Explanations of Figures and Case Reports with Individual Therapeutic Options

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All figures clearly present the clinical, radiological and morphological findings detected during everyday rheumatology practice. In accordance with their approximation to the morphological substrate of a condition or disease, they have been categorized into three divergent and loosely delimited groups:

A. *Condition-specific* syndromes, when the depicted stable combination of the assembled symptoms represents *a morphological substrate* or *morphological diagnosis* of a condition; subsequently *causal investigation* should ensue.
B. *Non-disease-specific* syndromes, when the figures can be assigned to more individual conditions and diseases.
C. *Disease-specific* syndromes, when pathognomonic (*Greek* "indicative of a disease") symptoms or the relevant diagnostic criteria of a certain disease can be identified.

The diagnostic value of all syndromes, particularly of the most representative subgroup B of *non-disease-specific syndromes*, can be decisively (but not absolutely) enhanced if they are considered together with the pertinent CS (Chap. 1.1.2).

The explanations of these pictures, with references to the relevant (sub) chapters of the text where the diagnosis is actually to be found (in *RSS*), and the implemented concepts of individual therapy, have been provided as teaching support in Chap. 2.

1. This picture best represents our discipline. This *classic pattern of targets* in rheumatology should be visualized with the other structures not presented, namely *connective tissues of the internal organs, nerves, vessels, immune and endocrine systems*.
2. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.2; see also Figs. 10, 11, 30, 31). Linked with the clinical data (weight loss and exhaustion, no organ involvement, *ANCA* negative, *histologically* involvement of the *small arterial vessels* in the subcutis *with perivascular eosinophilia and granulomatous changes*, capillary microscopy – highly pathological pattern consistent with vasculitis), this syndrome is to be assessed as certain vasculitis, though *not disease-specific*, most likely PAN *cutanea benigna*. *Therapy*: immunosuppression (Urbason® 30 mg and Imurek® 100 mg daily), nevertheless the course was resistant.
3. (C) *Two diseases* present here (*RSS*, Chaps. 1.3.1, 1.4.1, 3.1.1). *Therapy*: systemic (for primary disease) and as necessary local (cortisone injections).
4. (C) *A disease* (*RSS*, Chaps. 1.4 and 4.6; Fig. 8). *Therapy*: none since this patient had any *arthralgia,* evidently because she had been on several years of moderate immunosuppression (Urbason® 4 mg and Imurek® 100 mg) for the underlying disease (PM/DM).

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5. (C) *A disease* (*RSS*, Chap. 1.3, CS 1) with specific radiomorphological pattern (Fig. 9a). *Therapy*: during the last 8 years, strong immunosuppression (at present Decortin® 10 mg and MTX 15 mg/week *SC*, earlier Enbrel® and Remicade®, recently Rituximab and Humira®), 18 orthopedic operations (some of which can be seen in Fig. 9b). *Prognosis* (*RSS*, Chap. 7.4) and the course of the disease (only the 8-year-old medical history) in this case is extremely unfavorable in spite of modern therapy.
6. (B) *A clinical syndrome* (*RSS*, Chaps. 3.2.1, 9.4.1; see also Figs. 27, 71) can be explained by serological investigation (CS 1). *Therapy*: doxycycline 100 mg for 3 weeks, increase in cortisone doses. These changes were reversible after 3 weeks.

CS 1: Acute swelling and reddening in the ankle joint in immunosuppressed female patient, 42 years

In this patient with advanced disease (Figs. 5, 9a, b), an acute process with reddening, pain, and fever should probably be assessed first as sepsis, or erysipelas (this was the suspected diagnosis also in CS 5, 24, 34; Fig. 27). Septic arthritis of the ankle cannot be confirmed in this case, on the following grounds: non-synovialitic involvement (no dramatic functional deficits, no effusion in the joint), more likely the periarticular structures are affected, no septic fever, only moderate increase in CRP. Fresh *Yersinia infection* appears to be a good explanation for this process.

7. (B) *A clinical syndrome* (*RSS*, Chap. 4.6.2; see also Figs. 66, 115). Only in association with the clinical data (CS 2) can it be correctly interpreted in causal terms. *Therapy*: Decortin® 80 mg (!) more than 1 year (hardly appropriate in light of the activity and organ involvement, hence marked *Cushing's* syndrome developed) and azathioprine 150 mg/day. With additional administration of MTX 15 mg/week, the symptoms and findings regressed and at present no cortisone, normal CRP.

CS 2: *Puffy hands* and high-titer ANA in 26-year-old female patient

In this case a difference between *synovitis* and non-synovialitic, periarticular swelling of the joints (*puffy hands*) is first detectable (see also Fig. 128c). The term *synovitis* (like *arthritis*) implies that the swelling originates from the synovial membrane. That is not the case here. Diagnosis is found in the disease-specific immunology (*RSS*, Chap. 11.1), namely the high ANA titers with *U1-RNP* and *Sm* pattern with no anti-CCP-Ab and RF. Radiomorphological data (no enhancement on bone scan and no bone destruction on X-ray) also indicate an extra-articular cause for the swollen fingers. A definable, systemic disease is thereby involved. Increased immunosuppression produced clinical remission.

8. (C) *A radiological syndrome* (*X-ray* hands → *RSS*, Chap. 1.4.4; Fig. 4 belongs to the same patient). The destructive involvement of the *PIP* joints is the same, as in Fig. 9a. But here, we have the other disease. The polar differences between the two diseases,

which are the two most commonly confused, can be seen, as in Fig. 9b, particularly well in the MCP and wrist joints. *Therapy*: local, as necessary.

9a. (C) *A radiological syndrome* (*X-ray* hands → *RSS*, Chap. 1.3.4 prior to surgery), belonging to the female patient in Fig. 5. *Therapy*: systemic medicinal (see CS 1) and orthopedic (see Fig. 9b) treatment.

9b. (C) *A radiological syndrome* (*X-ray* hands, following surgery, see Fig. 9a). Here, a typical, individual pattern of involvement (mainly *MCP* involvement) should be implied, i.e., the *PIP* joints are typical of the condition for both diseases (OA and RA); though whether the *MCP* (in RA) or *DIP* (in OA) are affected at the same time is important.

10. (C) *A disease* (*RSS*, Chaps. 9.1.2, 9.2.2; see also Figs. 2, 30–32). Acute course of a disease developed 30 years ago, i.e., before the era of immunosuppression. The dramatic traits of such a disease would today, as at that time, be prognostically unfavorable. Changes are suggestive, clearly, of inflammatory thrombotic involvement with necroses of the medium vessels. There we have the entity already (see the nomenclature of systemic vasculitis, Jennette et al. 1994).

11. (C) *A disease* (*RSS*, Chap. 13.4), see comments on Fig. 10. Which other diseases are possible?

12. (A) *A radiological syndrome*: *Leriche's* syndrome (*aortic angiography* /*RSS*, Chaps. 9.2.5, 9.2.7, 9.2.9/ ascertained shortly before surgery and in fact Y-prosthesis). Causal interpretation in conjunction with clinical (CS 3) and above all lab findings (*RSS*, Chaps. 11.1, 11.4) only (the dramatic stenoses could also emerge from other diseases; see also CS 21, Fig. 132). *Therapy*: emergency OP (Y-prosthesis).

CS 3: Acute *Claudicatio arteriosa* manifested as weakness in the legs and lupus-type immunology in 40-year-old female patient (56 years at present)

Of clinical interest here is the acute development of *Claudicatio arteriosa*, which, on exertion, was not characterized by pain in the legs – as is the case with peripheral circulatory disorders – but by extreme weakness in the legs ("no strength in the legs, not a single step further without having to stop"). The acuteness of this condition and its morphological correlate can be seen in Fig. 12, i.e., the extreme narrowing of the abdominal aorta and *A. iliaca.* The causes for this are certainly associated with the abnormal immunology, i.e., the high ANA titers, anti-dsDNA-Ab (but with *negative Crithidia* test) and ACLA with lupus anticoagulant. Such a anti-constellation is at once to be regarded as a condition or, in my opinion, a disease (*RSS*, Chap. 11.4). Clinically, the deciding factors are the lack of organ/system involvement and the recent development of *livedo reticularis* in the legs (see histological findings in *RSS*, Chap. 11.6). The lifelong therapy with phenprocoumon (16 years already) certainly appears to be optimal. Earlier prescriptions of cortisone and Imurek® were ultimately discontinued.

13. (C) *A disease* (*RSS*, Chap. 1.3.1) on account of the pattern of involvement: sudden developments (monoarthritis with redness, widespread swelling, intense pain with movement deficits) are already the diagnosis of a disease, regardless of whether the

patient has stable hyperuricemia (as in this case) and which joint is affected (cf. Fig. 68 where there is also florid arthritis of the same joint, but with a completely different model). Pseudogout usually protects the schmall joints (*RSS*, Chap. 1.5.3). *Therapy:* Mainly anti-inflammatory (Arcoxia® 90 mg daily, prednisone 30 mg, later possibly colchicine). The patient cannot tolerate the allopurinol and benzbromarone, so could be eligible for *febuxostat* /Adenuric® 80–120 mg daily/, a novel non-purine selective inhibitor of xanthine oxidase or *pegloticase*, new uricosuric agent. The options with IL-1 blockers (*RSS,* Chap. 7.3.2) are also open.

14. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.2, 9.2.3, 9.2.5; see also Figs. 47, 52, 113) explicable only on account of the detailed history (CS 4); suspicion of systemic vasculitis could not be verified.

CS 4: Acute peripheral gangrene of unknown etiology in 48-year old male patient

Diagnostics for vasculitis were initially instigated (Jennette et al. 1994). In this regard, no criteria were established, i.e., (a) no organ involvement, except for the lungs (COLD due to nicotine abuse) and liver (transaminase increase due to alcohol abuse), (b) negative CTD and vasculitis serology, (c) negative capillaroscopy for CTD and vasculitis, (d) no signs of inflammation. Accordingly, vasculitis was questioned as the appropriate diagnosis. When asked, the patient claimed to have typical *Claudicatio intermittens* (cf. *Claudicatio arteriosa* in CS 3), and the affected fingers had already been painful and blue during the last 2 years approximately. The patient reported to have accidentally hit these fingers with a hammer. Thus, the patient was not rheumatic. Therapy and prophylaxis to be managed at a practice for internal medicine or angiology.

15a. (C) *A disease* (CS 5; see also Figs. 84a, b). A condition prior to *therapy*: conventional immunosuppression (Decortin® 30–10 mg for 4 months and MTX 15 mg/weekly *SC*) was effective, but the baseline condition was still clearly visible. Subsequently, experimental therapy (double-blind, randomized, controlled study with Apremilast®) as part of a study also ensued.

15b. (B) The *disease* in this picture is not identifiable (cf. Fig. 15a; CS 5). The condition resulted following experimental therapy (double blind randomized controlled study with Apremilast®).

CS 5: Pain and reddening in the toes and forefoot, massive CRP increase, 63-year-old male patient

The symmetrical *dactylitis* skin (reddening) and nail changes, leaves no doubt as to the diagnosis of the underlying disease. The suspected diagnosis of *erysipelas* seems rather unlikely on account of the symmetrical involvement. The degree of MRI changes would, in my opinion, be commensurate with the high CRP values. The response (ultimately complete regression of these changes due to intensified immunosuppression with MTX and Apremilast®) is an indirect confirmation of the immunological cause behind the process.

16. (A) *A clinical syndrome* (*RSS*, Chaps. 3.2.1 and 9.4.1) emerged in a female patient (Fig. 3) after subcutaneous Kineret® injections; this was completely reversible upon discontinuation of the medication.
17. (B) *A radiological syndrome* (*MRI* of the brain, native: large cortical defects and atrophic changes: *the demyelination areas periventricular and subcortical, predominantly in the region of the posterior horns of lateral ventricle, leukoencephalopathic changes in the frontal region, clear dilatation of lateral ventricles, particularly of 3rd ventricle, microangiopathy*). Such changes can be interpreted correctly only in conjunction with the medical history (CS 6) and immunology (*RSS*, Chaps. 10.6 and 11.4). *Therapy*: initially, on suspicion of an inflammatory/vasculitic etiology to the multi-infarct situation, anticoagulation (ASA and Clopedogrel®) and cortisone therapy were initiated. During such therapy media infarctions repeatedly developed, necessitating the use of phenprocoumon (no new clinically distinguishable processes have since occurred). In my opinion there was no indication for extension of the immunosuppression (without signs of further organ manifestations and no ACLA). Furthermore, life-long anticoagulation (phenprocoumon therapy) is being administered, if necessary minimal doses of cortisone, social and medicinal rehabilitation.

CS 6: Several insults (since age of 17), normal delivery and at present (after 12 years) dementia, deaf-muteness and spasticity, 41-year-old female

The patient had residual symptoms following *multiple infarctions*, such as anacusis, aphasia, impaired vision, intellectual deficit and spasticity, emphasized on the left and symptomatic epilepsy. These *media infarcts* could fundamentally be correlated to vasculitis, thromboses or both. Primary CNS vasculitis was at no time detected by MRI. The lack of lupus-specific organ involvement and dsDNA-Ab almost certainly rules out the existence of SLE, despite the histological examination of the skin (suspected LE). Immunology also revealed no ACLA in the blood. These contradictory clinical and immunological data are, in my opinion, most likely to be interpreted within the context of *primary APS* (*Sneddon's* syndrome). This concept, and the phenprocoumon therapy given as a consequence, achieved a certain degree of stability in the disease.

18. (C) *A disease* with several syndromes and symptoms (*RSS*, Chaps. 1.3.3, 3.1.4, 4.6.1, 9.1.4, 9.3.3, and 9.4.3). On DD, CREST syndrome could also be a possibility. *Therapy* was determined from the activity (some signs of activity /look at the right wrist/; the consequences of such inflammation /contractures/ are visible) and organ involvement. For the hands: heat, movement therapy, Dolobene Gel®.
19. (A) *A clinical syndrome* (*RSS*, Chaps. 1.3.3 and 9.3.3; see also Figs. 18, 43, 62, 80, 130a), here in a patient with *tetraplegia*. Condition not active. *Therapy*: only movement and physiotherapy, no surgery.

20a. (A) *A clinical syndrome* (*RSS*, Chaps. 9.1.1, 9.2.1, and 13.6) is explicable only in conjunction with clinical findings (CS 7).

20b. (B) *A clinical syndrome* following therapy (cf. Fig. 20a). Lasting regression of such symptoms from two cycles of doxycycline therapy infers causal involvement.

CS 7: Massive *Livedo racemosa*, reversible with doxycyclines, female, 53 years

Causality is a major problem in this case. Neither the biopsy nor CTD immunology was indicative. The positive borreliosis serology (*RSS*, Chap. 11.3.4) and curative effect of doxycyclines (Fig. 20b) are most likely to be seen as criteria for *Lymphadenitis cutis benigna* in *borreliosis* (Fig. 20a) (this is how the case was interpreted by Dr B. Heilig).

21. (B) *A clinical syndrome* (*RSS*, Chap. 1.3.1). Only is explicable causally in the context of Figs. 22–24 and CS 8. *Monoarthritis* is visible (where?). *Therapy*: biphosphonates and local cortisone injections; at the spread of arthritis, MTX option is to be considered.
22. (B) *A radiological syndrome* (*X-ray* hands): *cystic* changes in the same joint.
23. (B) *A radiological syndrome* (*CT* hands): marked *erosive* changes in this joint (two projections pictured). They can be interpreted only in conjunction with certain diseases (*RSS*, Chap. 1.3.4).
24. (B) *A clinical syndrome:* MTP *monoarthritis and oligoarthritis* represent, in an *HLA-B27*-positive female patient, the typical pattern of involvement for the relevant diseases (*RSS*, Chap. 2.2.1). Namely, not the individual clinical or radiological investigations, but together with CS 8, such findings may be *disease-specific*.

