Experimental FIP treatment application

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1. General presentation

FIP is a fatal disease affecting about 1% of cats worldwide, it stem from a common virus that occasionally mutate in the lethal form with high mortality rate within days or weeks.

There is no know official cure, but Dr pederson developed a cure that showed 80% of remission in a clinic trial in 2019. The disease being rare, the research is very slow and it's not very likely the cure is going to be on the market in the next years.

However some labs can manufacture the cure, but it's very expansive, 1000$ to 5000$ depending on the brand and the cat's weight, and one of the only way to get it is through a facebook group where most of the research happen with owners who attempt the cure at home and post the result on the group. Due to the drugs price, they usually have to go through a funding process, with self organization of owners to attempt at saving their cat in a peer 2 peer manner.

The process is very daunting, owner have to figure out dosage, brand, find supplier, organize a funding, going through different sites and facebook group, with some volunteering admin who try to help with the whole process, with only a few days before the disease become terminal.

The disease progress fast, with usually the cat not eating or drinking at the first stages, and symptoms progressing very fast which require intensive care only to keep the cat hydrated and fed, avoid anemia and other problems.

The identity of supplier has to be protected because of the illegal nature of the drug, and most vet won't get involved with it, or don't even know about it, and would recommend euthanasia upon diagnosis.

2. Overall process

I. Confirming the diagnosis

The disease is not easy to diagnose, the symptoms can be common with other pathology, it generally needs some advanced analysis on blood sample, or abdominal liquid sample for the wet form, and it's very often misdiagnosed either with false positive or negative.

II. Establishing treatment

There are different brands of treatment, the most reputed one is mutian, but it is also the most expansive, other cheaper brands exist such as shire, SAK, that are cheaper. It exist in pills or injection. There is not much information about which one has the best success rate, or which supplier are the more reliable, Owner have to figure it out from admin or other users feedback on the group.

Additionally to this, they need to compute the dosage depending on cat weight, type of FIP (wet, neuro, occular), establish the price for the 84 days of treatment, using some dull form from different websites for each brand.

III. Launching a funding

As the drug is very expansive, the course of action is generally buying the first dose to keep the cat alive, and then organize a go fund me through the facebook group. Some users also manage to lend each others the first doses to get the treatment started and giving more time to organize and put the fund together to pursue the full treatment which is 84 (12 weeks) days long.

Some users try to keep some emergency doses and making them available to users within a certain distance range to get the treatment started as soon as possible.

IV. Following the 84 days treatment

The treatment is 84 days long, with always risks of relapse and very little openly available information on how the disease is supposed to progress or relapse, it often involve posting blood samples or observation on the group to get feed back from other user experience or some vet who try to help figure out the situation.

There is no real structured tracking of all cases, users just post their result and evolution on the group and help each others with their own experience and the little research available so far.

3. Application steps

1) Registering cats with the relevant information, weight, age, breed, initial symptoms, date of the first symptom, diagnosis, and all relevant information at the start of the process.

2) Getting information on confirming diagnosis or not.

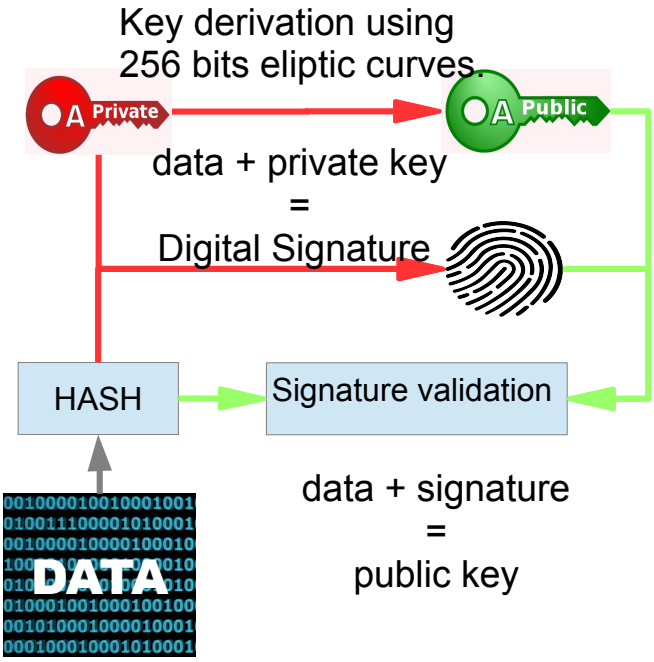
3) Registering supplier, or peer users with available dose, which brand are available, with some user rating and feed back on the result.

