Paediatric Vasculitis Assessment Training Manual:
A Practical Guide to Using PVAS and PVDI

Paediatric adaptation for the MYPAN trial
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Section 1 – Introduction

Welcome to the paediatric vasculitis training manual. This is the first part of your training in the standardised assessment of paediatric vasculitis patients in the MYPAN trial. Formal training has been shown to significantly improve validity of the data in previous clinical trials in adult patients with systemic vasculitis and it has become a pre-requisite to the participation in EUVAS trials. An international collaborative group of experts from both Paediatric Rheumatology European Society (PReS) Vasculitis Working Party and the North American Childhood Arthritis & Rheumatology Research Alliance (CARRA) Vasculitis Committee has developed paediatric adaptations of tools for the assessment of vasculitis activity and damage. The Paediatric Vasculitis Activity Score (PVAS) is based on the adult Birmingham Vasculitis Activity Score (BVAS) and has already been preliminarily validated in children with various forms of vasculitis and published recently (1). The Paediatric Vasculitis Damage Index (PVDI) has been adapted from the adult Vasculitis Damage Index (VDI) and has not yet been validated. It remains a tool under development and its use in this trial is considered exploratory.

Some of the evaluations developed for this program are straightforward and reflect everyday practice in managing patients with systemic vasculitis. Those who are familiar with evaluating these patients should have little difficulty with the evaluation process. However it is still important to standardise how we evaluate these patients so that we can all agree on definitions of disease activity and levels of disease damage. This manual is designed to help you understand the concepts of PVAS and PVDI, as well as provide you with the first simple practical exercises in completing PVAS and PVDI prior to the next training steps. We recommend that you print copies of blank PVAS and PVDI forms and accompanying Glossaries (provided in a separate file) before reading through the relevant sections on how to assess PVAS and PVDI, particularly the sections on the glossary and practical notes on completing the forms. This will make the manual easier to understand.

1.1 Aims and Objectives

Fortunately, because of advances in treatment, systemic vasculitis is now viewed as a chronic disease rather than an inevitably fatal condition. Reviews of previous clinical experiences in adult patients focused on death as a major outcome, but deaths from overwhelming vasculitis now comprise only a small minority of clinical outcomes in this disease, particularly in the hands of experienced clinicians. Because of this advance, alternative outcome measures are required, enhancing the need for thoroughly-validated assessment tools and investigators who are well-trained in their use. Such assessment tools concentrate on disease activity, flare and remission. The methods are practical and clinically based to enable standardised measurements of morbidity, which consist of:

- Current disease activity
- Increasing damage, which consists of non-healing scars developing as a consequence to the initial disease and its treatment.

Currently, two tools are available for the use in children:

1. PVAS - used to record current disease activity
2. PVDI - used to record damage as a result of vasculitis and its treatment

1.2 Methods

The whole training programme is designed to prepare you as a trial investigator for the standardised data collection. PVAS and PVDI can be evaluated by physicians with some basic training. The pack is composed of an explanation of PVAS and PVDI, followed by the original glossary for each. The footnotes are designed to add further information on a few items that may cause confusion.

Section 2 - Assessment of Vasculitis Disease Activity

2.1 PVAS (Paediatric Vasculitis Activity Score)

This is a scoring sheet that was designed to document new or worsening clinically active vasculitis that would be likely to require treatment. It consists of a set of items divided into nine organ-based systems. The scoring sheet simply records the presence or absence of each item. Each item is weighted and a maximum total score applied to each system. The total score on all nine organ systems gives an indication of the disease activity of each patient at the time of scoring.

The PVAS is designed to record features that are attributable to **current vasculitis**, after exclusion of other intercurrent co-morbidities such as infection or the presence of damage caused by vasculitis. This brings up a crucial point: **The PVAS is used to record active vasculitis only – not damage caused by previously active disease**. The PVAS reflects the need for immunosupressive therapy and is based on the intention to treat the patient**.**

2.2 Practical Notes on how to Complete PVAS

Only disease presentations that are attributable to active vasculitis are scored in the PVAS. Manifestation of new active disease should be scored if it has been present within a 28-day period preceding the PVAS assessment, even if it is not present on the day the PVAS is scored. As an example, if glucocorticoid therapy has been initiated for the symptom of arthritis, the inflammatory joint disease that a patient had ten days prior to the assessment may no longer be present on the day the PVAS is scored. Arthritis should still be recorded on the PVAS, because that manifestation of active disease was present within the 28 day period preceding the assessment.