CS 8: Stable mono-/oligoarthritis, HLA-B27-positive female patient, 18 years

Firstly, the clinical and radiomorphological syndrome diagnostics are to be interpreted. Clinical findings showed stable monoarthritis (more than 1 year); hand X-ray revealed suspected erosive arthritis (massive cystic changes). CT produced the most important feature of MCP 5 arthritis, which with such clinical findings and radiology is only to be suspected. In terms of cause, attention is to be paid mostly to stable monoarthritic involvement, and later onset of oligoarthritic involvement. At such an age, three diseases are possible. One can be differentiated immunologically (see above, negative RF and anti-CCP-Ab). The other two are to be suspected, rather, from the changes revealed by CT (*RSS*, Chaps. 1.3.4 and 2.2.1). Therapy should, in my opinion, first be local and later systemic (see comments on Fig. 21).

25. (B) *A clinical syndrome* (*RSS*, Chaps. 1.3.1, 1.4.7, and 4.10.1) only to be correctly interpreted within the context of the clinical findings (CS 9) and MRI (Fig. 26).
26. (C) *A radiological syndrome* (*MRI* of left knee → *RSS*, Chap. 1.4.6): *clear chondromalacia in medial femorotibial joint compartment, mild bone marrow edema of medial femoral condyle, medially emphasized capsulitis, manifest suprapatellar joint effusion.* This finding itself is a diagnosis and provides an exact explanation for CS 9. *Therapy* (local): Triam® 40 N 4, with MTX 20 mg N 2 twice, hyaluronic acid Synvisc® N 5. No pain during or after running a marathon (recently under 4 h).

CS 9: Acute arthritis of the knee at 50-year-old marathon runner

In such a case, MRI is highly appropriate for primary morphological diagnosis. A next step was joint puncture with subsequent punctate testing (leukocytes <1,000/µl, mostly lymphocytes, negative CRP and RF). To be thorough, certain serological tests (*RSS*, Chap. 11.3) could be conducted. The aforementioned therapy was functionally effective.

27. (B) *A clinical syndrome* (*RSS*, Chaps. 3.2.1 and 9.4.1; see also Figs. 6, 71, and 73 / following therapy/) should in this case /CS 34/ be causally ascribed to the underlying disease as with CS 24 (on exclusion of a septic process). *Therapy*: high-dose cortisone (Decortin® 40 mg/daily) and MTX, good response.
28. (C) *A disease* (*RSS*, Chaps. 1.3.1 and 3.8, CS 10) in initial stage. *Therapy*: provided the patient agreed (desire for children!), induction therapy was first undertaken for 4 months, namely with cortisone (Decortin® 30 mg to 0/daily with MTX 15 mg/week), then maintenance therapy (hydroxychloroquine Quensyl® 200 mg). No routine therapy in the last 8 months (patient takes cortisone for any minor episodes).

CS 10: PIP bursitis and MCP 2 arthritis, 26-year-old female

Stable (*bursitis* indicative thereof) PIP 2-3 *arthritis* in a young woman, highly suspicious of a diagnosis which can be confirmed by immunological investigations. Consequently, on consulting the patient (due to the desire for children) pathogenetic therapy was undertaken, resulting in immediate remission (see above). Patient is presently in the 24th week of pregnancy. Normal first-born.

29. (C) *A clinical syndrome* (*RSS*, Chaps. 3.11.6 and 9.8) with *cartilaginous inflammation* in typical areas that should be considered a rare condition. In this case, it first advances to a systemic inflammatory disease due to the symmetric infestation of the ears (5 months ago) and RA-like arthritis of the finger joints (2 months later), CRP increase (factor × 9). Other disorders (CTD, systemic vasculitis or myelodysplastic syndrome) or typical organ involvement (nose, trachea, airways, eyes, heart) are not apparent. Here, or even generally, a cartilage biopsy is not required to make the diagnosis (a traumatic event with morphological data, which is also seen clinically). *Therapy*: the patient, a 66-year-old male with persistent disease, has diabetes mellitus and did not respond to current therapy (prednisolone 25 mg daily), therefore he was prescribed MTX 15 mg/wk *SC*. Intensification of the immunosuppressive therapy as far as allogenic bone marrow transplantation cannot be ruled out.
30–31. (A) *A clinical syndrome* (*RSS*, Chaps. 9.1.2, 9.2.1, and 9.2.2; see also Fig. 2 with histologically defined disease) with disease not clearly definable (CS 11). *Therapy* (from my perspective): strong *immunosuppression* (cortisone and CYC pulse therapies), certainly accompanied by symptom-oriented therapy for *pulmonary hypertension*, ongoing at this time together with low doses of cortisone.

32. (A) *A clinical syndrome* (*RSS*, Chap. 9.1.2) after one year (complete scarring of the deep ulcerations presented in Figs. 30–31). *Therapy*: low-dose cortisone without immunosuppression.

CS 11: *Livedo racemosa* and deep ulcerations with pulmonary and renal involvement, ANCA negative, 42-year-old male patient

It is a serious clinical problem. Diagnosis: The diagnosis was formulated thus at a hospital abroad: *primary pulmonary hypertension, leg ulcer. Dyspnoea. Livedoid vasculopathy. Nephrotic range proteinuria, mild nephrosclerosis for biopsy, pulmonary hypertension, right ventricle dysfunction, monoclonalgammopathy, ANA positive 1/160.* Thereby, all syndromes are compiled without consideration of the development of the disease (initially there were the changes in the legs) and without formulating a common nosological concept which could unite such syndromes pathogenetically and would permit therapy to be devised in more than a syndrome-oriented way. Hence, with the exception of prednisone, only symptomatic therapy with a view to pulmonary hypertension (24 h) is being undertaken at present. My interpretation: *Livedo racemosa* and deep *ulcerations*, which were the first manifestations of the disease, signify the involvement of the small and medium vessels (establishment of this fact is virtually a diagnosis (*RSS*, Chaps. 9.1.1, 9.2.1, 9.2.2, and 9.2.9), although the biopsies performed in triplicate evidently were unable to furnish any clues regarding morphological diagnosis. The above mentioned pulmonary and renal symptoms are to be assessed within the context of such graphic pathomorphology.

In such patients, four diseases or states are most likely (Jennette et al. 1994). Two diseases (*APS* and *Cry-V*) can be identified from blood tests. The non-specific morphological and immunological findings do not, as is well known, rule out *vasculitis*, i.e., *PAN*. If this concept, which I favor, does not fit, such a situation can also be described as non-differentiated vasculitis, without pathognomonic symptoms – which in the case of CTD (see CS 16) or vasculitis is often the case. Such an assumption can justify the strong immunosuppression in similar, not very distinct cases – which in this event appears to be necessary. Even one state came into question, although *livedoid vasculopathy*. It has been recognized mainly as skin involvement and a nonvasculitic disorder of coagulation, but authentic vasculitis in the underlying subcutis can occur in cases of *CTD and PAN* with organ involvement typical of these diseases, as seen in this case. The association of the non-inflammatory *livedoid vasculopathy* with progressive *pulmonary hypertension* has not yet been addressed. *Therapy*: (from my perspective in terms of the inflammatory nature of this event) strong *immunosuppression* (cortisone and CYC pulse therapies), accompanied certainly by symptom-oriented therapy. In addition, place the full regression of these ulcerations (Fig. 32) and a certain stabilization of the disease (patient has been able to work for about 6 months). Over the course there was progressive right heart failure, despite maximal therapy for pulmonary hypertension, and the patient died 3 years after the outbreak of the disease (December 2009, you can see the dates of the images).

33. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.1, 9.2.1) appears, in conjunction with CS 12, to certainly be *disease-specific*. *Systemic therapy* to be conducted, also with the present

lack of organ involvement, primarily on account of the massive spread in skin changes; several medications were applied (CYC, MTX, Arava®) without success; moderate cortisone therapy (Decortin® 40 mg daily for 2 weeks) conducted, at present MMF therapy (up to about 4 months ago) so far achieving a certain stabilization of the disease and regression of *myositis*.

CS 12: Localized erythema, elevated CK and positive ANCA, 45-year-old male

All the clinical data suggest, in line with the criteria, a rare form of prognostically unfavorable vasculitis (most likely *MPA*) with cutaneous, subcutaneous, testicular and muscular involvement, but to date with no organ involvement, apart from selective hematuria with no renal insufficiency. Nevertheless, on account of the massive cutaneous/subcutaneous changes and the highly unpredictable course, intensified immunosuppression should be initiated (see comments on Fig. 33).

34. (B) *A radiological syndrome* (*CT* wrist bone left). A clear *radiomorphological* diagnosis (*RSS*, Chaps. 1.3.4, 3.10.1, and 4.5): *sharply demarcated cystic lesions around the bone of the wrist, particularly the Os lunatum, mainly on the left (small singular cysts on the right)*. Morphologically: *the bony tissue appears vital and free of inflammation; the soft tissue has localized necrotizing, florid inflammation with a predominance of neutrophilic granulocytes.* In conjunction with pain in the areas of both hands and unstable swelling of the wrists, for about 1 year, the causes for such multiple *osteolyses* in a 72-year-old woman are difficult to identify. The extensive sclerosis of the cyst walls and central localization of the cysts does not suggest bony lesions as part of *gout* (cf. Fig. 130b). A lack of immunological activity (anti-CCP-Ab, RF) and clinical evidence (no other joints involved, no previous illnesses, including psoriasis, no organ involvement) also does not seem to provide any indications. A colleague also believed this case to be RA. It is difficult, with a lack of RA criteria, to accept such a concept. With a localized problem, e.g., intraosseous ganglion, TB, sarcoidosis, possibly multiple myeloma, lymphoma, there was no indicative finding. Consideration should more likely be given, in my opinion, to an *osteolytic* syndrome (etiologically unexplained bone absorption /*vanishing bone disease*/ with "non-reactive" bone defects, as in Fig. 34).
35. (C) *A disease* (*RSS*, Chaps. 1.3.2, 1.3.3, and 3.1.1) based on the pattern of involvement, also with respect to symmetrical involvement. Other radiomorphological syndromes in this patient (see below) can be interpreted only in the context of this picture and CS 13.

36a. (B) *A radiological syndrome* (*X-ray* chest → *RSS*, Chaps. 1.6, 3.1.1, 10.2.2, and 13.3): such *nodules* should first be investigated from an oncology viewpoint. Open lung biopsy ensued, with diagnosis of "*rheumatoid nodules*" which were also visible in Fig. 35.

36b. (B) *A radiological syndrome* (*MRI* tibia → *RSS*, Chaps. 3.1.1, 13.3, and 3.11.8); these local bone changes are clinically consistent with cysts, enchondroma, possibly chondroblastoma or other tumors (e.g., *villonodular synovitis*). A morphological finding

from the bioptate was described as *granulomatous* inflammation with necrosis and interpreted as bone TB. Consequently, *tuberculostatic* therapy was undertaken for 1½ years. At present (2008) this morphological pattern is interpreted differently, namely in association with the *rheumatoid nodules* (see histological reference finding in CS 13, Chap. 1.1.2).

37. (B) *A radiological syndrome* (*X-ray* tibia → *RSS*, Chap. 13.3). *Ostitis cystoides multiplex.* Such a picture confirms the ultimate interpretation of the bone involvement (see above).
38. (B) *A radiological syndrome* (*X-ray* thorax → *RSS*, Chaps. 1.6, 3.1.1, 10.2.2, and 13.3): *Detection of disseminated and poorly demarcated, rounded swelling projecting onto the whole right and left lung. They are mostly consistent in terms of number and size with the previous examinations ... rounded transparency with horizontal reflection projecting onto the right mid lobes. Here, no radiomorphological differentiation can be made between disintegrated rheumatoid nodules and, for example, a tuberculous cavern or abscess cavity.* This picture poses the same questions as Fig. 36a (2004, see comments). A chest CT was arranged (see Fig. 39).
39. (B) *A radiological syndrome* (*CT* thorax → *RSS*, Chaps. 1.6, 3.1.1, 10.2.2, and 13.3) enables confirmation of Fig. 38: "*Detection of partly pleural nodules of a maximum of 3 cm in diameter. Ventrally, in the mid lobe, and touching the pleura, there is a cavern of 2 cm in diameter. These pulmonary lesions are highly consistent with necrobiotic rheumatoid nodes. Radiomorphologically, there is a concurrent malignant growth which cannot be ruled out with absolute certainty*"(all the more so in a chain-smoker). In comparison with Fig. 85, where a small-cell carcinoma was morphologically confirmed at almost the same localization as the nodules (dorsal, paravertebral), hardly any difference is to be found. One cavern (right front) is suggestive of TB (a diagnosis which was formulated in 2004). The third (my) version – involving several extra-articular *rheumatoid nodules* – can be justified over the course, since the general health was by no means impaired during the last 3 years. The patient refused a repeat lung biopsy.

CS 13: Pulmonary foci left, suspected to be tumors, and tuberculosis of the bone (2004), foci with caverns right (2007) in 58-year-old chain-smoker with RA

The diagnostic problems could and cannot be missed. *Initially* there were *nodules* in the left lung (Fig. 36a) in 2004 which were highly suspicious of a tumor or metastatic mass. The morphology – "pulmonary abscesses consistent with *rheumatoid nodules* with vasculitis in the marginal zone" – was in fact surprising (the first morphological finding was non-specific), but easily explained in the context of seropositive RA and peripheral rheumatoid nodules (Fig. 35). The diagnosis of bone TB can be established from the remarkable changes in the *tibia* (Fig. 36b), in addition there were the bone biopsy findings at this point (granulomatous inflammation with necrosis), leading to the conclusion of TB. This second disease could quite clearly even rule out the use of the possible TNF blockers. Another surprise was the negative outcome of in vivo *and* in vitro (QuantiFERON® TB) TB specimens, which actually questioned the history of the TB. Incidentally, on

morphological examination of this finding, this granulomatous tissue was interpreted as being different from TB – in fact, it was associated with the rheumatoid nodules (see reference finding CS 13, Chap. 2). The third surprise emerged from the latest radiomorphology of the lungs in 2007 (Figs. 38, 39). The three major causes for several foci, including one cavern, are to be considered – namely the *rheumatoid nodules* (a priority for me in light of the good health of the patient), *TB,* and ultimately the *tumors* (chain-smoker!). When further invasive diagnostics were refused by the patient, combination therapy (Arava® 20 mg/day with Enbrel® 50 mg/week) was initiated and produced a good response in the joints after a further 3 months. Over the course, pulmonary infestation in the form of acute *pneumothorax* developed as a complication and necessitated mechanical ventilation.

40. (C) *A disease* (*RSS*, Chap. 1.3.1; see also Fig. 49a) based on the pattern of involvement. *Therapy*: immunosuppression (cortisone with MTX and possible biologics, in this case *Enbrel®*, currently approved for early forms of this disease) *as early as possible* in order to achieve remission, as applicable.
41. (B) *A clinical syndrome* (*RSS*, Chaps. 1.3.1 and 4.6.3) in conjunction with CS 14, *disease-specific*. *Therapy*: immunosuppression (MTX with or without cortisone) a*s early as possible*; it was possible to use a *biologic* as part of a study.