4) Suggesting the available option to the owner to get the treatment started with the available supplier or other users who can have available dose in reachable distance, evaluating the doses, price, and options for crowd funding.

5) Updating new information and status alongside the treatment.

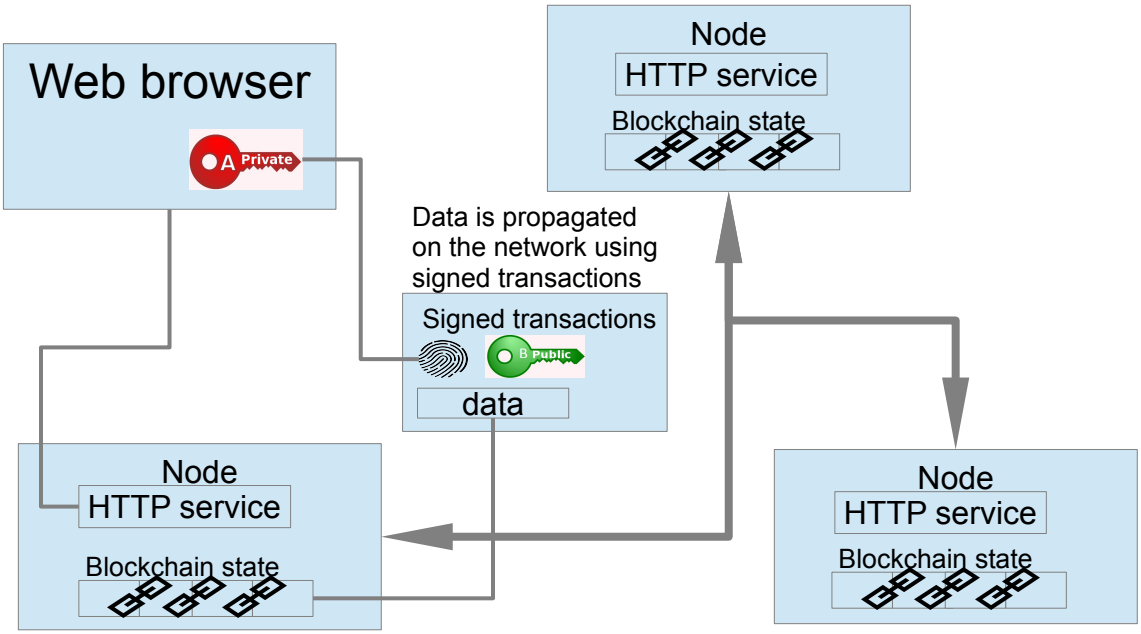
4. Blockchain solution

Unlike classic web applications, blockchain use asymmetric cryptography to identify users, the private part of the keys is kept by users, and a public key is derived from the private key to be used as identity on the network.



Each new data is added to the blockchain using cryptographic signature to prove user identity that can be verified by all users on the network.