When the patient is evaluated for the first time, usually at the time of diagnosis, all features of the disease are considered active/new, regardless their duration. On subsequent evaluations time has a more important role in distinguishing between disease activity that is “new” as opposed to “persistent”. In the box at the bottom right hand corner (“Persistent disease only”) persistent disease is recorded for those patients who still have active vasculitic features (lasting for less than 3 months), but none of them is new (present for less than 4 weeks) or worsening.

In other words, if all of the active features are persistent rather than new, the box in the bottom right hand corner labelled “Persistent disease only” should be ticked after all of the individual items still present have been ticked.

On this basis the calculated score for PVAS will contain only values representing persistent disease. By contrast if even one item amongst the item list represents either new or worse disease then you do not tick the “Persistent disease only” box. This will have the effect that all

items recorded whether they are new/worse or not will be calculated as if they are new/worse. Thus, patients with a mixture of persistent and new vasculitis features will be recorded as having new features for the purposes of the score calculation.

Three questions should be asked of each item on the scoring sheet on completion.
1. Is the abnormality present?
2. Can it be attributed to active vasculitis?
3. If it can be attributed to active vasculitis, is it newly present or worse or does it reflect persistent disease activity (present> 1 month, but less then 3 months)?

Scoring a new patient presenting for the first time
• Score all items that are present and attributable to vasculitis as **New/Worse.** In this case, the items can have been present for over 3 months or even longer.

Scoring a patient for review with known disease
• If any item is newly present (within the last 28-days period) or worse all the items will be scored as **New/Worse** and the "Persistent disease only" box **is not** ticked
• If **all** the ticked items have been present **within** the last 3 months and **are not new or worse,** the "Persistent disease only" **is ticked** and the calculated score for PVAS will contain only values representing persistent disease.
• If none of the items are present, an item has been present for over 3 months or, a patient reports having had a symptom more than 4 weeks ago but it is not present at the time of scoring on questioning or examination, the **none** box is ticked.

Scoring a patient with some new items and some persistent items
In this case all disease is scored as if it was **New/Worse**, even if there is only one item that is new/worse. This is simply to reflect the fact that in practical terms if patients have had a flare of the disease we tend to treat them for that flare. It is perfectly possible for patients to have some symptoms that are resolving whilst at the same time others that are deteriorating. Under those circumstances, one would regard that patient as having poor disease control of disease and initiate a higher level of therapy.

If one scores as New/Worse, this corresponds to **an intention to treat the patient on the basis of at least one of the ticked items.**

2.3 Overview of the PVAS Glossary
The full glossary for PVAS is found in a separate file.

GENERAL RULE: Disease features are scored only when they are due to active vasculitis, after excluding other causes (e.g. infection, drug side effects, etc.). If the feature is due to active disease, it is scored in the boxes. It is essential to apply these principles to each item below. Scores have been weighted according to the severity that each symptom or sign is thought to represent. Tick "Persistent disease only" box if all the abnormalities are due to active (but not new or worse) vasculitis. If any of the abnormalities is due to new/worse disease , DO NOT tick the "Persistent disease only" box.

For some features, further information (from specialist opinion or further tests) is required if abnormality is newly present or worse. Remember that in most instances, you will be able to

complete the whole record when you see the patient. However, you may need further information before entering some items. Please leave these items blank, until the information is available, and then complete them. For example, if the patient has new onset of stridor, you would usually ask an ENT colleague to investigate this further to determine whether or not it is due to active vasculitis.

Footnote for the PVAS glossary
(Refer to enclosed PVAS score sheet in a separate file)
Please refer to the PVAS glossary, retaining the principles of new/worse and persistent scoring but remembering that only patients who have persistent items throughout should have the "Persistent disease only" box ticked.