CS 14: Acute swelling of toe 5 on the left and emergency synovectomy with a suspected tumor, female, 52 years

This case should demonstrate the not untypical difficulties of early diagnosis of a classic disease. Instead of instigating immunological examinations *synovectomy* of MTP 5 left was carried out upon suspicion of *neoplasia* (this is how severe arthritis /see Figs. 41, 65/ looks). Once the arthritis had spread, especially symmetrically (Fig. 41), rheumatological examination ensued. About *synovectomy*: In the case of definable, earlier RA with (a) symmetrical involvement of a knee (but not the small joints), such surgery could even be *curative*.

42. (C) *A disease* (*RSS*, Chaps. 1.3.3 and 4.6.1) in light of the pattern of involvement; the late sequelae or damage from a medical history spanning more than 20 years, without basic therapy, are visible (cf. early forms of the same disease, Figs. 28, 40). *Telescopic finger* (shortened, slack and without function). *Therapy*: all therapies (currently taking only Decortin® 5 mg/day) were refused by this patient due to potential side effects (*compliance* difficulties). Optimization of *systemic* (at the sign of activity, possibly MTX with *biologics;* Enbrel® is approved without MTX) and *local* (cortisone injections, surgery due to risk of tendon rupture, orthesis, possibly TEP of PIP, MCP, MTP, see Fig. 9b) therapies should be considered, however.
43. (C) *A disease* (*RSS*, Chaps. 1.3.3 and 4.6.1) on account of the pattern of involvement (same patient as in Fig. 42); here, the late sequelae (fixed malpositioning of the toe joints) in the feet are visible (cf. early forms of the same disease, Figs. 41, 65). *Therapy*: only orthopedic care, as necessary.
44. (A) *A radiological syndrome* (*conventional X-ray* of sacroiliac joints → *RSS*, Chap. 6.8) produced a certain morphological diagnosis of sacroiliac joints involvement

bilaterally (*RSS*, Chap. 2.2.3). The nosological entity is to be considered in context with CS 15 and the radiological procedures (Figs. 45 and 46). On account of this picture, further diagnostics and *antiinflammatory therapy* (*local* essential, possibly *systemic*) are indicated.

CS 15: Asymmetrical pain and imaging of sacroiliac joints in HLA-B27-positive male patient, 42 years

The criterium for radiology was the inflammatory back pain (*RSS*, Chap. 2.1.5) on initial diagnosis of AS (*RSS*, Chap. 2.2). Thereby, *the methods* must be expected to *provide both possibilities and limitations*. Several methods can reveal the various clinical aspects of back pain, namely the *presence of involvement* (X-ray and bone scintigram, Fig. 44, show inflammatory or degenerative backgrounds), *activity* (Fig. 45) and *damage* (Fig. 46), which can be laterally different. Depending on the issue at hand, the relevant methods should be employed in a particular sequence. Such methods are to be regarded as the starting points for optimal *therapy*: initially local, CT-controlled cortisone injection into the *right* sacroiliac joints joint where the pain and activity are located, then *left*, where the erosions or damage are more to be found. Such therapy was initially successful, so that the need for *biologics* is not given at present (according to guidelines).

45. (A) *A radiological syndrome* (*CT* of sacroiliac joints → *RSS*, Chap. 6, Step 8) in the same patient with *left-sided* changes: bilateral *sacroiliitis* with erosions and subchondral sclerosis, emphasized on the left, "colorful picture", but with acute inflammatory, extensive *corticalis destruction* on the right.
46. (A) *A radiological syndrome* (*MRI* of sacroiliac joints → *RSS*, Chap. 6, Step 8) in the same patient revealed *more right-sided* changes (*bone edema in the right and increased sclerosis of the left* sacroiliac joint), confirming the diagnosis of *sacroiliitis* (*RSS*, Chap. 2.2.3) with therapeutic consequences (see above).
47. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.2, 9.2.3) even in conjunction with CS 16, difficult to assign causally during the short period of observation (3 months). Most such cases involve *non-differentiated* vasculitis associated with CTD, most likely *SSc or Buerger's* disease. *Therapy*: *immunosuppression* (high doses of cortisone with e.g., MTX SC) and *vasodilation* (Prostavasin®, Iloprost, Bosentan).

CS 16: Acute acral gangrene, high-titer ANA with no organ involvement, 36-year-old female

In this case the main difficulty was finding the cause of the acute acral gangrene. Initially this process is to be assessed as a true *Raynaud's* phenomenon, where the other – but not all (e.g., digits 4–5 not affected) – vessels of the hands (some with minor gangrene, others with cyanosis) are affected. Skin-muscle biopsy from the same side of the upper arm produced unremarkable findings. Thereby, there was no clinical involvement of the feet. Another pattern of circulatory disorders in the fingers can be seen from Fig. 14. No organ (endocarditis should be ruled out due to the risk of embolism) or connective tissue involvement could be ascertained. Some evidence of such is to be seen in the capillaroscopic

pattern (similar to *SSc*) and the *high ANA* titers, but with no differentiation, ruling out primary *Raynaud's* phenomenon. The slight CRP increase is attributable to the existing gangrene. In men, consideration is to be given more to *Buerger's* disease, which in this case is also relevant. Another, rare cause for such digital gangrene (*APS, cryoglobulinemia* or other forms of *vasculitis, cholesterol embolism*) was ruled out clinically, immunologically, morphologically and angiographically. The course could be stabilized by 2 weeks of therapy with Decortin® and MTX as well as Prostavasin® infusions. The underlying diagnosis was unclear during the follow-up period (6 months). Most likely, this case is in my opinion the initial manifestation of *SSc*.

48a. (A) *A radiological syndrome* (*MRI* of thoracic spine *before* therapy (*RSS*, Chap. 2.2.2): *Irregular contouring of the base and top plates with an indication of erosive character, clear edematous zone in the vertebral body and barrier disruption of the vertebral disc or reduction in the intervertebral space and edematous signal changes in the medullary cavity. At the same time, the base and top plates are poorly outlined.* Such changes can be clarified causally only in the context of CS 17. The same changes developed after a 2-week break during years of maintenance therapy (CS 17, Chap. 1.1.2).

48b. (A) *A radiological syndrome*, *MRI*-confirmed syndrome (after 3 months of therapy, see CS 17): the patient had no symptoms, clinical findings correlated with positive dynamics of the MRI changes in T6/7 and T8/9.

CS 17: Localized pain, small gibbus in thoracic spine and CRP elevation in HLA-B27-negative female, 50 years

A deciding factor in the *local diagnosis* of the five years of medical history is the *MRI* finding (Fig. 48a). The most common cause for this are infections (TB, among others) and tumors. They can be ruled out anamnestically, for certain. Indicative to the *causal diagnosis* of such relatively rare, but prognostically relevant, local thorax spine changes was the *sacroiliac jonts's* finding (as with CS 63 with isolierte *arthritis* of C1-C2, initially of unknown origin), in a similar way to Fig. 124. The *second* feature of such a case is its dependency on the strength of immunosuppression: only very intensive and sustained immunosuppression with cortisone was effective. During a therapeutic interval of 2 weeks, the same MRI changes developed as in Fig. 48a, and at the same time there was a dramatic rise in CRP (from normal to × 15) and moderate back pain (40 mm VAS). Therapy with Enbrel® 50 mg and Decortin® 40 mg left the patient free of symptoms in 3 days, with normal CRP. Maintenance therapy (Decortin® 5 mg and Enbrel® 25 mg in 3 weeks) was initiated. The further reduction of such therapy is noticeable clinically (from the mild back pain and rise in ESR and fibrinogen), hence treatment is continued.

49a. (C) *A disease* (*RSS*, Chap. 1.3.1, see also Fig. 40) on account of the *pattern of involvement*, pictured on a bone scan (Fig. 49b). The highly active, *anti-CCP-positive* female patient with a 2-year medical history did not respond to several basic medications (MTX, Arava® also in combination), biologics (Enbrel®, Rituximab, RoActembra®)

and RSO; high-dose cortisone is needed. At present, Remicade® is used with unconvincing efficacy.

49b. (B) *A radiological syndrome* (*bone scan → RSS*, Chap. 6, Step 8) is in the same patient as Fig. 49a. Without clinical findings it is hardly possible to draw any diagnostic conclusions (could also be PsA), initially showing accumulation in the early phase as an expression of exudative inflammation (*RSS*, Chap. 1.3.1); secondly, a *pattern of involvement* indicative to the distinctions between the various joint diseases and of the introduction of systemic and/or local therapy.

50. (A) *A radiological syndrome* (*MRI* of the skull): *extensive demyelination zones bilaterally, parietooccipital, with space-occupying nature and smaller, peripheral areas in the left frontal region.* In relation to the medical history (CS 18), such *CNS* involvement is consistent with an immunological disease, and also serves as a follow-up control (*demyelination of cortical structures*). *Therapy*: relatively mild immunosuppression (17-year-old female!) with Imurek® (100 mg daily) stabilized the disease quite rapidly but did not prevent the occasional, mild epidose.

CS 18: Recurrent neurological and visual deficits (since the age of 13), 3-year treatment of multiple sclerosis (MS), high-titer ANA, CNS involvement stabilized with Imurek® therapy, female patient, 17 years

This case of a 13-year-old girl is exquisite and is characterized by the episodic occurrence of *CNS* involvement with *optic neuritis* and *transverse myelitis* (all of which improved well with glucocorticoids). The case represents the *syndromal similarity* of a *disease which is easily definable using immunological examinations* (*RSS*, Chap. 11.1) on the one hand and MS on the basis of criteria on the other. MRI was performed upon diagnosis of known MS: *extensive demyelination zones bilaterally, parietooccipital, with space-occupying nature and smaller, peripheral areas in the left frontal region*. For 3 years, these diseases could not be differentiated either neurologically or radiologically, and were ultimately controllable only with high-dose cortisone (interferon was ineffective). This response to cortisone as well as the immunological (known since 2004) and histological (2006) aspects are to be regarded in discriminatory terms with a view to MS. Consequently, present therapy with Imurek® 150 mg and Decortin® 2.5 mg/day appears to effect clinical remission with rare episodes.

51. (C) *A radiological syndrome* (*conventional X-ray*; → *RSS*, Chaps. 1.3.3, 1.3.4, and 6, Step 8) revealed partially bony fusion of the *carpalia*, massive cysts and usures (stage IV), also in a visually normal wrist (Fig. 62). Bone destruction and erosion are a component of many types of articular diseases (see Figs. 8, 9a, 23, 59, 130b), and can be differentiated only in conjunction with the medical history and first and foremost the *pattern of involvement.*

52. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.4, and 9.2.3) easy to define in conjunction with CS 19 and Fig. 53. *Therapy* (during the last 2 years) daily: CYC 150 mg Decortin® 10 mg, Trental® 400 mg × 2, ASA 100 mg, ACE inhibitors. No episodes, full regression of *sclerodactyly and sclerodermia* on the thoracic wall.

53. (B) *A radiological syndrome* (*CT* lungs → *RSS*, Chap. 10.2.3): *finely streaked/reticular pattern* in the sense of inflammatory *fibrosing alveolitis* (the finding on the left can be

described as *pneumonitis* or *pulmonary fibrosis*). CT is the method of choice for interstitial diseases. This syndrome can be clarified in conjunction with the medical history (CS 19, Fig. 52; see also Figs. 79, 85, 91), and is highly significant to therapy (see above) and prognosis.

CS 19: Acute respiratory distress, pleural effusions and cold hands, male, 58 years

This disease, which is easy to define clinically and immunologically, should on the one hand show the association between the acute onset with multiorgan involvement and on the other hand the unfavorable course. Nevertheless, therapy (systematic immunosuppression with CYC and cortisone for 2 years) positively influenced the regression of *sclerodactyly and sclerodermia* on the trunk and the pulmonary fibrosis, without the occurrence of any clinically relevant adverse effects.

54. (A) *A radiological syndrome* (*MRI* of right ankle → *RSS*, Chap. 4.9): showing *an extensive osteolytic* process *approx. 3 cm distal to tip of fibula, right,* resulting in a pathological *fracture.* The 75-year-old female patient had suffered 5 months of painful *swelling* in the lower leg (as formulated in the referral diagnosis). Extensive diagnostics (blood count, immunology, infectious serology, conventional X-ray) produced no findings. MRI performed by a practitioner (I was asked by radiologists to assess the usefulness of such a procedure) produced the *suspicious malignant finding* (*bone tumor*, osteolytic metastasis with pathological fracture). Check-up revealed no signs of *primary tumor*, *metastasis* or *osteomyelitis* (also possible radiomorphologically). The diagnosis of a *stress fracture* emerged during the surgery.
55. (A) *A clinical syndrome* (*RSS*, Chaps. 9.1.2 and 9.2.2, see also Figs. 71, 101a), as if punched out, *Ulcera cruris* in a patient with RA (could also be the case with CTD or vasculitis). Thereby, massive extra-articular disease activity (*RSS*, Chap. 2.6) is to be expected. *Therapy*: systemic immunosuppression (see CS 11, 24).

56ab. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.1 and 9.2.1) only assignable precisely in context with CS 20, has the key role in the assessment of the activity of the immunological disease including renal involvement. *Therapy*: with existing *HCV* infection and renal involvement, there was a lack of efficacy with MTX and azathioprine and the patient could not tolerate CYC; initially responded well to MMF (CellCept® 1,500-2,000 mg/day with Decortin® 7.5–10 mg/day). In the last 2 years, the course has been recurrent (skin changes, abdominal pain, "black stools", anemia), necessitating several emergency hospital admissions with high-dose cortisone treatment.

CS 20: Palpable purpura, abdominal pain and renal insufficiency, active hepatitis C, female, 50 years

This case should demonstrate that the rheumatological aspects (Figs. 56a, b) of the underlying disease (in this case hepatitis C) could be predominant. Such skin changes (*palpable purpura of necrotizing venulitis*) are associated *clinically* with the current renal involvement

(stable hematuria, mild albuminuria and elevated creatinine) and recurrent abdominal pain. The *cryoglobulinemia (mixed type 2*) induced by the active hepatitis C caused the systemic affectation of small vessels; dermatohistologically: *leukocytoclastic vasculitis*. At this time there is no evidence of a progression to lymphoproliferative disease (in type 2 roughly 15% of patients). It is best to instigate *therapy* for the underlying disease (specific therapy with interferon and Ribavarin® was not effective and poorly tolerated). At the same time, immunosuppression was administered (daily Decortin® 10 mg and Cellcept® 2,000 mg), which proved to be ineffective (as above). In this refractory case, therapy with 500 mg rituximab weekly (four times) was undertaken. After the second infusion, there was a recurrence of the skin changes. The immediate effect was revealed after the fourth infusion (all were tolerated well), i.e., a symptom-free condition under reduction of Decortin® to 5 mg and CellCept® to 1,000 mg daily. Clinical remission was sustained for the following 18 months with such therapy.