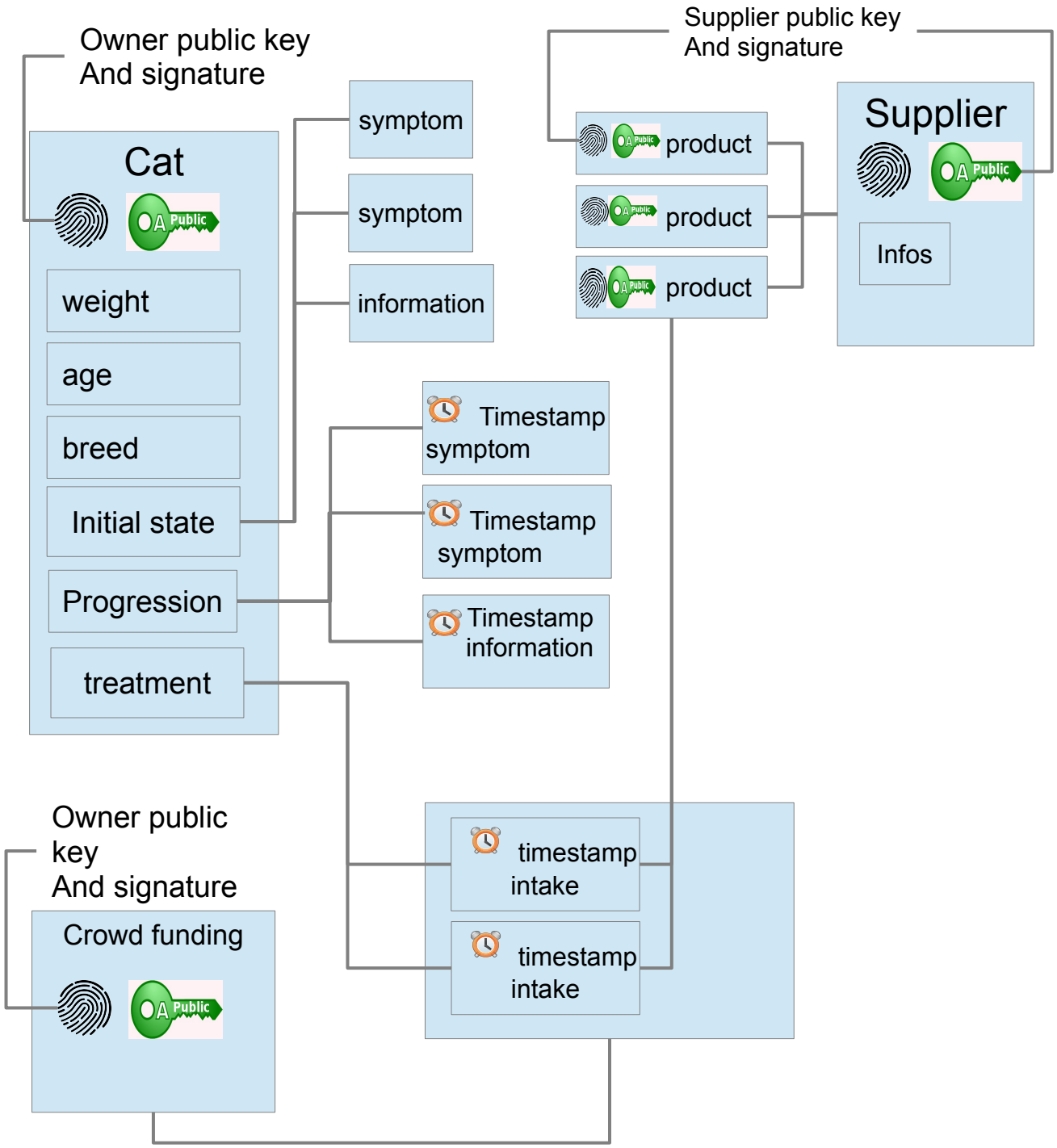
New data is propagated on the network as transaction that either add new data or link existing data together as a data graph.



5. General data graph

Owner register their cat with initial symptom, weight, age, breed, using their private key and select a treatment option, then add the treatment intake and new information along the course.

Supplier register themselves on the network using their private key and publish available stocks.



Treatment intake can be traced back to a supplier using crytographic signature.

Crowd funding can be organized either via blockchain tokenization or external site like go fund me.

The format for the symptoms and information relative to the cat need to be determined for ease of collecting the relevant information.

