Causes

- Primary IMT can be primary or secondary.
  - Primary IMT is an autoimmune disorder with production of antibodies directed against normal platelet antigens.
  - Secondary IMT occurs in association with infection, drug therapy, neoplasia, poly-immune syndromes, or complication of platelet transfusion.\(^1\)
    - Vaccination as a cause of secondary IMT is possible.\(^3\)

Pathophysiology

- IMT occurs when an animal’s immune system produces antibodies that bind directly or indirectly to its own platelets; this leads to accelerated platelet destruction by the mononuclear phagocyte system.\(^4,5\)
  - Primary IMT is usually mediated by immunoglobulin G directed against platelet antigens.
membrane glycoprotein IIb/IIIa.¹
- Secondary IMT occurs when antibodies target nonself antigens adsorbed onto the surface of platelets or when immune complexes become bound to platelet surfaces.⁶

History & Clinical Signs
- Travel, vaccination, medication, and tick prevention history are important in cases of thrombocytopenia to rule out causes of secondary IMT.
- Patients with IMT are often subclinically affected or are presented with clinical signs attributed to bleeding.
  - The GI tract can be a site of hemorrhage in these patients.
  - Intracavitary bleeding is uncommon.
- Systemic clinical signs are often seen only if a secondary anemia is present.
  - Some dogs without anemia will be presented for nonspecific clinical signs such as lethargy or anorexia.

Physical Examination
- Findings can include epistaxis, gingival bleeding, petechiae and ecchymoses (Figure 1), bruising, hematochezia, melena, and hematuria.
- An ophthalmologic examination is recommended to look for changes such as hyphema, anterior uveitis, and retinal hemorrhage.
- Clinical signs of anemia may be present.
  - This can include pale pink mucous membranes, weakness, tachycardia, bounding pulse, heart murmur, and tachypnea.

DIAGNOSIS

Definitive
- Diagnosis of thrombocytopenia is by manual platelet count.
- In order to diagnose primary IMT, all non-immunologic and secondary causes of IMT must be ruled out.
  - Diagnosis is confirmed when response to immunosuppressive therapy is observed.

Differentials
- Decreased platelet production: drugs, infection, irradiation, myelonecrosis, myelofibrosis, neoplasia⁴
- Platelet destruction: idiopathic, drugs, infection (tick-borne disease), neoplasia, platelet transfusion, systemic immune-mediated disease (systemic lupus erythematosus)⁴
- Platelet consumption: blood loss, disseminated intravascular coagulation, endotoxemia, vasculitis⁴
- Abnormal platelet distribution or sequestration: splenomegaly, endotoxemia⁴

Laboratory Findings
- Serum chemistry panel and coagulation profiles are often normal in cases of primary IMT.
- Hematuria may be evident on urinalysis.
- Cystocentesis should be avoided in patients with thrombocytopenia.
- CBC can give an automated platelet count.
  - The normal canine platelet count is 143 to 448 × 10³/µL.
  - If platelet clumping is present, a false
Thrombocytopenia may occur.

• All cell lines (WBCs, RBCs, platelets) should be evaluated.
  – Decreases in multiple cell lines can be associated with decreased cell production because of disease at the bone marrow level.
• A CBC with reticulocyte count should be performed to look for anemia secondary to blood loss from IMT or concurrent immune-mediated hemolytic anemia.

Manual platelet count
• The feathered edge and blood smear body should be scanned for an area of well-distributed platelets (Figure 2, previous page).
• The number of platelets per 1000× field should be estimated.
  – At least 5 to 10 fields should be evaluated and the average number of platelets/hpf calculated. 4
• The conversion factor of 1 platelet/1000× field equals 20 000 platelets/μL can be used to calculate the platelet count. 4
• Platelet counts in cases of IMT are usually <50 000/μL and often <10 000/μL.
  – Megakaryocytes may be present. 4,5
• With a mean platelet count of approximately 150 000/μL, healthy greyhounds can have lower platelet concentrations than other breeds. 1,4
• Healthy Cavalier King Charles spaniels can have a hereditary macrothrombocytopenia, with the platelet count in affected dogs ranging from 25 000 to 100 000/μL. 4

Imaging
• Thoracic radiographs are recommended to evaluate for thoracic infection or neoplasia.
  • These are usually normal in animals with primary IMT.
• Abdominal ultrasonography can evaluate for the presence of abdominal bleeding, infection, or neoplasia.
  • Homogenous splenomegaly can be seen with primary IMT, especially if secondary anemia is present.
  • If diffuse splenic mottling is present, fine-needle aspiration may be recommended once the platelet count is adequate.