57. (B) *A clinical syndrome* of *ocular involvement* (*RSS*, Chap. 10.8.1); such cases should be clarified and managed together with an ophthalmologist. In conjunction with the clinical findings (patient has similar changes to those in Fig. 44 and HLA-B27 antigen), the causes mostly were easily identifiable. *Therapy*: ciclosporin 150 mg/day, Ultralan® 10 mg/day, Humira® 40 mg at intervals of 2 weeks, careful monitoring of concomitant diseases (obesity class III, arterial hypertension, poorly controlled diabetes mellitus II, drug-toxic liver damage). Ophthalmological examination detected relatively rapid (within 6 weeks), positive dynamics of ocular involvement and vision. At the same time there was an increase in serum creatinine (1.40 mg/dl). After a break, CellCept® was administered with renal values normal thereafter.
58. (B) *A clinical syndrome* (*RSS*, Chaps. 1.3.2 and 1.5.3), namely MCP 2 involvement, could be interpreted only in the context of the clinical findings (polyarthritis, anti-CCP positivity) and radiomorphology (Fig. 59; see CS 50 with identical involvement and different diagnosis). *Therapy*: MTX and a *biologic* (Cimzia®/certolizumab as part of a study) resulted in remission in line with the criteria, with the exception of the affected joint (Fig. 59). Consequently, several cortisone injections and ultimately RSO were administered, with short-term regression of the local clinical activity.
59. (B) *A radiological syndrome* (*conventional X-ray* → *RSS*, Chap. 1.3.4) revealing selective destruction of the right MCP 2 and a cyst in MCP 4 of this female patient (see Fig. 58). Refer to the comments on CS 50.
60. (C) *A radiological syndrome* (*conventional X-rays* of C1-C2) with *absolute* disease specificity (*RSS*, Chap. 2.2.2), fresh *syndesmophyte* left); in this case the early disease was documented. *Therapy*: according to disease activity.
61. (C) *A radiological syndrome* (*aortoangiogram* → *RSS*, Chaps. 9.2.2, 9.2.6, 9.2.7, and 13.4). The pictured morphological diagnosis can be confirmed by the clinical data (CS 21). *Therapy*: angiological treatment (3 stents inserted into *A. brachiocephalica, A. carotis and A. iliaca*) and immunosuppression (azathioprine, then MTX with Decortin®, then Arava®). The course was stable, with no clinically relevant circulatory disorders.

CS 21: No pulse on one side (since the age of 20), cardiac arrhythmias and two acute myocardial infarctions, female, 36 years

Many years of disease with varied angiological/cardiological symptoms, not initially regarded as relevant in this young woman. Only after two *myocardial infarctions* in quick succession was a rheumatic disease first postulated. Angiological (4 stent implants into the coronary (1), supraaortic (2) vessels and *A. iliaca* (1)) and immunosuppressive (MTX, azathioprine, cortisone) therapies enabled stabilization of the course, apart from (a) the extremely painful, red and swollen scar (post thoracotomy; *synchondrosis /perichondritis/ manubriosternalis* /*RSS*, Chaps. 3.11.7 and 4.2.4/ suspected) and (b) the left thoracic pain during the last 4 years, which increased with exercise. These two syndromes are completely reversible with Arava® therapy.

62. (C) *A clinical syndrome* (*RSS*, Chap. 1.3.3; see also Figs. 35, 42, 80, 129c, where partly similar, but less pronounced changes are to be seen) which is virtually *disease specific*: *button-hole deformity* digits 2–5 left and 5 right, *flexion contractures* in the distal interphalangeal joints 2–4 right, so-called *claw hand* which here is *arthrogenically* fixed, in Fig. 18 *dermatogenic*, in Fig. 19 *neurogenic*, in Fig. 130a *osteoarthritis-induced*. The hands in Fig. 62 are a diagnosis, particularly in conjunction with radiomorphology (Fig. 51) and clinical findings (more than 20 years of *symmetrical polyarthritis* with restrictions to passive movement (why?) of the fingers and wrists; patient recently arrived from abroad). At the same time the patient currently has stable CRP elevations (×4–6) and therefore needs a more than moderate level of immunosuppression (cortisone, MTX + Arava®; if there is no response, *biologics* should be used), despite stage IV disease.
63. (A) *A clinical syndrome* (*RSS*, Chap. 3.3.1) with a clear morphological correlate (see Fig. 95), associated with arthritis of PIP 3 (as in Fig. 68), whereby two articular diseases are possible (serological diagnostics indicative, namely anti-CCP positivity). Therapy: basic therapy (Decortin® 5 mg/day and MTX 15 mg/week) were first intensified (Decortin® 30 mg/day + Remicade® N3) but unsuccessful, suggesting that orthopedic measures would be required.
64. (B) *A radiological syndrome* (*bone scan* → *RSS*, Chaps. 1.3.1 and 6, Step 8) revealing the *activity* of the disease (differing intensity in early-phase enhancement) and *pattern of involvement* ("hot-spot" affectation both DIP and PIP joints to be seen in left dig. 3), hence both RA and PsA would be possible. Clinically, these two diseases are *mostly* easily distinguishable. *Therapy*: according to nature and activity of disease.

65a. (B) *A clinical syndrome* causally identifiable only in the context of the clinical findings (*RSS*, Chap. 4.6.3) and imaging (*RSS*, Chap. 6, Step 8) (see Figs. 15a, 41). This case involves a young man with recurrent *Acne vulgaris* and *Tietze* syndrome (as in Fig. 69). The dactylitis visible in Figs. 65a, b would fit with *acne*-induced arthropathy (roughly the same as *SAPHO* syndrome → *RSS*, Chap. 4.2.1, but no psoriasis). Therapy: *systemic* (cortisone and MTX), response was registered.

65b. (B) *A radiological syndrome* (*bone scan* in the early phase → *RSS*, Chaps. 1.3.1 and 6, Step 8) confirms the *dactylitis* (→*RSS*, Chap. 4.6.3).

66. (B) *A clinical syndrome* (*RSS*, Chap. 4.6.2 see also Figs. 7 and 115) cannot, in fact, be clarified by the clinical findings (CS 22): no morphological correlate was found. The good response maintained with cortisone (Fig. 67) suggests that there is an (auto) immunological cause or *cortisone-dependent disease* (*RSS*, Chap. 13.3), most likely associated with vasculitis. Therapy: cortisone pulse therapy + MTX 15 mg/week, with hospitalized treatment for the flares.
67. (B) *A clinical syndrome* (see Fig. 66) following cortisone pulse therapy.

CS 22: *Puffy hands* and high CRP of unclear etiology in 17-year-old trainee painter

This case (Fig. 66) demonstrated the difficulties of morphological diagnosis in rheumatology (what should be biopsied here?). It is certainly an inflammatory/rheumatic disease, namely acute swelling in both hands (see also Fig. 7), massive CRP increase, good response to cortisone from the first episode (Fig. 67) with sustained remission also during the second episode and identical therapy. No organ involvement, non-specific immunology. Acute Sudeck's syndrome seems unlikely on account of the symmetrical involvement. Remitting seronegative symmetrical Synovitis with Pitting Edema (*RS3PE* syndrome) also seems unlikely because of the missing pattern of arthritides, young age of the patient and extremely high CRP.

Vasculitis of the small vessels cannot be confirmed morphologically or angiologically. An allergic process during painting work is not really consistent with elevated CRP. The fact remains that the dramatic disease or condition was healed without having secured a diagnosis.

68. (B) *A clinical syndrome* (*RSS*, Chap. 1.3.1; see also Figs. 3 and 64, a *radiomorphological correlate of such changes*). It cannot be clearly explained in conjunction with the clinical findings (CS 23). This case is more likely the joint disease associated with HIV (*RSS*, Chap. 12.4.3; see Fig. 88). Therapy: cortisone and MTX under CD4-level control produced a clear improvement.
69. (B) *A clinical syndrome* (*RSS*, Chap. 4.2.1). Only in conjunction with CS 23 and Fig. 68 can HIV-associated joint disease be postulated based on the almost specific pattern of joint involvement (*RSS*, Chap. 12.4.3). *Therapy*: (see comment to Fig. 68).

CS 23: Acute arthritis and Tietze syndrome with HIV, female, 36 years

The rheumatological question was whether this illness (whereby HIV is not implied) can be attributed to an inflammatory rheumatic disease. Most certainly is on account of the stable, florid *arthritis* with extremely *high CRP*. Which inflammatory and rheumatic disease with such a pattern of involvement in HIV (the disease in Fig. 84b) is involved? Other rheumatic diseases can almost certainly be ruled out on the basis of the immunological tests performed. The necessary, and effective, immunosuppression was administered in collaboration with infectiologists while carefully monitoring CD4.

70. (B) *A clinical syndrome* (*RSS*, Chap. 3.9, 4.6.1, and 9.3.4) described as *Jaccoud's arthropathy*. Only by taking an X-ray of the hands (Fig. 72) and considering CS 24

can such changes be correctly interpreted. *Therapy*: systemic, namely several years of Decortin® 5 mg/day + MTX 10–15 mg/week.

71. (B) *A clinical syndrome* (*RSS*, Chaps. 3.2.1, 9.1.2, 9.2.1, and 9.4.1) in the same female patient could only be interpreted on the basis of morphology and in the context of CS 24. An attempt was first made to consider this condition as an independent disease – *erysipelas*. *Therapy*: antibiotics for 3 weeks but with no success; intensified immunosuppression (Decortin® 30–20 mg/day + MTX 15 mg/week) produced a regression in the changes in 2 weeks and they were later (Fig. 73) totally reversible.
72. (B) *A radiological syndrome* (*conventional X-ray → RSS*, Chaps. 1.3.4, 6, Step 8, and 13.9), indicating the characteristics of deformed hands (Fig. 70), should be considered in conjunction with the medical history (CS 24).
73. (B) *A clinical syndrome* (*RSS*, Chaps. 3.2.1 and 9.4.1) showing the regressiveness of the changes (cf. Fig. 71) after cortisone therapy. This conveys an important generic term in rheumatology, namely *cortisone dependency* (*RSS*, Chap. 13, Step 3), which is to be regarded as an important criterium, but of no nosological specificity, for the presence of an inflammatory rheumatic disease.

CS 24: Deformities of the hands, myalgia, pacemaker, red feet with ulceration, female, 52 years (some episodes during 12-year follow-up period)

Over the course of this disease (which?), definable on the basis of clinical findings and immunological tests, various clinical patterns emerge which at times can be interpreted as independent diseases, e.g., are the problems with the hands related to RA (Fig. 70, *ulnar deviation, contractures, tendinitis → RSS*, Chaps. 1.3.2, 3.3, and 3.9)? This should be strictly contradicted on the basis of a *lack of erosions* (Fig. 72), *but also* RF and anti-CCP-Ab. The other manifestation of the changes depicted in Fig. 71 (*RSS*, Chaps. 3.2.1, 9.2.2, and 9.4.1) was initially interpreted as *erysipelas*. But there was no fever with chills, no migratory erythema, and no response to antibiotics - which thus contradict this. Such changes are certainly among the extra-articular symptoms of the disease. The response to intensified immunosuppression (Fig. 73) is indicative of the immunological basis of such changes.

74. (C) *A radiological syndrome* (*PET*, 2 positions → *RSS*, Chaps. 8.1, 9.2.2, and 9.2.7; cf. Fig. 77b) assigned to *fever of unknown origin* and suspected inflammatory changes in the vessels (in vasculitis of the *large vessels*) and perivascular (in Ormond's disease) structures, if other methods (*RSS*, Chap. 13, Step 9) furnished no evidence. Causes can only be interpreted in conjunction with CS 25. *Therapy*: relatively strong immunosuppression (moderate doses of cortisone and e.g., azathioprine or MMF) in this case brought satisfactory results.

CS 25: Fever, weight loss and increased inflammatory symptoms of initially unexplained origin in a 50-year-old female

This case presents the diagnostic problems and possibilities of causal investigation into months of unexplained *B symptoms* with fever, elevated CRP and ESR, weight loss,

especially *in young women*. This PET method should come last in the sequence of staged diagnostics (possibly after ultrasound, CT or MRI) for suspected vasculitis of the large vessels or Ormond's disease. *Therapy*: immunosuppression with Decortin® (40 mg/day) and azathioprine (150 mg/day). After a few days the remarkable symptoms were regressive, and remained so long-term.

75. (B) *A radiological syndrome* (*chest X-ray → RSS*, Chap. 10.2; cf. Fig. 79): *multiple nodular pulmonary infiltrations with caverns and bronchoectasis, fibrosis* - causally explicable only in the context of the medical history (patient suffered for approx. 10 years from cANCA-positive WG with involvement of the lungs). *Therapy*: lung transplantation was refused here on account of the advanced pulmonary and cardiac insufficiency (picture taken shortly before the fatal outcome). In other cases with pulmonary involvement, more or less strong immunosuppression should be instigated depending on the entity, activity, organ involvement and concurrent diseases and conditions.
76. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.5) only to be interpreted in association with other syndromes and constellations (CS 26). *Therapy*: immunosuppression, colchicine, sustained response generally to cortisone pulse therapy (Decortin® 250 mg *IV* N3).

CS 26: Mouth ulcers, heart attack, severely increased ESR and CRP, female, 73 years

These common problems (*acute myocardial infarction* in a 73-year-old woman, otherwise no risk factors) have remarkable clinical aspects, namely known *MB* with recurrent *mouth ulcers, extremely elevated ESR and CRP* during and shortly before the event. Such constellations are suggestive of vasculitis of the large and medium (*coronary*) vessels possible in association with *MB*. *Therapy*: cortisone pulse therapy produced a stable response (no vascular symptoms, no increase in CRP or ESR). No further diagnostics were undertaken, therefore. It must be noted that continued elevation of CRP, which is regarded as a significant *trigger* for atherosclerosis (*RSS,* Chap. 12.4.2), markedly increases the rate of myocardial infarction.

77a. (C) *A radiological syndrome* (*MRI angiogram → RSS*, Chaps. 9.2.2, and 13, Step 6): *Irregularities of the external aortic wall and A. iliaca bilaterally*. *Lumen fluctuations of A. iliaca communis bilaterally, but somewhat greater on the right than the left, but with no higher stages of stenosis*. Clinically there was severe *back pain*, initially treated intensively (reportedly 60 injections in one month), as well as episodic *fever and abdominal pain*. *A. temporalis* biopsy (before therapy) was normal. Such symptoms are dependent upon the strength of immunosuppression. No other large vessels affected. *Therapy*: relatively strong and systematic (for 5 years) immunosuppression (MTX 10 mg/week, Arava® 20 mg/day, Decortin® 15 mg/day). The thickness of the aortic wall (on MRI and ultrasound) could be reduced over the course. Nevertheless, intermittent abdominal pain and episodes of fever remain.
77b. (C) *A radiological syndrome* (*PET → RSS*, Chaps. 8.1, 9.2.2, and 9.2.7; cf. Fig. 74) in the same patient (see Fig. 77a): *band-shaped enhancement in abdominal aorta – (level approx. L 2/3), as with minimally active* aortitis, which is relatively rare (approx. 10–15% cases in such a rare disease), particularly in men (cf. Fig. 61, CS 21).

78. (A) *A clinical syndrome* → *RSS*, Chaps. 9.1.1 and 10.10.2; cf. Fig. 33, where are the differences? To be causally explained only in context (no organ involvement, specific Ab spectrum, cortisone dependency! cf. CS 27). *Therapy*: immunosuppression (more with induction therapy, less with maintenance therapy). Daily over the previous months: Decortin® 15–30 mg and CellCept® 2,000-3,000 mg, which are resulting in a serious urinary tract infection. Cellcept® was stopped for 1 month and then reissued. The above mentioned therapy, at high doses, was ineffective (platelet count was below 30,000–50,000/µl, whereupon rituximab (1,000 mg in two infusions) was prescribed.