HTML user friendly front end can be stored on the blockchain to display page and information and manage their identity key. The data can be queried using HTTP protocol.

6. Symptoms and diagnosis

I. merck book

i. Common symptoms

(a) Cat history

- is the cat in contact with other cats or alone, coming from cattery or shelter

ii. effusive

(a) Fluid analysis

- sterile
- viscous ropey
- yellow straw colored
- may contain fibrin strands
- high specific gravity (1.017- 1.047)
- high protein content (5 – 12g/L)
- mixed inflamatory cells (1,600 to 25,000/μL)
- Mixture of neutrophils,lymphocite, macrophages, fewer mesothelial cells in a granular, eosinophilic background are seen on wright-stained smears.

(b) Blood analysis

- Gamma globulin > 32% is 100% indicative of FIP
- albumin content > 48% or albumin albumin to globulin ratio > 0.81 100% ruling out FIP
- 50% of cats have increased total plasma protein (>7.8g/L)
- hyperglobulinemia (> 4.6 g/dL), hypergammaglobulinemia
- Serum protein electrophoresis may show increase in alpha2-globulin and polyclonal (occasionally monoclonal) increase in gamma globulin
- Hematologic changes show a neutrophilic leukocytosis (> 19,000 cells/μL)
- relative lymphopenia (> 1,500 cells/μL)
- 40 to 50% of cats have progressive normochromic,normocytic anemia (PCV < 24%) nonregenerative if FeLV or haemobartonella felis.
- Coronavirus titer is usually increased (1:100 to 1:3,200) some have very low titer.

(c) Differential diganosis

- Differentiated from ascite due to congestive hearth failure or hypoproteinemia (renal or liver disease, glomerulonephritis, malabsoption, parasitism), bacterial peritonitis, pansteatitis, toxoplasmosis, tuberculosis, pregnancy and trauma.

- Pleural effusion include cardiac insufficiency, neoplasia (lymphoma), pyothorax, chylothorax,cryptococcosis, lung lobe torsion, diaphragmatic hernia, trauma (hemothorax)

iii. Non effusive

- Serum protein abnormalities
- Debilatated cats
- non responsive fever
- weight loss
- multisystemic signs (occular and CNS signs)
- increased coronavirus titer
- Opthalmic examination 40% of non effusive have ocular lesion
- clinical chemistry can indicate failure in liver, kidney or pancreas
- If meningeal involvement, CSF analysis may show increased protein content (90 – 2,000 mg/dL) and increased number of cells (90 – 9,250 cells/μL) predominantly neutrophils.

II. Dr pederson study

i. *Monitoring during initial treatment period*

They were then monitored every 12 h for temperature, appetite, activity, urination and defecation. Blood was also taken at 1–3 day intervals to evaluate hematocrit, total protein, bilirubin, white blood cell count and white cell differential count.

Ascites samples were collected at entry and one or more day intervals for as long as possible and tested for the levels of FIPV 7b RNA transcripts by quantitative (q)RT-PCR (IDEXX Molecular Diagnostics)

daily logs on body temperature, activity, appetite, defecation and urination, and weekly body weight measurements.

A CBC and serum chemistry panel were done at monthly intervals by local veterinarians.

Gross signs of ocular disease consistent with underlying FIP was confirmed by ophthalmoscopic examination in three of the 31 cats (CT56, CT65, CT71). Two cats (CT71, CT80) were either reluctant or no longer able to jump to higher places,

suggestive of neurological involvement.