Infectious Disease Testing
• Ehrlichiosis, Rocky Mountain spotted fever, anaplasmosis, histoplasmosis, leishmaniasis, and distemper have been associated with secondary IMT. 4
• Tick-borne disease testing is recommended; complete panels include both polymerase chain reaction (PCR) and serology.
  • PCR is often positive early in active disease.
  • Negative PCR results do not rule out infection, and a positive serologic test does not necessarily confirm disease.
  • Serology is often positive after PCR because it takes time for antibodies to be produced.

Advanced Testing
• The benefit of bone marrow examination in cases of suspected IMT is equivocal.
  • Normal-to-increased numbers of bone marrow megakaryocytes may not be a consistent finding. 2
• Flow cytometric assays to detect antiplatelet antibodies are available but are not commonly performed in the clinical setting.
  • A positive test implicates an immune

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TREATMENT

Emergency Treatment

- Many IMT patients can be treated on an outpatient basis, but it is important for owners to monitor for signs of bleeding or anemia and to avoid trauma or injury.
- Patients are often hospitalized initially for monitoring or if they require a blood transfusion because of secondary anemia.
- Although uncommon, fatal bleeding into the brain, lungs, or spinal cord is possible.
- Bleeding risk increases as platelet count decreases below 20,000/μL, although spontaneous bleeding typically does not occur, even with marked thrombocytopenia.
- Platelet transfusions are usually reserved for cases of uncontrollable or life-threatening bleeding.
- Blood or platelet transfusions do not significantly raise the platelet count but can be used in an attempt to stop life-threatening bleeding.
- Vincristine (0.5–0.7 mg/m² IV once) may have some immunosuppressant activity and may induce thrombocytosis within 7 days.
- A peripheral catheter should be used for administration as extravasation of vincristine can cause skin necrosis.

Long-Term Treatment Options

- Immunosuppressive agents
  - Prednisone (1–2.2 mg/kg q12h) is the initial immunosuppressive therapy of choice for dogs with IMT; the majority of dogs will show a significantly increased platelet count within 7 days.
  - Additional immunosuppressive medications are usually needed only if significant prednisone side effects are present.
  - Azathioprine (2 mg/kg q24h, tapered to q48h after 1 week) has been described as an immunosuppressive option, but studies are lacking.
  - This medication can take more than 4 weeks to become effective.
  - Cyclosporine (5–10 mg/kg divided q12h) has been shown to be an effective immunosuppressive medication in dogs with IMT.
  - Mycophenolate mofetil (10 mg/kg PO q12h) has been reported to have variable response rates as an immunosuppressive medication for canine IMT in small studies.
  - This drug can be considered in refractory cases.
  - Leflunomide has shown efficacy in anecdotal reports, but studies on this immunosuppressive medication for IMT are limited.
- Melatonin (3 mg PO q12h) has been suggested anecdotally (based on clinical response in humans) to increase platelet counts in cases of IMT.
- Human IV immunoglobulin (0.28–1.5 g/kg IV) has been shown to significantly reduce platelet recovery time and hospitalization when combined with prednisone given slowly over 4 to 12 hours.
- Human IVIG should be used with caution in patients with renal dysfunction.
- Patients should be monitored for volume overload and hypersensitivity reactions.
- Splenectomy has shown variable response rates but can be considered in refractory cases.

FOLLOW-UP

- Immunosuppressive medications are tapered slowly once the platelet count has normalized.
- Prednisone is usually tapered first as many dogs will have significant side effects from this medication.
• If a second immunosuppressive medication is given, it is routinely tapered after the prednisone.
• Medication is generally reduced by about 25% every 3 to 4 weeks.
• Medications are usually tapered 1 medication at a time if multiple medications are given.
• The minimum duration of treatment is usually 4 to 6 months.
• The most common reason for treatment failure is an inadequate duration of therapy.
• Patients should be evaluated via a manual platelet count 1, 3, and 6 months after treatment has been discontinued and then every 6 to 12 months for life to monitor for disease relapse.
• A manual platelet count is usually performed before each medication adjustment.

References

IN GENERAL
Relative Cost
► $$$-$$$$

Prognosis
► The prognosis for patients with primary IMT can be good with reported long-term mortality rates of 10% to 15%.<sup>2,5</sup>
► Relapse has been reported in 9% to 40% of cases.<sup>2,5,8</sup>
► Poor prognostic indicators may include melena or a high blood urea nitrogen concentration.<sup>12</sup>

COST KEY
$ = up to $100
$ = $101–$250
$$$ = $251–$500
$$$$ = $501–$1000
$$$$$ = more than $1000