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Bone Health and Multiple Myeloma

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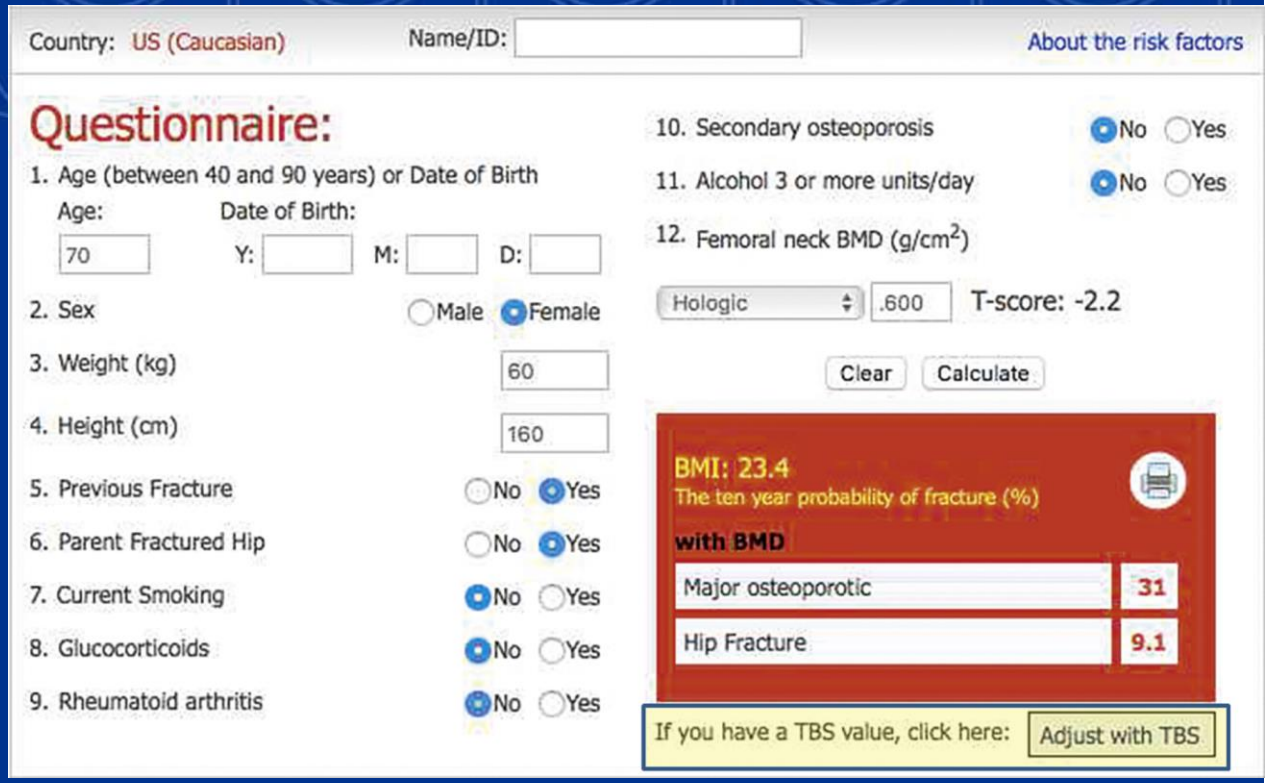
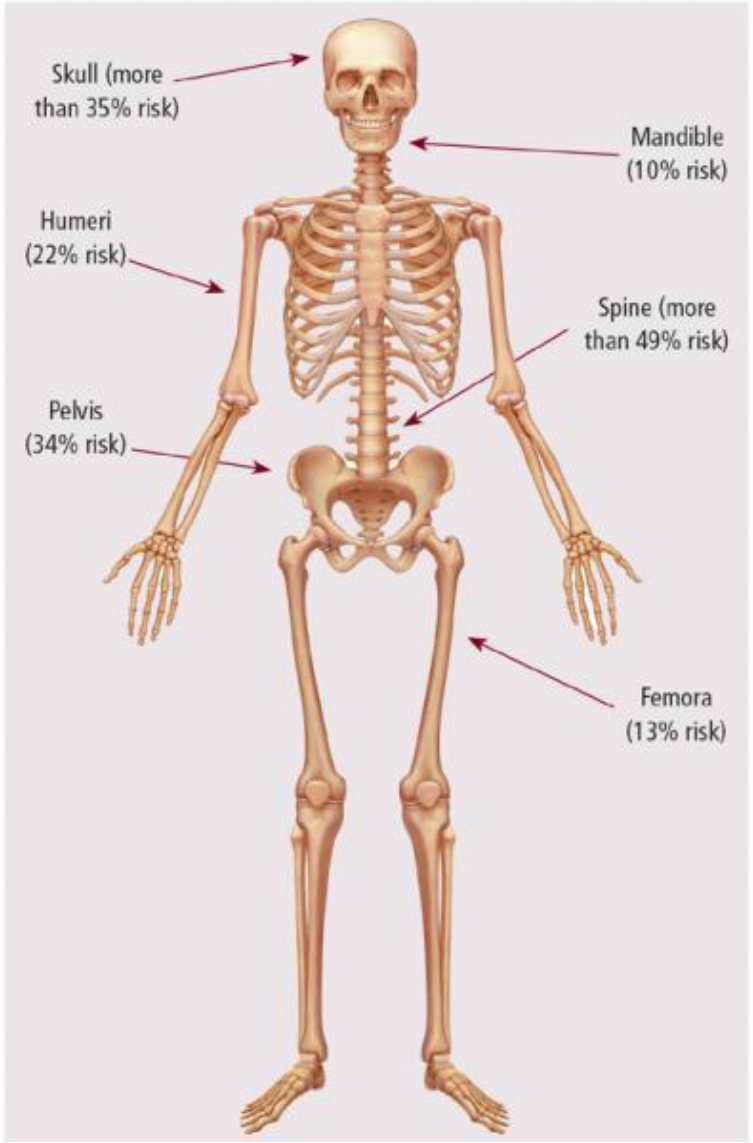
How are bones affected?