ii. Treatment outcome

Fever usually resolved within 12–36 h (Figure 2), concurrent with a marked daily improvement in appetite, activity levels and weight gain. Abdominal effusions rapidly disappeared over a 1–2 week period starting around 10–14 days post-treatment. Cats with thoracic effusions were usually dyspneic upon presentation to private veterinarians, prompting removal of pleural effusions prior to coming to UC Davis. Residual dyspnea and thoracic effusion responded rapidly to treatment and were no longer apparent after 7 days. Jaundice slowly resolved over 2–4 weeks, in parallel with decreasing hyperbilirubinemia. Signs of ocular disease began to clear within 24–48 h and were no longer apparent outwardly or by ophthalmoscopic examination by 7–14 days. Enlarged mesenteric and ileo/cecal/colic lymph nodes slowly decreased in size over the course of the treatment. All 26 cats appeared outwardly normal or near normal in the estimation of the owners after 2 weeks of treatment. The emphasis of treatment after 2 weeks was on monitoring several blood test parameters. Key values included packed cell volume (PCV), total white blood cells, absolute lymphocyte count, total serum protein, serum globulin, serum albumin and albumin:globulin (A:G) ratio.

Disease relapses in 2/8 cats (CT57, CT71) were clearly of a neurological nature with high fever and severe posterior ataxia and incoordination, while disease relapses in the remaining six cats consisted mainly of fever, anorexia and lack of activity.

24 surviving cats will be carefully monitored for any return of disease signs and periodically tested for total protein, globulin, albumin and A:G ratios for the first year.

iii. Favorable treatment response indicators

The simplest long-term measure of treatment efficacy was body weight. Weight gains of 20–120% occurred during and following treatment, even in cats 1 year of age and older at disease onset. Younger cats also appeared to grow in stature at an increased rate, as independently noted by owners. These post-treatment surges in growth indicated that FIP was subclinical in many of the cats for some time prior to diagnosis and had affected growth. CBCs and a chemistry profile also proved helpful in monitoring the later effects of treatment and observing for possible drug toxicities.

(a) CBCs

Cats presented with elevated white blood cell counts, which dropped to normal levels within the first 2 weeks of treatment (Figure 3a). Lymphopenia was noted at the time of entry and resolved over the first week of treatment (Figure 3b). A mild to moderately severe anemia was observed at entry, as reflected by the packed cell volume (PCV) (Figure 4). PCVs did not return to normal levels until after 6–8 weeks of treatment. Therefore, absolute total white cell and lymphocyte counts were only of value during the first week of treatment, while the PCV gave a more accurate picture of treatment progress over the first 8 weeks.

(b) Changes in serum proteins

Cats with FIP frequently presented with higher than normal total serum protein concentration, high serum globulin, low serum albumin levels and a low A:G ratio (Figures 5–7). Abnormal serum protein values improved progressively and reached normal levels after 8–10 weeks of treatment (Figures 5–7). The level of total protein was the least informative, as indicated by the weak R2 value (0.1883) for the trend line (Figure 5). However, a dramatic and transient rise in total protein levels occurred 3 weeks into treatment (Figure 5). It was associated with an increase in serum globulins (Figure 6a) and occurred at a time when abdominal effusions were rapidly resolving.

Plasma globulin levels rose during the first 3 weeks of treatment, peaked, and then slowly dropped to a maximum reference value of 4.5 g/dl or lower by week 9 (Figure 6a). Although globulin levels over time appeared to indicate the status of treatment, the low R2 value (0.3621) made this a less reliable indicator of treatment progress.
The levels of albumin in serum of the 26 cats treated for at least 12 weeks were usually low (⩽3.2 g/dl) at the time treatment was started (Figure 6b). Albumin levels then increased slowly and reached normal levels at 8 weeks. The trend line for this rise in

albumin had a strong R2 value (0.79), making serum albumin levels, as well as PCV, a good indicator of treatment progress. As is expected, the A:G ratio showed an equally strong trendline over time and reached a level above 0.70 at around week 8 of treatment (Figure 7).

(c) Decrease in viral RNA levels in cells from ascitic fluid associated with treatment

Sequential ascites samples were collected from eight cats over the first 2–9 days of antiviral treatment and tested for levels of viral RNA by qRT-PCR (Table 2). Whole effusions, or their cell fractions, were the most reliable sources of FIPV RNA. Viral RNA levels decreased, often to undetectable levels, by 2–5 days in 7/8 cats. Only one cat (CT54) failed to show a significant drop in viral RNA levels over a 9 day period.