Section 1 General- *Fever*
This is a reported sign. The temperature does not need to be present at the time of scoring.
Section 2 Cutaneous - *Infarct*
Look for line haemorrhages under the nails, or small black spots in the nail beds.
Section 2. Cutaneous - *Purpura*
Non-blanching petechial lesions that are sometimes palpable and represent bleeding into the skin because of damaged small blood vessels.
Section 5 Chest – *Endobronchial involvement*
These features are often detected on bronchoscopy or computed tomography and occasionally on radiographs. Patients may present with a cough or haemoptysis.
Section 8 Renal - *Hypertension*
Hypertension may be associated with active vasculitis if there is also proteinuria and haematuria, indicating renal inflammation.
Section 9 Nervous system - *Seizures*
Do not record an isolated seizure unless proved to be due to vasculitis. If several seizures occur in a patient who is not epileptic, this can then be scored. If the patient is a known epileptic and the condition deteriorates with persistent seizures it should be scored as New or Worse item.
Section 9 Nervous System - *Sensory Peripheral neuropathy*
Change in sensation. Symptoms of pins and needles or numbness in arms, hands, legs or feet. If symptoms present, patient should be examined by study doctor to confirm.
Section 9 Nervous System - *Cranial Nerve palsy*
Symptoms of pins and needles or numbness in the face, diplopia, disorders of extraocular muscles, facial asymmetry, and other manifestations of cranial nerve lesions. If symptoms, patient should be examined by study doctor to confirm.
Section 9 Nervous System - *Motor mononeuritis multiplex*
Weakness to a limb or part of a limb due to interruption of the blood supply to the nerve. A common manifestation of this is a foot- or wrist-drop. If symptoms, patient should be examined by study doctor to confirm.

Section 3 - Practical Exercises in Scoring PVAS

3.1 Introduction to the Practical Exercise in Scoring PVAS

We would like you to use the paper cases in order to broaden your understanding of PVAS and to test your ability to evaluate patients with systemic vasculitis. This is obviously an artificial situation because you are being presented with fixed information extracted from existing cases rather than seeing the patients yourself. If you accept that this is an artificial situation but allows for evaluation between observers then this is a useful exercise, it will serve as the basis in introduction to using PVAS and should be accompanied by real use in real patients. The exercises should be performed in order, if possible.

1. Please read and score example cases I–III using a blank PVAS form (in a separate file) and then review the ideal answers to these case exercises with the filled-in answer sheets.
2. Having reviewed the training manual for disease activity assessments by PVAS and the 3 example cases please confirm your understanding by scoring disease activity in the first set of 5 basic training paper cases 1-5 (Homework I).
3. Within 2 days from the receipt of your completed answer sheets you will get the feedback on your performance. Once you meet the training requirements (at least 85% agreement with "ideal" answers with no more than one scoring minimum of 50% agreement) you can proceed to the second set of advanced training paper cases 6-10 (Homework II).
4. Please score the Homework II cases using blank form as you did for the previous ones. The evaluation procedure will follow.
5. Successsful completion of all 10 training cases is required in order to receive a training certificate.
6. Once you fail in any above step you will receive additional set of 5 remedial training paper cases to complete.

General instructions:

- Indicate your name and the case number in the appripriate boxes in the upper right hand corner of the PVAS form
- You are not required to count the PVAS score by yourself, just tick the appropriate boxes with the bold pen.
- Please scan the scored answer sheets and send them to Pavla Dolezalova for evaluation (dolezalova.pavla@vfn.cz)
- If you have any concerns or questions that are not addressed by the manual, please feel free to contact Pavla Dolezalova

3.2 PVAS Example Cases I – III

In the following three practice cases, there is a short description of each patient. Please read the cases, score them using the PVAS evaluation form (sent in a separate file), and then review the "answers". Only after evaluating the three practice cases, please proceed to the first set of five basic training cases. The number of each case is indicated in the top right hand box of the PVAS evaluation sheet.
In all of the case histories, we provide you with "positive" data. **If there is no mention of any particular feature, you may assume that it is not present or that it is normal.**

Please remember to evaluate EVERY SINGLE SYSTEM CATEGORY by either ticking the box "None" if there is no item within that section to score, OR by ticking at least one active disease item within that category.

Example I
15-year-old boy (60 kg body weight) has noted a three week history of fatigue, 4kg weight loss, and joint pains in his hands and ankles. He has noticed some nasal crusting and bleeding, with severe tenderness over the cheeks. His past medical history includes a three-year history of anterior knee pain bilaterally due to Osgood-Schlatter disease. In his previous history you notice presence of mild left hemiparesis due to cerebral palsy from perinatal asphyxia. (This has subsided almost entirely following years of intensive physiotherapy). Examination reveals swollen, boggy ankles and MCP joints. He has increased reflexes in his left arm and leg, and an upgoing plantar response. His urine contains 15 red cells per high power field, and occasional RBC casts. The creatinine has risen from 110 umol/l on admission one week ago to 150 umol/l today.

A diagnosis of granulomatosis with polyangiitis was established on renal and nasal biopsy.

