Can laboratory investigations help us to decide when to discontinue larval therapy?

- **Objective:** This study investigated retrospectively whether three laboratory investigations — testing for leucocyte levels, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) — can be used to guide the decision of when to discontinue larval therapy.
- **Method:** Between 1999 and 2002 we administered larval therapy to 16 inpatients. In all cases the decision to discontinue therapy was a clinical one made by the surgeon who headed the trauma department. We retrospectively analysed laboratory investigations, testing for leucocyte levels, CRP and ESR, on the first and last days of therapy to ascertain if the results could have guided this decision.
- **Results:** The median leucocyte count on the first day of larval therapy was 10.5 (x 10e9/L) compared with 8.4 (x 10e9/L) on the last day (Friedman test: $p<0.05$). CRP and ESR showed a non-significant tendency towards lower values.
- **Conclusion:** Although the methodological limitations of this open-label non-comparative cohort study preclude a definite conclusion, we believe that laboratory investigations, particularly leucocyte count, can guide the decision of when to discontinue larval therapy. However, this objective parameter cannot replace clinical judgement.
- **Declaration of interest:** None.

larval therapy; maggots; leucocyte count; C-reactive protein; erythrocyte sedimentation rate

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Larval therapy was introduced in 1929 for the treatment of osteomyelitis and pyogenic infection.[1] Opposition from patients, complications of using non-sterile maggots (tetanus and gangrene), together with the introduction of antibiotics and improved aseptic technique, almost completely removed maggots from the therapeutic arsenal, although some case reports were published.[2-4] But the development of antibiotic-resistant bacteria led to larval therapy making a comeback in the 1980s.[5-7]

Clinical observations[8] indicate that larval therapy:

- Accelerates cleansing
- Combats infection
- Hastens the removal of necrotic tissue without damaging healthy tissue beneath
- Prevents (further) amputation.

It can facilitate rapid debridement,[9] although treatment times vary from 1–94 days.[10,11]

The literature suggests placing a maximum of 10 maggots per cm^2,[12] or using calculators such as the LarvE Calculator (SMTL, Bridgend, UK).[13] However, the size of the wound and amount of necrotic tissue determine the number of maggots required to achieve rapid debridement. It is often not clear when therapy should be discontinued, other than when 'there is complete debridement'.

Hersh et al.[14] showed that the extent of closure of infected postoperative deep sternal surgical wounds, treated early with topical negative pressure (TNP), is indicated by the level of plasma C-reactive protein (CRP), with a median CRP level at closure of 45mg/l.[15]

Guided by these studies, we explored, through a retrospective open-label non-comparative cohort study, whether the clinical decision to discontinue larval therapy can be confirmed by laboratory investigations, particularly significant reductions in leucocyte count, CRP levels and erythrocyte sedimentation rate (ESR).[15] We wanted to see if raised levels correlated with infection. We also used routine laboratory tests, including haemaglobin, haematocrit, sodium and potassium ions and creatinine tests.

Method

In 1999–2002, 16 patients received larval therapy at Leiden University Medical Centre in the Netherlands (Table 1). Locally, the most frequent indication for the therapy is osteomyelitis. It was initiated after surgical debridement and antibiotic therapy had failed. All patients gave informed consent.

Of the wounds, 50% had a multivariate aetiology:

- Trauma (50%)
- Diabetes mellitus (38%)
- Arterial disease (38%)
- Rheumatoid arthritis (13%)
- Steroid use (13%)
- Venous insufficiency (6%)
- Meningococcal sepsis (6%).

In all cases a clinical decision was made to discontinue treatment if there was complete debridement.

All wounds eventually responded to the therapy and healed within six months. Three patients died:

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Table 1. Characteristics of the patients treated with sterile maggots

Patient no.	Sex	Age (years)	Diagnosis	Region of therapy	Underlying condition	Period of larval therapy (days)	Technique: net or Biobag	No. of maggots applied	No. of maggot changes
1	M	50	Osteomyelitis	Lower leg	Vascular disease	32	Net	800	9
2	M	60	Osteomyelitis	Knee joint	Vascular disease/DM	12	Net	1000	4
3	M	41	Osteomyelitis	Both feet	Trauma	28	Net	2900	7
4	M	81	Osteomyelitis	Femur	Trauma/steroid/DM/ vascular disease	28	Biobag	550	8
5	F	62	Osteomyelitis	Lower leg	Trauma/vascular dis.	20	Biobag	360	6
6	M	70	Osteomyelitis	Lower leg	Trauma/DM	25	Biobag	260	6
7	M	33	Osteomyelitis	Lower leg	Trauma	37	Biobag	500	10
8	M	59	Osteomyelitis	Elbow	Trauma	24	Biobag	240	6
9	M	38	Osteomyelitis	Heel	DM	83	Biobag	780	21
10	M	50	Necrotising fasciitis	Neck/head	RA/trauma	13	Biobag	560	4
11	M	46	Necrotising fasciitis	Abdomen/ perineal region	Scrotal abscess	19	Biobag	1200	5
12	F	88	Soft-tissue infection	Upper leg	Trauma	27	Biobag	450	8
13	M	51	Soft-tissue infection	Upper leg	Trauma/vascular dis.	13	Biobag	100	4
14	M	54	Gangrene	Stump (lower limb)	Vascular disease/ DM	11	Net	2000	3
15	M	16	Gangrene	Both hands and feet	Meningococcal sepsis	27	Biobag	2100	8
16	M	61	Chronic ulcer	Lower leg	Venous insufficiency DM/RA/steroid use	34	Biobag	1000	10
Average		**54**				**27**		**925**	**7**