CS 27: Skin and mucous membrane bleeding, thrombocytopenia and high positive anti-dsDNA with no organ involvement, female, 54 years

The problem here is the *causal classification* of the *selective thrombocytopenia with anti-thrombocytic* Ab. Indicative of such are the high ANA and dsDNA-Ab titers with positive Crithidia test. In the event of disease with such specific serology → *RSS*, Chap. 11.1), intensified immunosuppression (cortisone and CYC pulse therapy, azathioprine) should first be attempted in accordance with current guidelines. Over the course, following splenectomy, the clinical findings under cortisone (Decortin® 10 mg and azathioprine 150 mg daily) during the 8 years of follow-up did not remain entirely stable: fluctuating thrombocytopenia, dependent on the cortisone doses, concurrent basic therapy and infections, especially after CellCept®, as is well known. As a result, close monitoring of organ involvement and platelet count, as well as the potential complications of immunosuppression (one of which was described above), is essential. In recent months, by increasing the doses of Decortin® (20 mg/day) and Myfortic® 360 mg (4 tabs/day) to way beyond those which are safe, clinically relevant thrombocytopenia (below the critical count) resulted, thereby necessitating introduction of *label of use* therapy with rituximab 1,000 mg (two infusions at 2-weekly intervals) which has recently been positively evaluated in the literature. Following such therapy, which was tolerated well, an improvement appeared to ensue and there was a rise in the platelet count up to 76,000/µl despite the reduction in maintenance therapy (Decortin® to 7.5 mg and Myfortic® to 720 mg daily). Clinical remission was seen from such therapy during the following 18 months.

79. (B) *A radiological syndrome* (*CT* thorax, → *RSS*, Chaps. 10.2.2 and 10.2.3). Honeycomb lung: *massive, multiple, cystic changes, confluent focal shadowing mainly in the upper lobe, interstitial shadow pattern left, pleural effusion, massive bihilar lymphadenopathy*. The case involves a 70-year-old male patient known to have had respiratory distress for about 15 years and *exophthalmos* (until recently evidently of unknown etiology → *RSS*, Chap. 10.8.5, though it belongs to the underlying disease). Histologically (lung, 12 years ago), chronic granulomatous inflammation was established (*RSS*, Chaps. 10.2.2, 10.2.3, and 11.6), and with ongoing cortisone therapy the patient was able to work until recently. Rapid deterioration in general health and pulmonary function were ascertained on discontinuation of cortisone (*chest X-ray* taken shortly before death). The cortisone (Decortin® 1,000 mg – 5 days) and CYC (1,000 mg – 3 days) pulse therapy was ineffective.

80. (C) *A disease* (*RSS*, Chap. 1.3; see Figs. 3, 5, 35, 42, 62, 104, 129c). Can the differences to Figs. 4, 13, 81, 89, where the other diseases was illustrated, be seen? *Therapy*: mostly immunosuppression.
81. (A) *A clinical syndrome* (*RSS*, Chap. 1.4.2), definable in conjunction with CS 28 (see Fig. 80, where are the differences? or Fig. 4, where similar changes can be seen). *Therapy*: prescription of MTX should not be deemed appropriate; local therapy is to be applied (cortisone injections, RSO or Dolobene Gel®).

CS 28: Arthritis of the finger joints, rheumatoid factors and appropriate (?) MTX therapy, 64-year-old male

The patient was referred for continuation of basic therapy in existing RA. The distinction from *inflammatory osteoarthritis* (*OA*) was the main problem here as well as generally in arthrology. In terms of the *pattern of involvement* (*MCP* joints not affected, see Figs. 8, 80, 128a, b), the arthritis of the individual *PIP* joints (*Bouchard's* OA) is to be interpreted, in conjunction with *Heberden's* OA, *clearly* as OA of the fingers. The patient does not need MTX.

82. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.6) definable as a sign of vasculitis of the small vessels only in conjunction with the clinical findings (CS 29). *Therapy*: after the effective immunosuppression (see below), these changes disappeared completely.

CS 29: Alopecia, acute abdominal pain and massive proteinuria, 27-year-old male

This case initially showed, over the course, *peculiar clinical masks* of a disease. Acute onset of systemic organ involvement characterized mostly by an unfavorable course. In such a case, the non-typical symptoms predominated: severe *abdominal pain* (due to *pseudoileus* on account of *lymphadenopathy*, another time due to *renal vein thromboses*), severe *headaches* (due to *cerebral edema*), and *edema of the legs* (due to marked *nephrotic* syndrome). *Therapy*: Cellcept® 2,000 mg and ciclosporin 50 mg × 2, CYC, azathioprine, 4 × rituximab 1,000 mg. The nephrotic syndrome proved resistant to all basic therapy, hence autologous cell transplantation has been carried out successfully.

83. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.4 and 9.4.1) in a male patient with tattoos can be considered only *morphologically* (in this case *granulomatous inflammation, large nodular-type Lupus pernio compared with small nodular, disseminated type*, Fig. 90) and *radiologically* (here, *bihilar lymphadenopathy* was found, but only on CT). Such a constellation is typical for sarcoidosis but also for lymphoma, hence these diseases are hardly distinguishable. The lack of B symptoms and only hilar involvement are more indicative of *sarcoidosis*, despite the negative finding of ACE. Such changes should be differentiated from pigment granuloma (the deciding factor, thereby, is the pulmonary involvement). *Therapy*: due to the massive proliferation of skin changes, cortisone therapy was instigated. The skin changes and hilar lymphoma were reversible (except for the slight growth at the location of the Fig.).

84ab. (C) *A clinical syndrome* (*RSS*, Chap. 9.1.1) which is of great diversity (a – *Psoriasis hyperkeratotica* and b – *Psoriasis vulgaris)*, with great specificity and clinical significance on investigation of the joint and back pain. Should also be checked as a potential occurrence in relatives (has the same indicative, clinical value). *Induration* of the skin is similar to *leukemic infiltration*. *Therapy*: in collaboration with dermatologists, particularly for similar (as in Fig. 84a) cases.

85. (B) *A radiological syndrome* (*CT thorax*, compare against Fig. 53, CS 19). Radiomorphological diagnosis of new onset (when comparing with previous imaging from 06/2007), clearly pronounced *mediastinal and hilar lymphoma* as well as *solid nodule* of 2.5 cm subpleurally in S6 left. The *finely streaked, reticular pattern* of the lung parenchyma presented here, was known. The finding should be investigated immediately (see below) and compared against Fig. 79.

CS 30: Pulmonary fibrosis, Raynaud's syndrome, Scl-70 positive, HAP with response, deterioration in general condition and drop in DLCO transfer, abnormal thorax CT, 66-year-old female

The present, primary finding is seen in Fig. 85 (see above). The moderate interstitial fibrosis (increased reticular streaking, emphasized hilus region bilaterally) reflects the underlying disease. Consideration must be given thereby to: multiorgan involvement without *sclerodactyly* and with positive Scl-70 tends to contradict *SSc*. The extent of the pulmonary fibrosis is not proportionate to the highly impaired pulmonary function and general health deteriorating in the previous 3–4 months. The decisive explanation for this was furnished by the *perthoracal punch biopsy of the mass* on the left, namely the proof of small-cell, anaplastic *carcinoma*. *Metastases* were found in the liver. Chemotherapy was instigated. The decisive question: should the entire medical case history be viewed as a *paraneoplastic process* or are two diseases involved (→ *RSS*, Chap. 5, CS 73 with virtually the same issues as in the patient with WG and colon carcinoma)? Thereby, the other possible triggers are to be considered, i.e., the systematic azathioprine therapy during the last 4 years.

86. (A) *A radiological syndrome* (*MRI* of the skull for ENT → *RSS*, Chap. 10.9.2 following CYC therapy): *an almost circular, soft-tissue structure in the left maxillary sinus* (*T2-T1-weighted, hypointense*). This is a *radiomorphological diagnosis* to be interpreted causally only in conjunction with the medical history (CS 31); the maxillary sinuses were affected (*sinusitis*) after four cycles of CYC pulse therapy. *Induction therapy*: 6 cycles of HAP (Benenson et al. 2005).
87. (A) *A radiological syndrome* (*MRI* of the skull → *RSS*, Chap. 10.9.2 after HAP therapy): *significant structures of soft-tissue density no longer detectable in sinus region*. The method would be suitable for follow-up control. *Maintenance therapy*: immunosuppression (Decortin® 10–5 mg/day and MTX 10 mg/week). With 2-year clinical remission under the aforementioned therapy, an attempt to stop MTX was made. Shortly thereafter there was a *cerebral insult*, which cannot be ruled out as the sign of a flare.

CS 31: Multiorgan involvement and MRI of the ENT region under immunosuppression, 62-year-old male

This case, with multiorgan involvement and pANCA positivity, poses few diagnostic difficulties. Perhaps there is just one aspect with a view to the activity of the disease during many years of maintenance therapy (with MTX), and justification for such therapy is to be highlighted. This question can be answered only by attempting to stop MTX, as a detector for the initial activity. Stroke after the 5-week break in MTX appears to be causally related to dormant, minimal activity. For this reason, I would in future continue with the immunosuppressive maintenance therapy in the remission of such (and perhaps other) diseases. Another aspect is a new therapeutic option in WG with refractory ENT involvement. HAP achieved full regression of the specific mass (Benenson et al. 2005).

88. (B) *A clinical syndrome* (*RSS*, Chap. 4.6.4) explicable causally only in association with clinical findings. The case involves a 29-year-old HIV-positive patient with no cardiac or lung disease, no skin changes; he was evaluated as one case (CS 23, Figs. 68, 69).
89. (B) *A clinical syndrome* (*RSS*, Chaps. 1.4, 4.6.1, 9.3.2), behind which are two other systemic diseases which can only be diagnosed by disease-specific immunology (CS 32). *Therapy*: mild immunosuppression (daily Decortin® 20 mg – at present 5 mg + Arava® 20 mg); consequently stabilized.

CS 32: Arthritis, sicca syndrome and SS-A, CenpB- and anti-CCP antibodies, female, 67 years

This case in fact involves all *4* rheumatic diseases. *One* is to be seen in the *DIP nodules* (Fig. 89 and radiologically, as in Fig. 8). The *second* is noticeable from the *MCP swellings* (MCP 2-3) and high-titer anti-CCP antibodies. The *third* can be established from the clinical findings (Calcinosis cutis, Raynaud's syndrome, Teleangiectases, swallowing difficulties) and first and foremost from the CenpB-Ab (*RSS*, Chap. 11.1). The *fourth* can be postulated from the *sicca* syndrome and possibly SS-A-Ab, but viewed as *secondary*. All inflammatory rheumatic diseases have relatively minimal activity at present, with no organ involvement and thus are easy to control with mild immunosuppression (Arava® 20 mg + Decortin® 5 mg/day). The further reduction in such therapy was always associated with deterioration in general health, arthritis and elevated CRP, which can be described as drug-induced remission.

90. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.1) can be clarified nosologically only by the morphology (*granulomatous changes, small-nodule, disseminated type* compared with *large-nodule* type *Lupus pernio* Fig. 83), though in association with the clinical findings, chest findings (Fig. 91) and lab findings (CS 33). *Therapy*: strong immunosuppression (due to broad spread of efflorescences and pulmonary involvement). High-dose cortisone therapy (70 mg/day for 3 months) was administered by family doctor, but without any effect and long-term adverse effects (*diabetes mellitus*, requiring treatment). No response (during 2 years) to CYC, MTX, azathioprine *PO* and pulse therapy, MMF, Arava® also in combination with Humira® (3 months). Ultimately, a clear response was achieved with Remicade® (three infusions) with full regression of ACE and IL2r, lasting no longer than 8 weeks.

CS 33: Multiple focal erythema, high ACE and pulmonary fibrosis, 42-year-old male

The *nature of the skin changes* can be identified by biopsy. However, such morphological data should be viewed in a clinical context, namely with highly specific chest X-ray findings (Fig. 91) in the form of the hilar lymphoma. The potential, prognostically unfavorable involvements of the CNS, heart and liver, could not be verified. Due to *pulmonary involvement* (stage II) and primarily because of the *massive skin changes, systemic therapy* was initiated, but had no effect (see comments on Fig. 90). The 2-month response was registered only with Remicade® (three infusions). Measurement of ACE and IL2r, which was normal only under such therapy, is suitable as a follow-up control. Incidentally, the same morphological finding could look completely different in this disease (Fig. 83) and respond completely differently to cortisone (in the latter case very well, and not at all in CS 33).

91. (B) *A radiological syndrome* (*CT thorax → RSS*, Chap. 10.2.3) – *bihilar lymphadenopathy*, increased small-nodule interstitial streaking (see also Figs. 53, 85) – can be explained causally only in conduction with clinical findings (CS 33) and morphologically confirmed skin changes (Fig. 90). *Therapy* was in this case based mainly on these changes and less so on the lung involvement.
92. (A) *A morphological syndrome* of lupus nephritis /LN/ (*RSS*, Chap. 10.1) on renal biopsy after 16 cycles of CYC pulse therapy (CS 34). *Top*: *2 damaged and 1 intact glomeruli with tubular atrophy* (*A*); *Bottom*: *fibrinoid necrosis* (*big arrow*)*, extracapillary proliferation* (*small arrow*) (*activity index 9/24*; *chronicity index 4/12*). This implies signs of specific *lupus activity* and moderate *chronicity*. *Induction therapy* is in refractory LN in the form of HAP (18 *cycles*) (Benenson et al. 2005).
93. (B) *A morphological syndrome* of LN (*RSS*, Chap. 10.1, CS 34) renal biopsy after *intensified HAP* with healing of a defect as focal segmental glomerulosclerosis. *Top left*: biopsy with extracapillary proliferation (*arrow*). Top right: normal glomerulus. *Bottom*: segmental sclerotic glomerulus (activity index 1/24; chronicity index 8/12) (Benenson et al. 2005). Thereby, *no lupus-specific* changes, significant *regression of activity* or *increased chronicity* of LN are to be seen. In the subsequent 6 years, sustained remission is to be evaluated under *maintenance therapy* (azathioprine 100 mg or 50 mg and Decortin® 10 mg/daily). At present there are no indications for secondary neoplasia.

CS 34: CYC-resistant nephrotic syndrome, unexplained subcutaneous involvement; activity and chronicity of LN from the perspective of renal biopsy, response to HAP, female, 52 years

The multiorgan involvement and specific immunology enable confirmation of the diagnosis. The *emergency aspects* developed *initially* from acute onset of *arterial hypertension* (260/160 mm Hg for one week); at the emergency department, hypotensives were prescribed, with pain and swelling of the entire right leg appearing later. The *pelvic/leg vein thrombosis* was confirmed by ultrasound and CT, since which time the patient has been on phenprocoumon. A *second acute process* (firstly in the elbow region, then lower leg/foot, Fig. 27) occurred twice during 4 years. This was initially considered to be an infection in

an immunosuppressed patient, treated with antibiotics but to no effect. A response to intensified immunosuppression indicates specific *panniculitis* within the context of the underlying disease. The *therapeutic aspects* of this case are found firstly in the CYC-resistant course of LN (Fig. 92). The new option, namely intensified HAP, triggers clinical remission of the disease and GN, sustained over the last 6 years by 100 or 50 mg azathioprine *PO.* The successive renal biopsies taken during this period enable the favorable (minimal renal insufficiency, *no lupus-specific* changes) yet progressive (increasing chronicity index) course of LN to be easily controlled (Benenson et al. 2005).

94. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.1) which can only be interpreted in conjunction with the anamnestic evidence of acute *myasthenia* syndrome and *myalgia* (*RSS*, Chap. 9.6). At present, there is minimal activity in the disease (*myalgia*, CK elevation). *Therapy*: Decortin® 10 mg and azathioprine 100 mg (daily) with response in the skin.
95. (A) *A clinical syndrome* (*RSS*, Chaps. 3.3.1, 3.7.1 and 9.5) with consistent morphological correlate (see also Fig. 63). *Therapy*: during the early stage of inflammatory activity of the process and underlying disease, respectively, antiinflammatory therapy (cortisone *PO* or locally – but *no crystal suspension*! – preferably Lipotalon® or if possible laser therapy); for late-onset forms and fibrosing changes surgery may be indicated.
96. (A) *A radiological syndrome* (*CT* of the skull → *RSS*, Chap. 10.8.5) should be diagnosed not only radiomorphologically, but histologically (*granulomatous inflammation* is detectable, no lymphoma) and immunologically (cANCA, ACE are in this case not detectable). Such *orbital granuloma* is to be regarded as a progression of the inflammation in the sinuses, as in Fig. 86 (same disease). *Therapy*: immunosuppression (incidentally not tolerated in a 72-year-old woman with certain RA).
97. (A) *A radiological syndrome* (*conventional X-ray* → *RSS*, Chaps. 1.4.4, 4.11.2, and 6, Step 8) only explicable in the context of the medical history (CS 35). The intensified pain symptoms in the right hip, on response to rituximab, necessitate orthopedic consultation. *Therapy*: total hip replacement was highly successful.

CS 35: Severe hip pain in RA patient with minimal activity, 53 years

The inflammatory and noninflammatory joint diseases may present a unique mixture of the symptoms, depending on the clinical and radiological pattern of involvement. This patient, with standard RA and *minimal activity*, developed *severe hip pain* during drug-induced remission which was mostly load-dependent and accompanied on initial steps (*run-in pain*) by asymmetrical *narrowing of the joint space* and *osteophytes* (Fig. 97). When interpreting this case, a unique disease in the right hip with RA is most likely.

98. (A) *A radiological syndrome* (*MRI* of the feet → *RSS*, Chaps. 3.7.2 and 4.7) represented the certain *morphological diagnosis* in the *Fascia plantaris* region, explicable in the context possibly of the Yersinia infection (CS 36). Mostly this has a mechanical cause (Fig. 108 shows a different radiomorphological correlate for this process). Therapy: *local* (several cortisone injections in the heel region were only effective

short-term, physiotherapy) or *systemic* (cortisone, *biologics* would be possible only within the framework of AS).

99. (B) *Radiological syndrome* (*MRI* of the feet → *RSS*, Chaps. 3.7.2 and 4.7; CS 36), with full regression of the changes presented in Fig. 98, which should be regarded as a parameter for follow-up control (after laser therapy). Subsequently the patient is free of symptoms (2 years).

CS 36: Refractory heel pain and MRI confirmed response to laser therapy, 63-year-old female (Benenson et al. 2006)

This is initially a *diagnostic problem* which can be solved by MRI. Then it becomes a *causal problem*, namely with the associations of such changes to the intestine and Yersinia infection, possible linked to mechanical causes. Resistant heel pain was treated with the new option, namely *curatively* with soft laser therapy (confirmed clinically and by MRI).

100. (A) *A clinical syndrome* (*RSS*, Chaps. 2.6 and 9.1.1): *palmar erythema* associated with pain in the finger tips, in this case in a 36-year-old female patient with RA. *Therapy*: these changes were regressive upon intensification of the immunosuppression.

101a. (B) *A clinical syndrome* (*leg ulcers* → *RSS*, Chaps. 2.6 and 9.1.2, see also Figs. 2, 30, 31, 55) which can be explained only in conjunction with the medical history (severe RA, long-term cortisone therapy, venous insufficiency, resistance to TNF blockers and basic medication). *Therapy*: strong immunosuppression (CYC, rituximab).

101b. (B) *A clinical syndrome* (*RSS*, Chap. 9.1.2) in the same patient (after rituximab therapy, Dr A. Rubbert). The *scarring* should be considered when making a diagnosis just as much as the *ulcerations* (see also Fig. 32).

102. (A) *A radiological syndrome* (*MRI* of the calcaneus → *RSS*, Chaps. 3.3.2, 4.7.1, and 9.5), prior to laser therapy: *marked plantar fasciitis: edema of calcaneus (osteitis), perifascial, surrounding of soft tissue and m. flexor digitorum brevis* (Benenson et al. 2006). This is a *morphological diagnosis* with resistant heel and Achilles tendon pain. Causes can only be interpreted in conjunction with CS 37. *Therapy*: anti-inflammatory, systemic and/or local therapy (irrespective of cause, extent and bone marrow involvement) indicated.

103. (B) *A radiological syndrome* (*MRI* of the heel after therapy in CS 37, complete regression (*restitution*) of the changes which were to be seen in Fig. 102) used as a radiomorphological *parameter for follow-up control* (Benenson et al. 2006).

CS 37: Recurrent arthritis, tendinitis, enthesitis, associated with Yersinia infection. Response to laser therapy, 32-year-old female

The clinical aspects of this case, documented over 8 years, consist of *recurrent arthritis* of the small joints (MCP, MTP, and PIP), *dactylitis* (Digito 2), *tenosynovitis, enthesitis and plantar fasciitis*. Only the association with the 3 years of serologically fresh Yersinia infection can be verified thereby. Fig. 102 shows the *tendinitis with bone marrow edema*

around the heel. *Therapy*: *systemic* cortisone boosts and MTX for flares, recently Arava®. Laser therapy was used for *localized* problems (Benenson et al. 2006).

104. (C) *A disease* (*RSS*, Chaps. 1.3.2, 3.1.1, and 3.3, see also Figs. 3, 35, 80, 112, 122a, b, 129c). Therapy: systemic (*RSS*, Chaps. 7.3 and 12.3).
105. (A) *A radiological syndrome* (*CT* of the abdomen → *RSS*, Chaps. 10.1, and 13, Step 9), a morphological diagnosis /*nephrocalcinosis/* with unclear clinical significance in a patient with SLE (CS 38) and status post acute renal failure. In other cases, namely in *primary hyperparathyroidism* and Sjögren's syndrome, this syndrome is associated with an unfavorable prognosis for the kidneys. *Clinically* the renal problems present as a *nephrotic* syndrome (*RSS*, Chaps. 10.1.2 and 10.1.5). *Therapy*: systemic, i.e., daily Decortin® (15 mg, 5 mg at present) and MMF (CellCept® 3,000 mg, 1,000 mg at present); patient currently has no symptoms, proteinuria up to 500 mg/24 h.

CS 38: ANA-positive mastitis, resistant nephrotic syndrome, nephrocalcinosis, questionable APS, phenprocoumon therapy, iatrogenic renal failure, 27-year-old female

This case is of clinical interest first and foremost because of the *untypical onset* of the disease at the age of 16 with *ANA-positive mastitis* following exposure to the sun. Six years later, *exudative pleuritis* developed, pronounced *nephrotic* syndrome (proteinuria up to *9.0* g per 24 h), thirdly *iatrogenic renal damage* resulting in *acute renal failure* after abdominal *hemorrhage* which occurred during the unnecessary phenprocoumon therapy. *Too systematic a therapy with ciclosporin* is, incidentally, known to increase the creatinine levels. Furthermore, it is highly likely that diagnosis of APS (due to proof of ACLA) was not standardized and hence the phenprocoumon therapy was stringent. I also find the stringent therapy with erythropoietin for *Coombs-positive anemia* (this substance was too highly quantified in the serum) superfluous (in the absence of renal insufficiency). The positive dynamics of proteinuria were seen during CellCept® therapy. Thereby, mixed proteinuria is to be evaluated as *glomerular* on the one hand and *tubular* on the other (*RSS*, Chap. 10.1.2). The latter could be connected to *nephrocalcinosis* (Fig. 105). If so, limitations to immunosuppressive therapy are possible (in the event of a flare). The switch to rituximab does not at this time seem appropriate due to the clearly reduced proteinuria (to 0.5 g/24 h).

106. (A) *A radiological syndrome* (*MRI* of the shoulder → *RSS*, Chaps. 3.3, 3.6, and 4.1): *subdeltoid and subcoracoid bursitis in combination with tendinitis and peritendinitis of the supraspinatus tendon, small amount of joint effusion* (Benenson et al. 2006). This is a radiomorphological diagnosis in resistant shoulder pain (CS 39). *Therapy*: local (physiotherapy, cortisone injections) was ineffective; laser therapy was undertaken.
107. (B) *A radiological syndrome* (*MRI* of the shoulder, CS 39) following *laser therapy* (Benenson et al. 2006): the inflammatory changes in the clinical and MRI findings regressed completely over the long term. MRI should be employed in such a condition for follow-up.

CS 39: Refractory shoulder pain, MRI-assured response to laser therapy, 61-year-old female

This is a presentation, *initially*, of an appropriate radiomorphological procedure for unexplained *shoulder pain*. *Secondly*, we have a relatively new therapeutic option for a common process, i.e., mechanically induced, persistent pain in the shoulder. The complex inflammation was treated effectively with laser therapy confirmed clinically and by MRI (Benenson et al. 2006).

108. (A) *A radiological syndrome* (*X-ray* of the heel→ *RSS*, Chaps. 3.6.2 and 4.7.1), a radiomorphological diagnosis for fresh, not yet calcified *osteophytes*. In this case the patient could hardly walk; in other cases the radiological changes are not consistent necessarily with the symptoms of pain. *Therapy*: local (physiotherapy, cortisone injections, radiotherapy, laser therapy).
109. (B) *A clinical syndrome* (*RSS*, Chaps. 3.2.1 and 9.4.1) and clinical diagnosis, respectively, explicable causally only in relation to the medical history (CS 40). *Therapy*: cortisone (Decortin® 20–10 mg/day, approx. 2 weeks). Discontinuation upon regression of the symptoms.

CS 40: Attacks of fever with high CRP and *Erythema nodosum*, 26-year-old female

The problem was the *causal* investigation of the last 16 years of *feverish episodes* and *skin changes* (Fig. 109). One of the most common causes thereof is sarcoidosis and streptococcal infection, followed by *Yersinia* infection, which in this case was detected (*RSS*, Chap. 11.3.2). The diagnosis certainly could have been ascertained sooner. *Therapy*: most effective is cortisone therapy with e.g., Decortin® 30 mg/day. Antibiotic therapy (tetracyclines/quinolones) is recommended only if the infection is fresh (e.g., positive stool culture).

110. (A) and 111ab. (A) *A clinical syndrome* (*RSS*, Chaps. 9.1.1 and 9.1.3; see also Figs. 15a, 84a, b) developed *suddenly*, with generalization, 2 days after Humira® injection (CS 41): in the extremities and the whole body, except the face, and particularly dense on the hands and soles of the feet, in the following sequence: first *pustules* (Fig. 111a), after 2–3 days massive *vasculitic and hemorrhagic* (massive on the heels), *epidermal* patches of *necrolysis* with *Urticaria vasculitis*, somewhat later *psoriasis* (Figs. 110 and 111b). *Therapy*: prescription by dermatologists of mostly local therapy, with good effect.

CS 41: Drug-induced generalized polymorphic efflorescences following TNF blockers, female doctor, 49 years

Such changes (Figs. 110, 111a, b) are to be viewed as drug-induced (*RSS*, Chap. 9.1.3); they developed simultaneously, without prior signs, following injection of Humira® in a patient with *psoriatic SpA* who was HLA-B27 positive. There is a history of regular intake of this medication for 1.5 years, with good response, also in the plaques, without any

adverse effects. Also remarkable was the extent and the step-wise progression of these changes: *initially pustulous* efflorescences, *then* the *vasculitic* component and *ultimately* in those areas the massive superficial *plaques*. Also remarkable was the efficacy of the local therapy prescribed by dermatologists. Despite the known associations of such changes with TNF blockers the question must be asked whether the other members of this TNF family should be prescribed upon increased activity of the underlying disease. In one almost identical case a patient with AS was effectively treated with Remicade® for 3 years. Thereafter, the changes on the hands and soles of the feet developed after the 4th injection when switching to Humira® /Fig. 129b/. Such *pustulous keratoderma blenorrhagica* (*RSS*, Chaps. 9.1.1 and 9.1.3) could be regarded as another variant of *pustulous psoriasis* in SpA, particularly in ReA or SAPHO syndrome. A switch to Remicade® (together with local therapy) produced a marked improvement in the skin symptoms. The known *psoriasis-inducing effect of TNF blockers*, however, in the form of *Psoriasis vulgaris*, appears from the last summary (Wollina et al. 2008) to be family-specific. Recently we have seen such changes using Cimzia®.

112. (B) *A radiological syndrome* (*CT* thorax → *RSS*, Chap. 10.2.2) in ANCA-positive female patient, 63 years, demonstrated *a progression in size of bipulmonary and intrapulmonary infiltrates and caverns: in the mid lobe clearly connected to the bronchial system (caverns almost 6 × 5 cm), in the right dorsocaudal lower lobe (cavern approx. 4.3 × 6.2 cm). The two granulomas in the left lungula were confluent and now measure 4.3 cm in diameter.* At the time of examination (after 3rd cycle of CYC bolus therapy) the general condition was seriously deteriorated, CRP increased (to factor × 30), and procalcitonin normal. Having ruled out superinfection and neoplasia, rituximab therapy (two infusions of 1,000 mg each) and CellCept® 2,000 mg per day were initiated (Dr A. Rubbert). Complete regression of the aforementioned pulmonary changes ensued in 6 weeks.
113. (B) *A clinical syndrome* (*RSS*, Chaps. 9.1.2 and 9.2.2, see also Fig. 14) can be assessed *causally* only in the context of the medical history (CS 42). *Therapy*: at present the disease appears to be self-limiting and not in need of therapy.

CS 42: Depression and treatment-associated gangrene, 50-year-old male

The *diagnosis* of vasculitis (2 years ago) had very certain criteria (status post amputation of toes 2 and 3 on the right shown in Fig. 113). On the *cause*. Previous history: treatment with *psychopharmaceuticals* (for depression) ensued at the same time as the above mentioned *acute condition*. From the *first event* onwards, *Trevilol*® was prescribed but the correlation to the product was not evident, or such a correlation was not questioned. Prior to the *second event* other antidepressants were taken (*Remergil*® *and Edronax*®), and the changes were not reversible. *On the nature of the vasculitis*. To obtain a true picture, cortisone was first stopped. Subsequently, *no criteria* for *systemic vasculitis* were found: neither *Raynaud's* syndrome, nor organ or connective tissue involvement, nor laboratory parameters (CRP, ANA, ANCA, coagulation problems were not indicative). The *pulmonary hypertension* (40 mmHg) which developed shortly after stopping cortisone was seen

as related to COLD, with diminished one-second capacity (48%) and no diffusion disorders. We could find no criteria as to whether the vasculitic symptoms existed whatsoever 2 years following surgery. Such constellations could almost exclusively involve *drug-induced vasculitis*. This form of *hypersensivity angiitis* often has, as in this case, a *terminated, self-limiting course* (upon discontinuation of medication) as well as *untypical symptoms*, e.g., no organ involvement (cerebellar infarction is to be seen as an independent problem) or Raynaud's phenomenon. Therefore it is not wise, in my opinion, to undertake further diagnostics, e.g., muscle biopsy or MRI of the thighs. The diagnosis could ultimately be established from the extensive *history,* namely by determining the *close time-related connections of the two episodes of bleeding disorders with the intake of psychopharmaceuticals*. *The basic therapy* appears, on account of the lack of activity, *not to be indicated*.

