The performance characteristics of diagnostic tests are usually described in terms of sensitivity and specificity. Although this information is useful for estimating a test's predictive value, it provides little information to guide its use in clinical practice. A case in point is canine heartworm disease, a potentially severe but treatable disease whose signs mimic scores of other diseases. Infections may be microfilaremic or amicrofilaremic (occult), the latter frequently diagnosed with the aid of serologic tests for the detection of *Dirofilaria immitis* antigen. When faced with clinical signs compatible with occult heartworm infection three options typically exist: (1) rule-out other diseases on the differential list first, (2) treat empirically for heartworm infection regardless of the result of serologic testing, or (3) let the results of a heartworm serodiagnostic test guide treatment decisions. Although commercially-available antigen detection kits are good, none are 100% sensitive and specific (Brunner et al, 1988; Courtney and Cornell, 1990). Therefore we pursue other diseases when the probability of heartworm disease is low, treat empirically when the probability of heartworm disease is high, and test when the probability is intermediate. But how high is high and how low is low? The best management option may not be readily apparent because of the number of interactive variables that must be considered.

CONSTRUCTION OF A HEARTWORM DECISION TREE

Figure 1 depicts a decision tree for clinical management of a suspected case of occult heartworm disease. The tree was created using *D-Maker®* (Digital Medicine, Inc., Hanover, NH) on a *Macintosh* microcomputer. Prognostic values were derived from studies on the clinical course of advanced heartworm disease (pulmonary embolism or right heart failure) by Calvert and Thrall (1982) and Hoskins et al (1985). With the exception of death, whose utility is 0, all other probabilities and utilities are variables whose values can change for the purpose of sensitivity analysis. All variables were assigned a baseline value for initial fold back of the tree. A description of branches, specific nodes and their associated variables follows.

Rule Outs. This branch represents the decision to rule out other diseases on the differential list before considering heartworm disease. This option might be chosen if the likelihood of heartworm disease is considered to be low either because it is uncommon in the area or because of characteristics of the case. The prior probability (pD) of heartworm disease was given a baseline value of 20% to reflect the prevalence of infection among dogs serologically tested at this College's diagnostic laboratory. This baseline value for pD is used throughout the tree. The utility of untreated heartworm disease (Htwm) is no greater than 5%, reflecting the likelihood of recovery with supportive therapy only (Calvert and Thrall, 1982). The prognosis for recovery from diagnosis and treatment of other diseases on the differential list (OtherRx) was set at 50%, equal to that assigned to heartworm disease (HtwmRx).

Htwm Rx. This branch represents the decision to treat the case as if it were heartworm, even if a serodiagnostic test is run and the result is negative. This alternative might be chosen when the likelihood of heartworm disease is high, due either to high prevalence in the area or characteristics of the case. If the dog is suffering from heartworm disease (Heartworm) then there is a probability of complications from thiacetarsamide treatment (pUHtwmRx) leading to death (utility = 0) in no more than 20% of cases (Calvert and Thrall, 1982; Hoskins et al, 1985). The same authors reported that at least half of those cases without treatment complications

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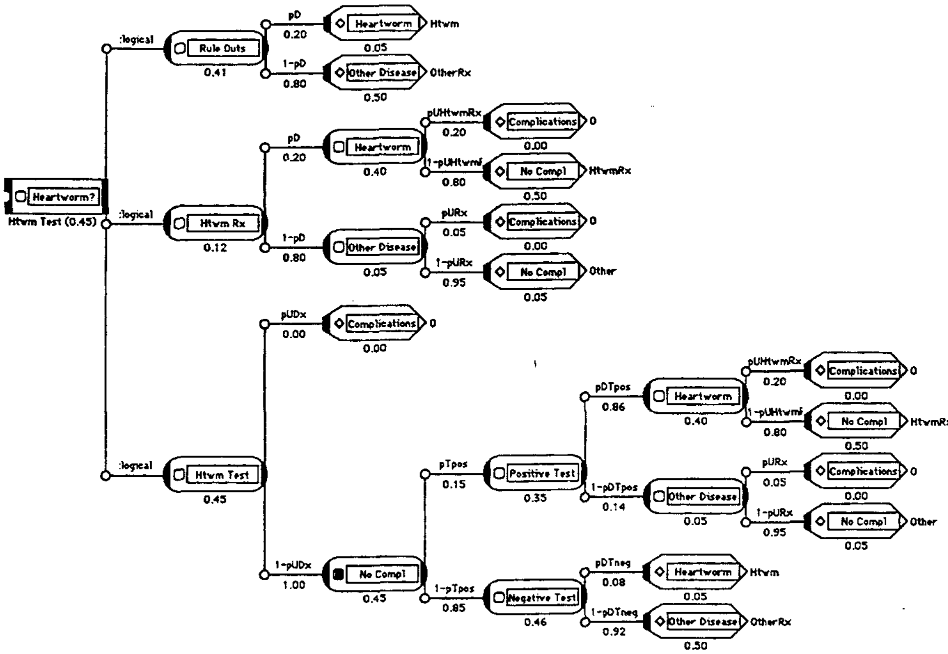