Please score his ***PVAS.***

Example II
A 16-year-old boy presents with acute onset of hearing loss, aural discharge, epistaxis, nasal discharge, crusting, and fever. Examination reveals bilateral conductive hearing loss, a temperature of 38.3°C, normal urine sediment, and normal creatinine. A nasal biopsy shows granulomatous inflammation with poorly-formed granulomas, and he has a positive ANCA by immunofluorescence, with a cytoplasmic staining pattern. Chest radiograph is normal. He is started on methotrexate and prednisolone. Three weeks later, he attends the clinic feeling worse. He has been tired, with increasing amounts of epistaxis (daily instead of alternate days), less aural discharge, with some improvement in hearing. The nasal crusting is worse. He now complains of sinus discomfort, and on examination he has tender maxillary sinuses. Urine testing shows haematuria (++), proteinuria (++), and no RBC casts. Urine chemistry is negative.

Creatinine is still normal. Blood pressure has gone up to 145/95. He is afebrile. He is sent for a renal opinion.

Please score his ***PVAS.***

Example III
A 12-year-old girl presented with ischaemic fingers, splinter haemorrhages and gangrene twelve months prior to the current visit. At that time, she was found to have a serum creatinine of 150 umol/L, too numerous to count RBCs in her urine, RBC casts and proteinuria (+++). Several months before that presentation, she had developed an inflammatory arthritis and bilateral hearing difficulties, for which an ENT surgeon had inserted tympanostomy tubes. The diagnosis of granulomatosis with polyangiitis (formerly Wegener's) was confirmed by a renal biopsy, which demonstrated segmental, necrotizing glomerulonephritis of a pauci-immune nature. She was strongly C-ANCA and PR3-ANCA positive.

In retrospect, her mother recalled being told two years ago that the girl had a "deviated" nasal septum. In fact, at the time of presentation she was found to have a nasal septal perforation and bloody nasal crusts. She responded promptly to cyclophosphamide and prednisolone. At the time of her current evaluation, she has been now off cyclophosphamide for five months

and is taking methotrexate 20 mg/week. She has also tapered off prednisolone four months prior to the current visit. Her serum creatinine has been stable in the 70-90 umol/l range since discharge from her initial hospitalization. She underwent amputation of a couple of gangrenous fingertips 6 months ago and occasionally has pain at the amputation site, but there is no coolness or evidence of further digital ischaemia. Her haematuria has never completely resolved, remaining on the order of 5-10 RBCs/hpf, and she continues to have stable proteinuria (+). She reports occasional sinus stuffiness and a general lack of energy, but has returned to school full-time.

Please score her ***PVAS.***

3.4 PVAS Example Cases I – III Answers

Please see the scored PVAS forms for example cases in a separate file.

As there are New/Worse items in cases I and II the PVAS persistent values are automatically zero.

Example I

PVAS new/worse = 21, PVAS persistent = 0

The relevant abnormalities for example I are: general: (*arthralgia, weight loss* ≥5% body weight*),* ENT (*bloody nasal discharge*/, *crusts* and the cheek tenderness represents *paranasal sinus involvement),* renal (*haematuria, rise in creatinine >10%).* Because this is the first visit, you would score the actual creatinine value. The anterior knee pain and old hemiparesis are irrelevant as are the clinical signs relating to that. You should record the *malaise* in the "other section" but it does not count towards the calculation of the score.

These items represent new active disease and therefore the "Persistent disease only" box is not ticked and automatically PVAS persistent is zero whereas PVAS new/worse will score all the points. This gives a total calculated PVAS new/worse score of 21: general 3, cutaneous 0, mucous membranes 0, ENT 6, chest 0, cardiovascular 0, abdominal 0, renal 12, nervous system 0.

Please note that we have not ticked the "Persistent disease only" box.

Example II PVAS new/worse = 20, PVAS persistent = 0

We have asked you to score this for the current visit but remember that all of the features occurring within the previous month count towards the current visit therefore both sets of assessment are relevant.

The relevant features are: general (*fever ≥38.0°C),* ENT *(bloody nasal discharge*/*nasal crusts, paranasal sinus involvement, conductive hearing loss),* renal (*hypertension, proteinuria, haematuria).* Although not listed on the PVAS form, *malaise* and *aural discharge* are relevant findings and should be added to the "other" section although they do not score any points.

These items represent new active disease and therefore the "Persistent disease only" box is not ticked and automatically PVAS new/worse will score all the points.

The total PVAS new/worse score is 20: general 2, cutaneous 0, mucous membranes 0, ENT 6, chest 0, cardiovascular 0, abdominal 0, renal 12, nervous system 0.

Please note that we have not ticked the “Persistent disease only” box.