114. (A) *A clinical syndrome* (*RSS*, Chaps. 3.1.2 and 4.7), post-operative status of 1st toe (CS 43).

CS 43: Acute *puffy hand* right after tophus ablation of first toe, 56-year-old male patient

This patient's problems emerged 3 days after outpatient surgery, manifested as acute *puffy hand*-like changes (Fig. 115; cf. Figs. 7, 66), but accompanied by asymmetrical joint involvement (!), *fever* and extreme *pain in the wrist* as well as elevated CRP. Such an association between surgery and distant arthritis should always raise the suspicion of *septic arthritis*. *Positive pathogen* diagnostics ensued (from blood and joint punctate). Conservative *therapy* (see comments on Fig. 115) is most commonly employed, lasted 4 weeks and was effective.

115. (B) *A clinical syndrome* (*RSS*, Chaps. 1.3.1, 4.4, and 4.6.2) can be clarified causally only in the context of the medical history (CS 43). *Therapy*: wrist puncture (repeated, preferably with irrigation /lavage/ of the joint), long-term antibiotic therapy; if such therapy is inadequate, synovectomy is indicated.
116. (C) *A radiological syndrome* (*X-ray* spine → *RSS*, Chaps. 2.3 and 6, Step 8, see also Figs. 118, 123), radiomorphological diagnosis, not necessarily consistent with the pain and other spinal syndromes. Therapy (orthopedic): depending on concomitant syndromes (*RSS*, Chaps. 3.4 and 3.12.1), could be surgical in the case of spinal canal stenosis, for example.
117. (C) *A radiological syndrome* (*X-ray* spine → *RSS*, Chaps. 2.2.1 and 6, Step 8, see also Figs. 60, 124) is absolutely specific (diagnostic criterium) in the causal investigation of back pain. *Therapy* (rheumatological): according to disease activity.
118. (C) *A radiological syndrome* (*CT* spine → *RSS*, Chaps. 1.5.2, 2.3, and 6, Step 8), marked *spondylophytes*, described as DISH (*diffuse idiopathic skeletal hyperostosis*) syndrome, with high diagnostic value in the causal investigation of back pain; is not necessarily consistent with its intensity, common in patients with *Diabetes mellitus*, often confused with *syndesmophytes* (cf. Figs. 116, 117). *Therapy* (orthopedic): depends on concurrent symptoms (*RSS*, Chaps. 3.4 and 3.12.1).

119. (B) *A radiological syndrome* (*conventional X-ray* hip → *RSS*, Chaps. 1.3.3, 2.4.1, 4.10.1, and 6, Step 8), radiomorphological diagnosis (*concentric narrowing of joint space*) which can be causally explained only in conjunction with the medical history. It is important to find *symmetrical involvement* (see also Fig. 97). At the same time, there is increased *subchondral sclerosis* in the *symphysis* region which, at the time, appeared together with pain in this area. To be regarded as *symphysitis* (see Fig. 120). *Therapy*: surgical (Fig. 120). Figs. 119, 120, 124 belong to the same patient.
120. (B) *A radiological syndrome* (*conventional X-ray* hip → *RSS*, Chaps. 1.3.3, 2.4, 4.11, and 6, Step 8). Postoperative status in patient in Fig. 119 (total hip replacement bilaterally and stabilization of lower *sacroiliac joints*). Can another radiomorphological syndrome be identified? Yes.
121. (A) *A radiological syndrome* (*MRI* of the hip → *RSS*, Chaps. 2.4.3, 3.10.1, and 4.11), highly specific morphological finding: *marked signal changes in left acetabulum, following application of contrast agent the changes in the acetabular roof show strong enhancement, entire left acetabulum clearly surrounded by bone marrow edema.* The finding can be clarified causally in relation to the medical history (CS 44). Is spontaneous *osteonecrosis* in the *acetabulum or coxitis* most likely? *Therapy*: primary disease not active at present, hence cortisone should be discontinued. In terms of the acute process, MTX should be applied. A good response could be achieved immediately: the patient remains mobile, and almost free of pain. Prognosis of the process is unclear.

CS 44: Polyarthritis, cortisone therapy, acute motion deficits in the hip, female, 25 years

Once the morphological correlate to severe hip pain has been clarified by MRI (Fig. 121), the question of *causes* for this condition and the underlying disease arises. *Asymmetrical arthritis* of the large joints and proven *fresh Yersinia* infection are the criteria for diagnosis of ReA → *RSS*, Chap. 11.3.2. This was possibly treated too systematically with cortisone, resulting in the new onset of left-sided hip pain influencing the clinical picture. This is a common occurrence sometimes unavoidable with long-term cortisone therapy (*RSS*, Chaps. 3.10.1 and 12.1) and should be dealt with separately - in our case with MTX and good functional results.

122ab. (B) *A radiological syndrome* (*MRI* of the right forearm, 2 projections): *extensive linear mass of soft-tissue density with a diameter of 17 × 2.5 × 3 cm, inhomogeneous contrast enhancement, producing a wall around the distal ulna which partly causes destruction of bone as well as the immediate tendons). Recommendation: schedule surgery.* Such *tumor-type,* painless changes were first assessed as a *malignant tumor* e.g., sarcoma (CS 45) and biopsied three times (!). Thereafter, surgery ensued with fusion of the right wrist joint (Fig. 122c).
122c. (C) *A radiological syndrome* (*conventional X-ray* of forearm, → *RSS*, Chaps. 1.3.4, 3.1.1, and 4.4); post arthrodesis of the wrist (stabilized with a plate) for instability of the joint (see comments on Figs. 122a, b). The underlying disease can be seen from the histological finding of the above mentioned tumorous changes (*massive*

mass of rheumatoid nodules) and the considerable *destruction of the wrist bones* (also as in Fig. 9a; a different form of destruction and a different disease can be seen in Fig. 34). Surgery ensued to prevent luxation in this joint with deficits in hand mobility. The hand function was thus clearly improved.

CS 45: Massive tumor on lower arm with bone destruction and ulnar compression syndrome in female patient with RA aged 55 years

This patient appears to be "exquisite", initially by diagnosis and then therapeutic outcome. The seropositive RA *without rheumatoid nodules* and anamnestic evidence of *bone TB* revealed a massive linear mass in the lower arm, suspected to be tumorous, infiltrating the surrounding structures (nerves, tendons, muscles, synovial membrane) and destroying the bones. Hence there is a variety of rheumatological and neurological symptoms. Painless soft-tissue swelling should generally lead to the suspicion of sarcoma. During surgery, an *enormous*, histologically confirmed *rheumatoid nodule* was found as a liquid mass and was *curatively* removed; the wrist and wrist bone were fused for the purposes of stabilization. The peculiarities of this case are: (1) the extent of the only linear rheumatoid nodule with necrosis which developed following the ineffective rituximab therapy, or this therapy was not able to prevent growth of the nodule, (2) the specific malignancy of the local symptoms (*N. ulnar* compression syndrome, bone destruction, tendon damage), (3) local symptoms treated *curatively* by orthopedic colleagues. As basic therapy, other biologics – namely Enbrel® (with a view to the history of TB) – are used successfully but not persistent. The disease activity was minimized in the last 4 months with Simponi® (50 mg monthly *SC*).

123. (C) *A radiological syndrome* (*conventional X-ray* of the lumbar spine and sacroiliac joints), a radiomorphological diagnosis (*RSS*, Chaps. 2.3 and 6, Step 8, see also Fig. 116) in the form of massive *osteophytes, sacroiliac* joints have in this case a key role in the assessment of the *lumbar* problems (cf. Fig. 124). *Therapy*: orthopedic.
124. (C) *A radiological syndrome* (*conventional X-ray* of sacroiliac joints; → *RSS*, Chap. 2.2.2), radiomorphological diagnosis in the form of massive *syndesmophytes* in lumbar region, no sacroiliac joints space (total ankylosis). *Therapy*: predominantly rheumatological and as necessary orthopedic.
125. (B) *A radiological syndrome* (*conventional X-ray* of thoracic spine at level of thoracic vertebrae 6–8, → *RSS*, Chap. 3.11.1). Post *osteosynthesis* of a fracture to the thoracic spine (1995) with incorporated osteosynthetic material (cage and pedicle screws).
126. (A) *A radiological syndrome* (*CT* of thoracic spine of 17.01.08 → *RSS*, Chaps. 2.1.2, 3.11.1, and 3.12.1): *narrowing of the spinal canal at level* T3 *with collapsed posterior edge of vertebra from* fracture *at the same level, of unexplained etiopathology.*
127a. (B) *A radiological syndrome* (*CT* of thoracic spine of 17.01.08 → *RSS*, Chap. 3.11.1): *osteoporotic sintering fracture of vertebra* T3.
127b. (B) *A radiological syndrome* (*CT* of thoracic spine of 19.08.08): status post emergency surgery, *spondylodesis* T2 (thoracic vertebra)/T4, open repositioning of spine by *osteosynthesis*, computer-navigated (Drs W. P. Groß and G. Schiffer, Neurosurgery, Cologne University).

CS 46: Years of cortisone therapy in RA, vertebral fracture and acute paraplegia, 73-year-old male

Patient taking maintenance therapy for RA for 15 years (MTX and Decortin® 5–10 mg/day), also since surgery in 1995 (*acute event* at that time considered as related to *osteoporosis*). The patient has since been relatively well mobilized, with regular outpatient follow-up, lastly on 08/01/2008. The *acute paraplegia* is causally related to a fall and osteoporosis-induced *compression fracture of the spine*, clearly visible in Figs. 127a, b. The case illustrates the almost *unavoidable consequences of long-term cortisone therapy* in an elderly patient with RA and restricted mobility. The patient died 2 months after the event (probably as a result of pulmonary embolism).

128 (abc) Visual diagnosis hands
129 (abc) Visual diagnosis hands/feet
130 (abc) Visual diagnosis hands/feet
131 Visual diagnosis of the systemic rheumatic disease
132 Visual diagnosis of the systemic rheumatic disease

CS 47: Unclear arthritis and contractures of the fingers, referral diagnosis of RA, radiological signs of OA and gout, 70-year-old male patient

The patient was referred several times in about 5 years for rheumatological consultation. In terms of the pattern of involvement, there is a mixture of clinical and radiological data most likely attributable to *OA* (flexor *contractures*, Fig. 130a) and *chronic gout arthritis* (intermittent florid, asymmetrical arthritis in toe 1, wrist, knee and ankle joints), tophi in toe 1 /Fig. 130b/, auricles (as in a 10-year-old girl, CS 55). Seronegative *RA* appears rather unlikely.

CS 48: Acute, severe pain in the legs, dramatic weight loss, abdominal pain, intestinal infarctions and positive cANCA, 30-year-old male patient

This case of a *life-threatening condition* initially posed enormous difficulties with diagnosis in a 30-year-old man. Acute *sensory and motor deficits* developed in the legs and feet (*polyneuropathy*), then rapid *weight loss* (retrospectively it is clear that this was linked to *malabsorption* or with the involvement of the small intestine) and, following *abdominal pain* with mild tension (of unclear etiology at that time) there were several *intestinal perforations*. A further problem: how is such intestinal involvement to be evaluated in an ANCA-positive patient: on the one hand as *ANCA-associated vasculitis* with involvement of the medium and small vessels or as an entity, namely PAN. Subsequent therapy (40 cm of small intestine removed), basic therapy with CYC (discontinued due to liver damage) and rituximab, then maintenance therapy with MMF, resulted in complete restitution of the symptoms (normal weight, no vasculitic symptoms, ability to work). In a further 3 years, showed the increasing renal insufficiency.

CS 49: Exudative pleuritis, lymphadenopathy and morphological diagnosis of lupus in skin biopsy, female, 40 years

This case demonstrated the significant value of immunological data as compared to morphological data when considering the diagnosis of CTD. In this case, the disease-specific immunology (ANA, SS-A, SS-B, high RF) is pivotal to the diagnosis (*RSS*, Chap. 11.1) and morphological diagnosis must be considered for skin biopsy (of LE). This morphological finding depicts the common changes typical to CTD and should not be described as an entity (*RSS*, Chap. 11.6). This also applies to the biopsy of the lymph nodes in this disease, which is not entirely indicated (was almost always carried out, as in CS 66), particularly with such a constellation. In such a symptom-free state, the patient certainly does not require treatment.

CS 50: MCP 2-3 and other forms of arthritis, status post MTX therapy, ferritin increase, male, 56 years

Stable polyarthritis is commensurate with RA, which in this case had been treated by colleagues systematically, for several years. Whether this term – *arthritis* – is correct in this case depends on the cause of the condition. A disease-specific laboratory value can explain the causal diagnosis. Other keys to this case lead from the pattern of involvement, namely *asymmetrical oligoarthritis* of the large joints, as with *inflammatory OA*, primarily MCP 2-3 (Figs. 58, 59) bilaterally, with no inflammatory signs. Isolated *MCP 2-3 arthritis* should always be indicative of a fairly common genetic disease in which, incidentally, *primary* arthrotic and *secondary* arthritic changes predominate. Thus, first identify the underlying disease and then the pattern of joint involvement! Or vice versa. In terms of therapy, *pathogenetic* (what is meant by this?) comes first (*RSS*, Chap. 1.5.4) and then *symptom-oriented* (joint punctures with cortisone injection, RSO, orthopedic measures) therapy.

CS 51: Acute hemolytic anemia and pneumonia associated with Chlamydia and dsDNA antibodies, female, 25 years

This case first demonstrated the diagnostic problems in explaining the new onset of *hemolytic anemia*. In a young woman with *hemolytic anemia* and *pneumonia*, the systemic disease should primarily be ruled out immunologically. In this case, these syndromes were associated with *Chlamydia* infection. This could well be the case, or more specifically that hemolytic anemia presents as a mono symptom in chronic SLE. Over the course the patient experienced involvement of other organs and systems, namely the CNS, kidneys, lungs, APS. As a consequence, the diagnosis of SLE appears to be certain. The basic therapy required should be adjusted to the patient's explicit wish to have children. To treat the CNS involvement, pulse therapy with cortisone, then maintenance therapy (Decortin® 10 mg/day and for a short period over 5 weeks MTX 15 mg/week *SC*) was initiated. Stabilization was achieved (Decortin® 5 mg and azathioprine 100 mg daily).

CS 52: Minimal RA activity, excessively high CRP and ESR, male, 68 years

This case demonstrated how, with RA already established, diagnostic problems may arise if the deterioration in *general health* (fatigue, massive myalgias and elevated CRP and ESR → *RSS*, Chaps. 8.4 and 8.5) is not proportionate to the (minimal) activity of RA. At such an age, *tumor* and *infection screening* should basically be initiated. The next step was to clarify whether this condition was dependent on cortisone or not. *Therapy*: no response to intensified immunosuppression (MTX 25 mg/week *SC* combined with Arava® 20 mg/day, Decortin® 20 mg/day, Humira® 40 mg/2 weeks). The cortisone pulse therapy administered twice (Fortecortin® 8–2 mg over 3 weeks *PO*) was clearly effective, clinically as well as in terms of CRP and ESR. On reducing the cortisone dosage, the neck/shoulder pain returned along with minimal *arthritis* in individual PIP joints, higher CRP and ESR values. At present, therapy is ongoing with Decortin® 7.5 mg and Azathioprin 100 mg daily and MTX 10 mg per week, with no arthritis or signs of inflammation.