DM=diabetes mellitus, RA=rheumatoid arthritis

one due to a traffic accident and two of underlying disease (cancer and autoimmune vasculitis).

Patients only received standard antibiotic therapy if clinical signs of infection were present, such as necrotising fasciitis or meningococcal sepsis.

After adequate debridement with larval therapy, most wounds were treated with TNP and split-skin grafting.[16,17] For the larval therapy:

- Average treatment time was 27 days (range: 12–83)
- An average of seven dressings was used (range: 3–21)
- Almost 15,000 maggots were used (average per patient: 925 maggots; range: 100–2900).

Four patients used the net technique. The rest had Biobags (Polymedics Bioproducts, Peer, Belgium).

Laboratory investigations were performed on the first and last day of treatment (Table 2).

Results

For CRP and ESR, there was no significant difference between values on the first and last day, although there was a trend towards lower values.

However, the Friedman statistical test showed there was a significant reduction in leucocyte count on the last day of treatment: the median leucocyte count at baseline was 10.5 (x 10e9/L) compared with an endpoint of 8.4 (x 10e9/L) ($p<0.05$). Normal leucocyte levels are <10.0, so the baseline value of 10.5 was indicative of infection. After treatment and debridement, the leucocyte level was normal at 8.4.

Average laboratory values for all three tests one month before and one month after larval therapy were the same as those recorded on the first and last days of treatment. There was a non-significant

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Table 2. Laboratory test results for leucocytes (x 10e9/L), CRP (mg/L) and ESR (mm/h) at the first and last days of treatment

Patient no.	Leucocytes First day	Leucocytes Last day	CRP First day	CRP Last day	ESR First day	ESR Last day
1	14.1	8.4	163	59	58	64
2	13.0	13.1	26	218	86	91
3	9.7	11.2	29	193	52	98
4	11.1	5.2	47	0	125	37
5	4.2	4.0	32	77	134	138
6	10.3	10.4	5	9	18	34
7	7.3	7.0	3	2	5	4
8	10.1	6.4	227	26	140	140
9	9.1	6.6	17	5	19	8
10	10.6	7.0	30	6	21	9
11	11.6	10.5	123	26	140	84
12	7.6	6.9	29	24	59	60
13	22.4	8.4	61	19	—	39
14	9.6	8.5	124	68	123	80
15	11.5	11.9	16	36	41	70
16	12.4	9.9	87	42	57	44
Average	**10.45**	**8.4***	**31**	**26**	**58**	**64**
Range	**4.2–22.4**	**4.0–13.1**	**3–227**	**2–218**	**5–140**	**4–140**

*Significant Friedman test ($p<0.05$)

reduction in CRP levels and ESR, again with a trend towards lower values following treatment: the average CRP level was 86mg/l one month before treatment and 40mg/l one month after (non-significant) and the average ESR was 70mm/h before and 58mm/h after (non-significant).

Discussion

Larval therapy is a very potent form of debridement. In our patients, removal of necrotic tissue or infection from infected, sloughy, necrotic wounds led to lower infectious parameters.

The results demonstrated a significant reduction in leucocyte levels one month following discontinuation of larval therapy. This indicates that larval therapy could be used instead of antibiotics in simple soft-tissue infection.

In line with a previous study on TNP,[15] we expected that CRP would be the best laboratory value for guiding decisions on when to discontinue larval therapy. However, CRP showed a non-significant trend only.

Conclusion

The methodological limitations of this cohort study, which was open-label and non-comparative, preclude a definite conclusion on whether laboratory investigations can be used to guide discontinuation of larval therapy.

However, we believe that, for our patients, laboratory investigations, especially leucocyte count, can help aid this decision, although they cannot replace clinical judgement.

While they did not achieve significant results in this study, in our opinion other laboratory investigations, such as CRP and ESR, also have a value in demonstrating the astounding detoxificating effects of larval therapy. A longer follow-up period might have demonstrated this.

More work needs to be done to evaluate which wound characteristics indicate that treatment should be discontinued. The value of wound cultures and pathologic examination also needs to be established. ■

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