Example III PVAS new/worse = 0, PVAS persistent = 0
This patient has had three separate assessments and we are really asking you to concentrate on the most recent assessment when he has been off treatment for several months. All of the presenting features would have been scored at the time but are not currently relevant since they do not represent current disease activity. Therefore the ischaemic fingers, splinter haemorrhages, gangrene, haematuria, red cell casts, proteinuria, inflammatory arthritis, bilateral conductive hearing loss, septal perforation and bloody nasal crusts do not count for the current assessment.

This girl has a lot of damage but no current disease activity. The creatinine level is stable and does not count. The gangrenous fingers have been treated with amputation; the haematuria is chronic and has not increased. The proteinuria is stable and the nasal stuffiness is damage and the general lack of energy is also not relevant.

Her PVAS new/worse score is therefore 0 and no items should be scored on this current visit. The PVAS persistent score is also zero.

Section 4 - Assessment of Vasculitis Disease Damage

4.1 PVDI (Paediatric Vasculitis Damage Index)

This is a scoring system to document those features that are due to disease damage rather than disease activity. This is quite separate from PVAS and PVDI gives no indication of current disease activity. Damage is defined as the presence of scars (arbitrarily defined as any item present ≥ 3 months) that **develop as a consequence of the initial disease or its treatment.** For example, hypertension would score as a damage item if present for ≥ 3 months and if caused by either chronic renal disease associated with vasculitis or by the treatment of vasculitis (i.e. with corticosteroids). Thus, the damage items are often the direct result of previous disease activity, but may occur from treatment or other co-morbidity if this occurs after the onset of vasculitis. This is an important concept because we know that some vasculitis treatments are toxic and contribute significantly to the burden of disease.

The PVDI can be used in different ways in both clinical trials and routine clinical practice. First, the PVDI can serve as a measure of treatment failure/inadequacy. The mounting of damage items over time indicates that the treatment regimen employed did not control the disease activity adequately to prevent damage, or did not suppress the disease without causing treatment-related morbidity. In addition, the PVDI can reflect clinically significant delay in diagnosis since damage can accrue in the prediagnostic phase of vasculitis, before effective treatments are started. Finally, it is known from adult studies that the accumulation of damage such as that measured by the PVDI appears to be a predictor of mortality. A baseline score of >4 for the adult tool (the VDI) is associated with an increased risk of mortality at 2 years. The paediatric version (PVDI) is currently under development and has not yet been formally validated in children, but we are hopeful that this tool for children (derived from the VDI) will be as important as the adult VDI for capturing disease damage as an outcome measure in clinical trials.

4.2 Practical Notes on how to Complete PVDI

The Vasculitis Damage Index addresses features that have occurred since the onset of vasculitis, regardless of whether or not they are attributable to vasculitis. *This is where the PVDI differs conceptually from the PVAS, which only scores items that are directly attributable to active vasculitis.*

- PVDI is used to record **any condition** that has occurred and lasted for at least 3 months since the start of vasculitis and refers to chronic damage present for ≥ 3 months (consistent with the definition of chronicity employed in the VDI in studies of adults).
- The PVDI items may be present:
    1. As a direct consequence of vasculitis disease activity
    2. As a consequence of vasculitis therapy
    3. Or as a consequence of related or unrelated comorbidity that develops or deteriorates after the onset of vasculitis

In the PVDI scoring, damage is defined as an item having been present for ≥3 months. If the item had been present for ≥3 months but has completely disappeared by the time of evaluation, then this item still scores in the box labelled "NLP" (for "no longer present"). PVDI will thus capture damage that was present for ≥3 months but has resolved. This scenario is particularly relevant to children, who may have greater capacity to heal than

adults. *This is the major conceptual difference between PVDI and the adult VDI.* For example, cutaneous ulcers present for > 3months in the past that have completely healed at the time of assessment would score in the "NLP" box for that item, but not in the "present" box.

Thus, in order to record potential resolution of some damage items PVDI captures:

1. Features of damage that had been present in the past starting after the vasculitis onset, lasting for ≥3 months but resolving by the time of the assessment by ticking the NLP box for those features (NLP = "No Longer Present").
2. Features of damage that have been present for ≥3 months and are still present at the time of the assessment by ticking the "present" box for those items.

Note also that you cannot score any single item as "present" and "NLP" at the same time.