In summary, a response to cortisone must be specifically evaluated. This leads to the suspicion – particularly at the given age – of another inflammatory/rheumatic concomitant disease. One of which involves shoulder and neck pain – of that I am certain.

CS 53: Pain and swelling of the finger joints and high-titer RF, ANA and ENA, long-standing diagnosis of RA revised, female, 45 years

This case showed that periarticular *arthralgias*, *non-synovialitic swelling* of the fingers and high-titer *RF* may have other causes than RA. The lack of erosions and signs of arthritic activity on bone scan were the criteria for further causal investigation. The *unremarkable sicca symptoms* (*RSS*, Chap. 10.7) and *remarkable,* specific CTD *serology* (*RSS*, Chap. 11.1) produced other diagnostic aspects which could explain all the syndromes ascertained in one concept, better than RA.

CS 54: Raynaud's syndrome, massive increase in CK and TSH in Scl-70-positive female patient, 30 years (some episodes during 5-year follow-up)

The 5-year period of follow-up in this patient showed that systematic immunosuppression (CYC and Decortin®) for SSc can be effective: the swelling (Fig. 130c), induration, *livid discoloration* and substance defects in the fingers, as well as extensive sclerosis of the skin on the arms and shoulders receded. Over the course, two different masks of this disease were seen, with virtually identical symptoms: *fatigue* and *myasthenia*, accompanied initially by a *massive increase in CK* (with normal TSH). Somewhat later, there was a noticeable, *massive increase in TSH* with low readings of free T3 and T4, but at that time *no CK* elevation. These common syndromes of SSc were largely stabilized by increasing the immunosuppression for the *myositis* syndrome on the one hand and L-thyroxine therapy for the massive *hypothyroidism* (*RSS*, Chap. 12.4.4).

CS 55: Acute recurrent attacks of pain in toe 1 in 10-year-old girl, polyarthritis with deformities and elevated creatinine (20 years later)

This case has been described under the heading "juvenile gout in women" (Kurmanalieva et al. 1986). It revealed the classic variant of "male" gout at that age and over the course, characterized by the serious consequences of *hyperuricemia*, as far as concerns the joints (*destruction, deformity*, *motion deficits*) and renal involvement (*interstitial nephritis* with renal insufficiency). The initial diagnosis of *seronegative RA* certainly did not have a positive influence on such damage. The potential pathogenetic background is evidently found in the endogenic, hereditary enzyme deficiency (excess purine load excluded). The therapeutic options are the same as those for adults with gout.

CS 56: Sicca syndrome, enlarged parotid, acute increase in serum calcium epistaxis (three emergency situations over a 12-year follow-up period, female, 65 years)

This case showed that *lymphoma* possibly developed from Sjögren's syndrome. The question is how to identify as early as possible the degeneration or relapse in the lymphoma. This concept, or postulation of such, should be reached based on (1) the *clinical* (deteriorated general health, increase in *parotid mass* and *lymphadenopathy*, development of *systemic vasculitis* /*small vessel disease*/, could at the same time be part of Sjögren's syndrome), (2) the *biochemical* (*hypercalcemia* with no increase in parathormone; increased anemia, polyclonal B-activation, β-2-microglobulins) and (3) the *morphological* (*cell transformation* in the parotid and bone marrow) *data*. The case also demonstrates that complete remission is highly likely if lymphoma is diagnosed early.

CS 57: Known PsA with minimal activity, polyarthralgias, long-term incapacity to work, discharge from cure therapy because of acute relapse, engineer, 46 years

The inflammatory joint disease appears certain, but with minimal activity (no florid arthritis, even on bone scan, no increase in CRP or ESR). The many months of incapacity to work and sudden discharge from cure therapy have, in my opinion, other causes – namely the diffuse pain symptoms or undiscovered *fibromyalgia*, which represented the justification for such organizational measures. *Therapy*: MTX 15 mg/week *SC* appears to have an effect on the skin changes, but less on the arthralgia. The trial use of Remicade® (three times) was ineffective in terms of the joint and back pain.

The prognosis of PsA (*RSS*, Chap. 7.4) in this case seems to me to be better than that of *fibromyalgia*, which is often associated with depression and disability (see CS 59).

CS 58: Arthritis, dramatic weight loss, swallowing difficulties, ANA with anti-Cenp differentiation, female patient, 68 years

Such a case should be viewed from two angles. Firstly, a systemic rheumatic disease (stable, non-erosive arthritis, swallowing difficulties, calcinosis, telenagiectases and, above all, *anti-Cenp*-Ab) is identifiable. The *paraneoplastic aspects* are possible on account of the loss of up to 15 kg in weight without changes in appetite (over a period of 6 months); they could not be confirmed by *tumor screening*. In such circumstances, massive *esophageal motility disorders* are involved, in my opinion, developing as part of the CREST syndrome and possibly affecting the small intestine by means of *malabsorption*. The excessive increases in TSH and low values for T_3 and T_4, which are often association with such an illness, are not insignificant when considering the general condition. Such a condition is always to be found with CREST syndrome and always requires treatment.

CS 59: 31-year-old female patient with general symptoms, fever and discrete lymphadenopathy (histology NHL). After 14 years of general symptoms, "pain all over", fatigue, depression, incapacitated

In this patient, the *two entirely distinct diseases*, with partly *identical symptoms*, should not be overlooked. 14 years ago the clinical pattern was entirely non-specific until a colleague (Dr E. Erdmann, Cardiology, Cologne University) reached the unobvious conclusion to have a minimally enlarged, *iliac lymph node biopsied*. Consequently, the diagnosis of *B-cell NHL* was ascertained and treated effectively.

Another clinical pattern developed 14 years later, also with general symptoms, fever, abdominal symptoms and mainly with diffuse pain, leaving the patient reliant on strong analgesics. Once a relapse of the underlying disease, infections and CTD had been ruled out, the condition was interpreted as *fibromyalgia* with diffuse pain syndrome. This was certainly a secondary somatogenic fibromyalgia as a result of the previous serious disease, with medicinal and social sequelae. The referral diagnosis, namely PMR (from age alone), appears to be ruled out.

CS 60: Fever of unknown etiology, polyarthritis, positive Yersinia serology, lack of RF and anti-CCP-Ab in 40-year-old male patient

The diagnostic problems were considerable with an unexplained clinical pattern over 6 months, with *septic pathology* (fever, nocturnal sweating, asymmetrical arthritis of the large joints, extremely high CRP). *Polyarthritic involvement* ensued with symmetrical arthritis of both wrist joints and individual *PIP* joints. The initial clinical pattern can be explained in association with the later detection of Yersinia infection as its rare variant (*RSS*, Chap. 11.3.2). The subsequent development of polyarthritis would be characteristic on account of the pattern of involvement of the second joint disease, which did not reveal any immunological markers, however. *Therapy*: initially resistance and in the last 2 years response to basic medication (Decortin® 20 to 5 mg/day, MTX 15 mg/wks *SC*, Arava® 20 mg/day, Remicade® N2, Rituximab N2, several RSO). Hence, the distinctions between

seronegative RA and ReA are sometimes difficult, particularly if two diseases exist, as I would suggest in this case.

CS 61: Minimal activity of RA, diffuse pain, stable requirement for Durogesic® over the last 5 years, female patient, 80 years

This case represents a disease or condition causing the need for Durogesic®. Whatever the case it is not RA, which is certainly very well controlled. It is a *diffuse pain* syndrome which can possibly be described as *secondary to* RA. Pain therapy with opiates should, in my opinion, be administered at a pain management clinic.

CS 62: Fever, polyserosis, elevated CRP, GGT, LDH and anti-dsDNA antibodies in 70-year-old male patient

Two important criteria for further diagnosis and therapy were identified at the hospital, namely the *exclusion of other diseases* and the cortisone dependency. The individual syndromes of the disease are entirely non-specific and suggestive of many diseases, but the combination of these syndromes is highly specific for an inflammatory/rheumatic disease which can be distinguished from SLE. The *minimal* increase in anti-*dsDNA*-Ab in such constellations should not carry *any lupus specificity*, since the other components of SLE, namely connective tissue symptoms, renal involvement and even vascular problems, are absent (*RSS*, Chaps. 8.1 and 8.4). What is the concept for *Still's in adults*? To be certain, the quantity of cortisone should first be reduced, if possible, at least as far as the clinical threshold. Rheumatological check-up should then be repeated. *Therapy*: Arava® 40 mg/day once per week, then 20 mg/day and Decortin® for 2 months, reducing from 70 to 10 mg/day, without any reactivation of the clinical symptoms.

CS 63: Severe cervical syndrome and isolated C1-C2 arthritis, initially of unknown etiology, female, 53 years

The initially, apparently isolated *C1-C2 involvement* (cervical syndrome, no other joint or back pain) was interpreted, by myself, as *secondary inflammatory osteoarthritis* with *osteitis* (thus explaining the high CRP and ESR) on the basis of the MRI finding, and scheduled for local therapy (cortisone installation). A colleague devised and confirmed a different concept by verifying *sacroiliitis*, but with HLA-B27-negativity. I would still adhere to this procedure, have the entire spine examined despite the local symptoms and commence with local therapy.

CS 64: Acute myelitis with paraplegia, mouth ulcers, hemolytic anemia with thrombocytopenia and positive cANCA, female, 47 years

The systemic nature of the disease, with extraordinarily varied clinical, laboratory and immunological symptoms, is evident. The inflammatory nature of the disease is also clear. What was unclear, in particular, upon admission, was the question whether vasculitis or

CTD was involved. The atypical *pneumonia* and pronounced *Moschkowitz* syndrome with ANCA positivity are more suggestive of primary (which?) or secondary *vasculitis.* Ultimately, this prognostically very unfavorable *Moschkowitz* syndrome was treated (cortisone, vincristine and rituximab, but also antibiotics) successfully. Nevertheless, the entity remains unexplained. To this aim, analysis of previous history should help. The first question to be answered is which vessels are affected. Acute *brain stem encephalitis, butterfly erythema, GN* with renal insufficiency, *oronasal ulcerations, cytopenias*, all suggest involvement of the *small vessels*, most likely as part of SLE. But this concept is contradicted by the *immunological* (no anti-dsDNA-Ab but ANCA) and *morphological* (not a typical pattern for SLE in main bioptate, rather fibrosis and sclerosis, as is typical for SSc) *data*. In the context of clinical findings, such results should be assessed retrospectively as non-specific (ANCA) or common with SLE (ulcerations). They certainly do not rule out SLE. Over the course, therapy with Decortin® 10–5 mg and CellCept® 1,000 mg daily enabled stabilization and release from the symptoms, which can be described as a clinical and immunological (no ANCA detectable) *remission* of SLE.

CS 65: Pain and swelling in the ankles of a physically active woman, 62 years, with known psoriasis

When investigating the resistant pain in the feet and heels, radiomorphological diagnosis should initially be the aim (with MRI), thereby revealing polydimensional, inflammatory involvement of, namely, the tendon sheath (*tendinitis*), attachments (*enthesitis*) and bones (*osteitis*). The causal explanation is reliant on the distinction between *mechanical and inflammatory pain*. *Based on the pattern* (at rest, better than on exercise), history (*psoriasis vulgaris, arthritis of the knee*) and clearly elevated CRP and ESR, such constellations are more likely to be interpreted as *inflammatory in nature* due to the known *psoriasis*, if serological and immunological markers of other diseases are absent. After *therapy* (5 weeks: Decortin® 20–0 mg/day and MTX 15 mg/week *SC*, then soft laser therapy 785 μm N10 (Benenson et al. 2006)), the patient was free of symptoms (8-month follow-up).

CS 66: Fever of unknown etiology, lymphadenopathy and cough in a male patient aged 15 at the time (six episodes during the last 12 years)

When the disease first appeared, there were considerable diagnostic problems when investigating the multitude of clinical and laboratory symptoms. The *exclusion of the most common diseases* in such constellations is to be seen as the *first necessary step*, in which case the *similar* (infections such as sepsis or infectious mononucleosis) and the *distinct* (possible malignancies) *DD spectrum* should be introduced in the case of younger (this case) and older (CS 62) patients. When ruling out such diseases, “consideration is necessary”: namely of a relatively rare disease with no specific, morphological, radiological or immunological markers but luckily virtually stable clinical and biochemical constellations, whereby *fever of unknown etiology* with elevated *CRP* and *liver enzyme-LDH*, but also *macular exanthem* and *arthralgias* should be prioritized. Such a disease is always an *exclusion diagnosis*. The virtually stable clinical and biochemical constellations, and

cortisone (dose) dependency, are helpful in this case. *Therapy*: initially high-dose cortisone (pulse and then maintenance therapy for 3–4 months), then combined with MTX (good response); with no response and adverse effects (nausea) to such therapy, Arava® (initially 100 mg – 3 days, then 20 mg/day) without cortisone was used 2004–2005, with prompt response and full clinical remission (2 years); patient was convinced that Arava® achieved more than high-dose cortisone.

CS 67: Emergency hospitalization of 42-year-old RA patient, female, after outpatient attendance with increased serum calcium levels

This patient, whose general health was not diminished, was clinically diagnosed at the first visit (28.02.04) as having seropositive RA (polyarthritis, positive RF and anti-CCP-Ab). A couple of hours later, increased levels of *calcium in the blood* (3.37 mmol/l; *upper limit* 2.6 mmol/l) were ascertained. Such an emergency situation developed during the asymptomatic phase of the newly discovered condition. To avoid *hypercalcemic crisis*, which without precursors could have been exacerbated (cardiac arrhythmias with sudden death, polyuria, and somnolence), such patients should be sent to a hospital immediately. At a serum calcium level > *3 mmol/l*, surgery is indicated in an asymptomatic state. Consideration should be given to the cause of the condition prior to surgery. *Paraneoplastic hypercalcemia* takes a different course (see CS 56). In such a case (CS 67) the patient was suffering from a *primary disease* (the *myeloma* was excluded) and was cured long-term by surgery.

CS 68: Female patient with known RA, long-term MTX therapy and leukopenia. Response to CellCept®, 62 years

To obtain the correct diagnosis, it is important to establish the following constellations: firstly, confirmed RA, then absolute, pronounced *neutropenia*, postulated as a result of one-year administration of MTX. Subsequently, isolated middler doses cortisone therapy (Decortin® 20–10 mg/day) was applied with no basic preparations. This concept of *drug-induced myeloplasia* cannot be confirmed by bone-marrow biopsy (more a regenerative condition). *Hepatolienal* syndrome suggests *activation of the reticuloendothelial* system, which is to be regarded as the target for immunosuppression.

Determination of *antineutrophil* antibodies is pivotal to the diagnosis. *Therapy*: to begin with, immunosuppressive therapy for neutropenia (by hematologists) was refused and, on account of the high RA activity, only high-dose cortisone (no basic therapy) was prescribed. Addition of CellCept® 2,000 mg per day for 2 months produced a successive rise in leukocytes (to *3,500/µl*) and neutrophils (abs. *1,400/µl*). The antineutrophil antibodies were no longer detectable. After reduction of therapy (to Decortin® 5 mg and CellCept® 1,000 mg daily), neutropenia again developed and the antineutrophil antibodies could again be detected. Intensified immunosuppression for 2 years already had a positive influence (incidentally without side effects) on the clinic state and relevant laboratory parameters (currently under treatment CellCept® 1,000 mg and Decortin® 5–7.5 mg daily). If such therapy were ineffective, rituximab would be a possibility.

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