Figure 1. Heartworm decision tree based on properties of the *DiroChek®* antigen detection test.

will recover from heartworm disease (HtwmRx). In the event that the patient is not suffering from heartworm disease (Other Disease) then there is still a chance (no greater than 5%) of an unfavorable reaction to thiacetarsamide heartworm therapy (pURx) leading to death. The prognosis for recovery from non heartworm disease without specific therapy (Other) is no greater than 5%, as for untreated heartworm disease.

Htwm Test. The third branch of the tree represents the decision to let the results of a heartworm test guide subsequent management of the case. The probability of complications from the testing procedure (pUDx) is included in the tree only for completeness. Realistically, however, there is no risk associated with the act of heartworm serologic testing. The alternate path includes several formulas, embedded in the "No Compl" probability node, to calculate the likelihood of a positive test (pTpos) or negative test (1-pTpos), and the Bayesian probabilities that the dog is or is not infected given a positive (pDTpos, 1-pDTpos) or negative (pDTneg, 1-pDTneg) test result. The expressions pDTpos and 1-pDTneg correspond to the positive and negative predictive values of the test. The likelihood of heartworm disease given a positive or negative test is calculated from disease prevalence (pD), test sensitivity (Sens) and specificity (Spec). The latter were set at 65% and 97.3% respectively, based on characteristics reported for the *DiroChek®* heartworm test for 140 dogs with occult infections and 183 dogs free of heartworms and their microfilaria (Courtney et al, 1990). *DiroChek* is used at this College's diagnostic laboratory.

RESULTS OF DECISION TREE ANALYSIS

A fold back of the heartworm decision tree (Figure 1) reveals that use of the *DiroChek* diagnostic test provides the highest expected utility (0.45) followed by rule out of other diseases (0.41) and empiric heartworm therapy (0.12). This does not mean that performance of a diagnostic test will always lead to a favorable outcome under the baseline conditions. Risk profile analysis reveals that the expected utility will be >0.45 88% of the time if a diagnostic test guides case management versus 80% and 16% of the time when rule outs and empiric therapy are pursued, respectively. The performance of another serodiagnostic test, *CITE®*, can be compared by substituting corresponding sensitivity and specificity values of 62.1% and 100% respectively (Courtney et al, 1990) and folding back the tree. The expected utilities of management strategies are identical to those obtained with the *DiroChek* test. Thus, choice of *DiroChek* versus *CITE* can be based on criteria other than test performance, such as cost, convenience or user preference without jeopardizing the quality of patient care.

There is a direct relationship between worm burden and test sensitivity (Courtney et al, 1990). The *DiroChek* testing band (range of prevalence values over which testing is the preferred strategy) was evaluated over a range of sensitivities from 53.2% to 100%, corresponding to increasing worm burdens. The testing band ranged from 5% to 70% for detection of infections with 1-2 worms, to 5% to 100% for >20 worms. Thus, when the likelihood of infection is below 5% the rule out of other diseases is the preferred option. If the likelihood of infection is greater than 70% then heartworm therapy should be instituted, even if test results are negative. Test results should guide treatment decisions in all other cases.

CONCLUSION

One of the principal benefits of decision tree analysis of heartworm tests is that sensitivity of a choice to its underlying assumptions can be tested in a clinical context. The preceding analysis focused on heartworm test properties, but the analysis could just as easily have focused on other variables, such as prognosis. Pulmonary thromboembolism is an inevitable consequence of successful adulticide therapy (Anonymous, 1990). However, the decision to incorporate prognostic data from dogs in advanced stages of heartworm disease into the model probably represents a "worst case scenario." In general, as the efficacy of heartworm therapy increases, both the testing and treatment thresholds (prior probability at which either testing or empiric therapy is the best choice) decreases.

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