For the purposes of PVDI scoring, damage is defined as persistence of an item ≥3 months, but not necessarily causing a life-long persistent physical scar. As examples, failure to thrive, steroid-induced diabetes, or delayed puberty may all resolve. Nevertheless, the majority of PVDI items cannot disappear and therefore represent true scarring. Examples of this include tissue loss due to digital ischemia or collapse of the nasal bridge.

Definitions of individual items are provided in the attached PVDI Glossary. Additional items that are not specifically listed on the PVDI form can be added to the section titled **"Other"** based on their clinical significance as assessed by the physician and/or the patient. For example, if the patient undergoes renal transplantation, or insertion of a dialysis catheter, these events could be captured under **"Other".** Even if during long-term follow-up some damage items may move from the "Present" box to the "NLP" (No Longer Present) box, ***the PVDI score can only remain stable or deteriorate over time, since both "NLP" damage items and "Present" damage items carry a numeric score of 1 and all PVDI items carry an equal score of 1.*** Thus. there is currently no severity rating for individual items in PVDI; future refinements of the tool may examine this more closely.

Items should NOT be scored at the same time on both the PVAS and PVDI: events are either disease activity or damage, but never both at the same time. If an item on the PVAS form such as bowel ischaemia or stroke is ticked as an activity item, this will eventually be counted as damage on the PVDI score sheet if still present after 3 months, ***but is not scored on the PVDI sheet until it has been present for ≥ 3months.*** Note also that you cannot score any single item as "present" and "NLP" at the same time.

Note that the following items in the PVDI form are nearly always ticked if specific items are present:

- "Subglottic stenosis (no surgery)" prior to "Subglottic stenosis (with surgery)"
- "Impaired visual acuity" precedes "Blindness" **UNLESS** the blindness truly occurs with acute onset (< 3 months) and then persists for ≥3 months; e.g., due to retinal detachment.
- "GFR 15-60 ml/min/1.73 m^2" prior to "End stage renal disease" (GFR <15 ml/min/1.73 m^2) **UNLESS** the end stage renal disease definitely developed from normal renal function (GFR >60 ml/min/1.73m^2) within a 3-month period (rare in clinical practice, but occasionally observed).

Other points of note are:

- "Chronic nasal blockage/discharge/crusting" could indicate chronic disease damage if present on its own for more than three months.
- "Chronic breathlessness" should only be scored if it is not attributable to a predefined outcome such as subglottic stenosis or other pulmonary (e.g., pulmonary fibrosis) or cardiac (e.g., cardiomyopathy) manifestation.

If a patient has had surgery that repairs an item of damage (for example, a saddlenose repair), that item remains on the PVDI as "present" since the tissue is never truly normal post-operatively.

4.3 Overview of the PVDI Glossary

The full glossary for PVDI is found in a separate file.

- This is a score of damage due to items present ≥3 months and is not a score of active vasculitis. Damage is defined as items having ever been present for ≥3 months if they occurred since the onset of vasculitis. Damage that has resolved is scored as NLP (=No Longer Present). Thus, as previously highlighted, the PVDI score can only remain stable or deteriorate even if some items resolve.

- Although many of the features of the PVDI may reflect drug related damage and are captured with this tool, for the MYPAN trial there is also a separate form to record adverse drug reactions (ADR).

- In the case of blindness, myocardial infarction, loss of pulses, major tissue loss, or stroke, **repeat episodes** may be recorded (in Other section) but these must be **at least 3 months apart** to score. For example, blindess in left eye would score if present for ≥3 months; if blindness in the right eye then developed, this would only score on the PVDI when present for ≥3 months.

- Note that the **same pathological feature cannot be scored in more than one organ/system section** of the PVDI scoring sheet, even though it may appear to fit in different parts of the index. For example, if optic atrophy is scored in the ocular section, it should not be recorded as a cranial nerve lesion. Similarly, typical atrophy of interosseal hand muscles associated with ulnar neuropathy might be scored as "Peripheral neuropathy" but not also as "Significant muscle atrophy" for two reasons: 1. it is a typical feature of chronic ulnar nerve neuropathy and 2. it appears in a different system category. The principle is to ensure that each feature of damage is scored, but not more than once except in cases in which the same item of damage has occurred in the contralateral organ.

- Each underlying **pathological event causing damage may be scored by one or more damage items within that system category**, which may reflect its clinical importance/severity. E.g. cataract may or may not cause visual impairment, hence it would be possible to score cataract AND visual impairment if both were present. Also, pulmonary fibrosis is not always associated with pulmonary hypertension, coronary stenosis may or may not cause myocardial infarction etc.

Section 5 - Practical Exercises in Scoring PVDI

5.1 Introduction to the Practical Exercise in Scoring PVDI

Please use the paper cases to teach yourself and test your ability to evaluate disease damage in paediatric patients with systemic vasculitis.

1. Please read and score example cases I–III using a blank PVDI form (in a separate file) and then review the ideal answers to these case exercises with the filled-in answer sheets.
2. Having reviewed the training manuals for disease damage assessments by PVDI and the 3 example cases please confirm your understanding by scoring disease damage in the first set of 5 training paper cases 1-5 (Homework I).
3. Within 2 days from the receipt of your completed answer sheets you will get the feedback on your performance. Once you meet the training requirements (at least 85% agreement with "ideal" answers with no more than one scoring minimum of 50% agreement) you will be sent the second set of training paper cases 6-10 (Homework II).
4. Please score the Homework II cases using blank PVDI form as you did for the previous ones. The evaluation procedure will follow.
5. Successsful completion of all 10 training cases is required in order to receive a training certificate.
6. Once you fail in any above step you will receive additional set of 5 remedial training paper cases to complete.

General instructions:

- Indicate your name and the case number in the appripriate boxes in the upper right hand corner of the PVDI form
- You are not required to count the PVDI score by yourself, just tick the appropriate boxes with the bold pen and calculate the school absence as per instructions (see PVDI Glossary)
- Please scan the scored answer sheets and send them to Pavla Dolezalova for evaluation (dolezalova.pavla@vfn.cz)
- If you have any concerns or questions that are not addressed by the manual, please feel free to contact Pavla Dolezalova

5.2 PVDI Example Cases I – III Questions

In the three practice cases, there is a short description of each patient. Please read the cases, score them using the PVDI form and then review the answers provided both in the following text and in the PVDI forms in the file PVDI Example Case Answers. After evaluating the three practice cases, please proceed to the first set of paper test cases. The number of each case is indicated in the top right hand corner box of the evaluation sheet.

Remember that we are interested in scoring damage, not disease activity, even though we might tell you something about disease activity in the case history.

In all case histories, we **provide you with "positive" data**. If there is no mention of any particular feature, you may assume that it is not present, although in real life cases, you would of course need to assess all the items individually on the PVDI form during the patient review.

Please remember to evaluate EVERY SINGLE SYSTEM CATEGORY by either ticking the box "None" if there is no item within that section to score, OR by ticking at least one damage item within that category. If an item is present at the time of evaluation, it is scored in the column "Present". If it was recorded before and is now resolved , it is scored in the column "NLP" (No Longer Present).

Example I

A 11-year-old boy with a diagnosis of granulomatosis with polyangitis (formerly Wegener's) presented with nasal blockage, discharge and crusting two years prior to the current assessment date. Over the last six months he has noticed no change in the persistent nasal crusts and the nasal blockage and is generally tired and miserable. He is on no regular medication at present. You previously treated him with methotrexate and prednisolone and at the last clinical visit by the ENT specialist, no active disease was documented two weeks prior to his visit with you.

The patient had Perthe's disease of his right hip managed conservatively when 4 years old, but resolution has been incomplete which is making him feel even more unhappy. One year ago he sustained a thoracic vertebral crush fracture which caused him pain for approximately three weeks and he has lost about 2 cm in height. He has never had renal involvement with his GPA. Six months after starting corticosteroid treatment for his disease he developed hypertension requiring two different antihypertensive medications given concurrently and he continues on this treatment to date. For a period of eight months within the first year of therapy he required hypoglycaemic drugs because of steroid induced diabetes. Since the steroids have been cut this has completely resolved and he is off all diabetic treatment. He was last reviewed for PVAS and PVDI 6 months ago and has missed no school over this period.

Please score his PVDI and school absence for the current visit.

Example II

A 15-year-old girl presents with a two-year history of granulomatosis with polyangiitis (formerly Wegener's). She presented with deafness due to a combination of sensorineural hearing loss, which was of sudden onset and in keeping with vasculitis of the eighth nerve. In addition she has had chronic otitis media for more than one year with some hearing loss and had grommets inserted with partial improvement in hearing for which she now uses a hearing aid. Within the first six months of her disease she developed nasal bridge collapse despite the use of methotrexate and prednisolone. Within two months of nasal bridge collapse she developed an active urinary sediment and biopsy of her kidney showed active glomerulonephritis with crescentic changes.

The patient was treated with cyclophosphamide, prednisolone, and plasma exchange. During the course of her plasma exchanges she had transient leucopenia. After six months of cyclophosphamide she became amenorrhoeic, having had regular periods from a year prior to onset of the vasculitis. Her amenorrhoea lasted for about one year and now she reports having regular periods. After initial decline her renal function stabilised and since the last review by her nephrologist 3 months ago it has remained at 50 ml/min/1.73 m^2. Neverheless, she has had difficult to control hypertension requiring two anti-hypertensive medications for about 6 months. For the last nine months she has been complaining of cramps in her calves when she walks any distance but this clearly improves with rest. Four months ago she noticed

worsening of her vision and the ophthalmologist confirmed the presence of bilateral cataract. She has been complaining of breathlessness on exertion for at least eight months and you have investigated this thoroughly and found no significant pulmonary abnormality to account for it. She was last reviewed for PVAS and PVDI 6 months ago and has missed 5 days of school in total due to breathlessness exacerbated by a viral infection and hospital appointment attendance.

Please score her PVDI and school absence for the current visit.

Example III

A 17-year-old girl with a diagnosis of microscopic polyangiitis established five years prior to the current visit on the basis of purpuric vasculitis, pulmonary haemorrhage and active urinary sediment with biopsy proven glomerulonephritis comes for assessment today. Two years ago she had a myocardial infarction and continues to suffer intermittent chest pain on exertion due to coronary artery stenosis. One year ago she had an episode of severe abdominal pain due to bowel ischaemia and despite aggressive treatment she had to be admitted to hospital for resection of approximately 20cm of small bowel and had a defunctioning enterostomy for approximately six months, which was eventually reversed.

When she was initially treated with cyclophosphamide and prednisolone four years previously, she had significant hair loss which did not return until five months after stopping cyclophosphamide. Six months ago she had a minor left hemiparesis from which she made a partial recovery but still has some residual weakness in the left leg. She was last reviewed for PVAS and PVDI 3 months ago and has missed 5 days of school for hospital appointments with renal and cardiology teams including an exercise stress test and a follow up cranial MRI.

Please score her PVDI and school absence.

5.4 PVDI Example Cases I – III Answers

Example I **PVDI = 4**

This patient has long-standing granulomatosis with polyangitis with a number of items representing chronic damage and they include: *chronic nasal blockage/discharge/crusting (Present), osteoporosis/vertebral collapse (Present), hypertension > 95th centile or requiring antihypertensives (Present)* and *diabetes (NLP).*

The steroid induced diabetes counts even though it has resolved because it persisted for more than three months, and is scored as an NLP item.

The Perthe's disease in his hip is long-standing and not related to his vasculitis diagnosis, and does not score on the PVDI.

Therefore his total PVDI score is 4 (one point for each item).

School absence is scored as *6 months* since PVDI last assessed and average monthly non-attendance is recorded as ≤ *1 day / month.*

Example II **PVDI = 8**

This girl has a large number of damage items. The hearing loss should be recorded since it has been present for more than 1 year. The nasal bridge collapse is another damage item to score. The transient leucopenia should not be recorded since it did not last any significant length of time and did not require G-CSF support. The deteriorated renal function has been stable long enough to score as a damage and not disease activity item at the time of assessment. From ocular items only cataract is scored as it clearly accounts for her impaired vision.

The following items should be scored: *hearing loss (Present), nasal bridge collapse (Present), secondary gonadal failure (NLP), hypertension > 95th centile or requiring antihypertensives (Present), GFR 15-60 ml/min/1.73m2 (Present), chronic claudication of extremities (Present), cataract (Present), chronic breathlessness (Present).*

This gives her a total PVDI score of 8.

School absence is scored as *6 months* since PVDI last assessed. Average monthly non-attendance is recorded as ≤ *1 day / month.*

Example III **PVDI = 5**

This patient has quite a number of PVDI items of damage to record. From Cardiovascular items, myocardial infarction scores as well as Coronary artery aneurysm/stenosis as the latter accounts for chronic symptoms of angina. The alopecia should count because it lasted five months. From abdominal items Gut infarction/resection is the only damage item (Present) – remember that if a patient has had surgery that repairs an item of damage (for example, a saddlenose repair, or in this case abdominal surgery), that item remains on the PVDI as "present" since the tissue is never truly normal post-operatively.

The following items should be scored: *major alopecia (NLP), myocardial infarction (Present), coronary artery aneurysm or stenosis (Present),* and *stroke (Present).*

In total the PVDI score is therefore 5.

School absence is scored as *3 months* from the last review and >*1-4 days / month.*