- Sufficient calcium and vitamin D levels
- Physical activity and exercise
- Tobacco and alcohol use
- Early onset menopause / low testosterone
- Older age
- Body size
- Family history
- High thyroid levels
- Steroids, anti-seizure medications, methotrexate, SSRIs

Myeloma and bone involvement

- 90% of patients
- Uniquely located IN the bone and bone marrow but also manipulates bone biology.
- Bone mineral density peaks at age 30 and then starts to decline slowly afterwards, especially after age 50.
- Bone is constantly undergoing growth and resorption.
- Entire skeleton is slowly replaced over the course of several years (7-10).
- Concurrent osteoporosis portends poorer prognosis in women





Which bones tend to be involved?

Which ones need immediate treatment?

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Clin J Oncol Nurs. 2011 Aug; 15(0): 9–23

bones imaged?

Imaging Examination	Advantages	Disadvantages
Whole-body radiographs	Cost; readily available; detects skull and limb injuries - findings consist of punch injuries, osteoporosis, or fractures in 75% of patients.	Low sensitivity and positivity; detects lesions only after apparent bone destruction (30 to 50% bone loss)
Whole-body low-dose CT	High sensitivity and positivity; allows aspiration biopsy and surgery guided by 3D images; defines radiotherapy planning; demonstrates the measurement of extramedullary lesions, detects bone marrow invasion and osteolysis; allows to evaluate the tumor load; data collection is fast; lower cost than MRI or PET-CT; little discomfort for the patient.	Cost; may miss skull and costal arch injuries; difficult determination of the number of injuries; when lytic bone lesions are not identified, the negative predictive value is low (59%), not excluding the diagnosis, requiring follow-up and complementation with MRI, WBMRI and/or PET-CT.
MRI	There is no exposure to radiation; allows locating and measuring infiltrative lesions in the bone marrow and focal lesions; it allows accurately diagnosing eventual spinal cord compression; the number of lesions may indicate prognosis; displays extramedullary lesions; 3D reconstruction imaging can help with biopsy and planning surgery and radiotherapy.	Cost; lengthy process for data collection; unsuitable for patients with claustrophobia or metal implant wearers; the drug used as a contrast agent is contraindicated in patients with severe renal impairment; bone marrow infiltration may be misdiagnosed as an osteolytic lesion; presence of electric field limitations and motion artifacts.
WBMRI	No ionizing radiation or need for contrast; faster image acquisition than PET/CT; well tolerated; superior spatial resolution; High accuracy in the study of bone marrow, especially when there is no detectable bone destruction on radiographs or CT; more sensitive than PET-CT in detecting bone involvement; better differentiation between therapeutic response and disease progression; provides information with prognostic value (number and extent of lesions, prediction of fracture risk).	Cost; accessibility and availability; time for image acquisition may require sedation; as it is a very sensitive methodology, it may lead to unnecessary tests and biopsies; same contraindications as MRI.
PET-CT	Reflects the activity of the lesions; it allows evaluating the activity of the lesions in the pre and postoperative period; extramedullary lesions can be imaged; it facilitates the evaluation of the prognosis in the pre and postoperative period; the use of new radionuclides makes it possible to identify different diseases.	Cost; accessibility and availability; low resolution in lesions smaller than 0.5 mm; MM insensitive with low fluorodexyglucose activity; limited diagnostic value (false-positive results due to inflammation, infection, fractures, bone remodeling, post-surgical or post-biopsy changes, recent chemotherapy and radiotherapy).

Abbreviations: 3D, three-dimensional; MM, multiple myeloma; PET-CT, positron emission tomography-computed tomography; MRI, magnetic resonance; WBMRI, whole body MRI; CT, computed tomography.

Source: Orthop Surg. 2016;8(3):263-269.

Lesions in the bone – “lytic”

- A “hole” or shadow is seen on xrays due to bone destruction
- No bone growth around the lesions
- Accelerated bone loss
- Bone lesions do not heal completely

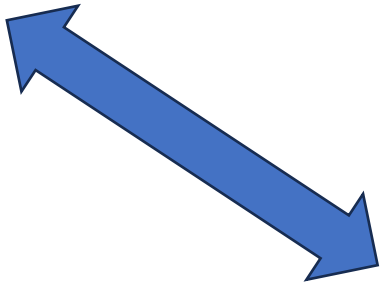
Types of cells in bone

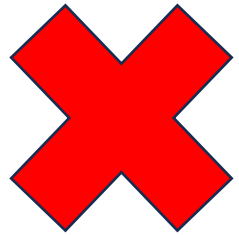
- Osteoclasts: breaks down bone
- Osteoblasts: builds up bone

Remove bone mineral and matrix

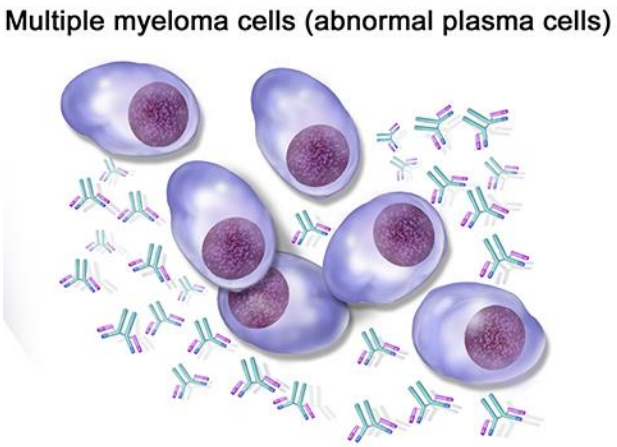
Create an eroded cavity

Create a matrix to replace resorbed bone with new bone





High calcium



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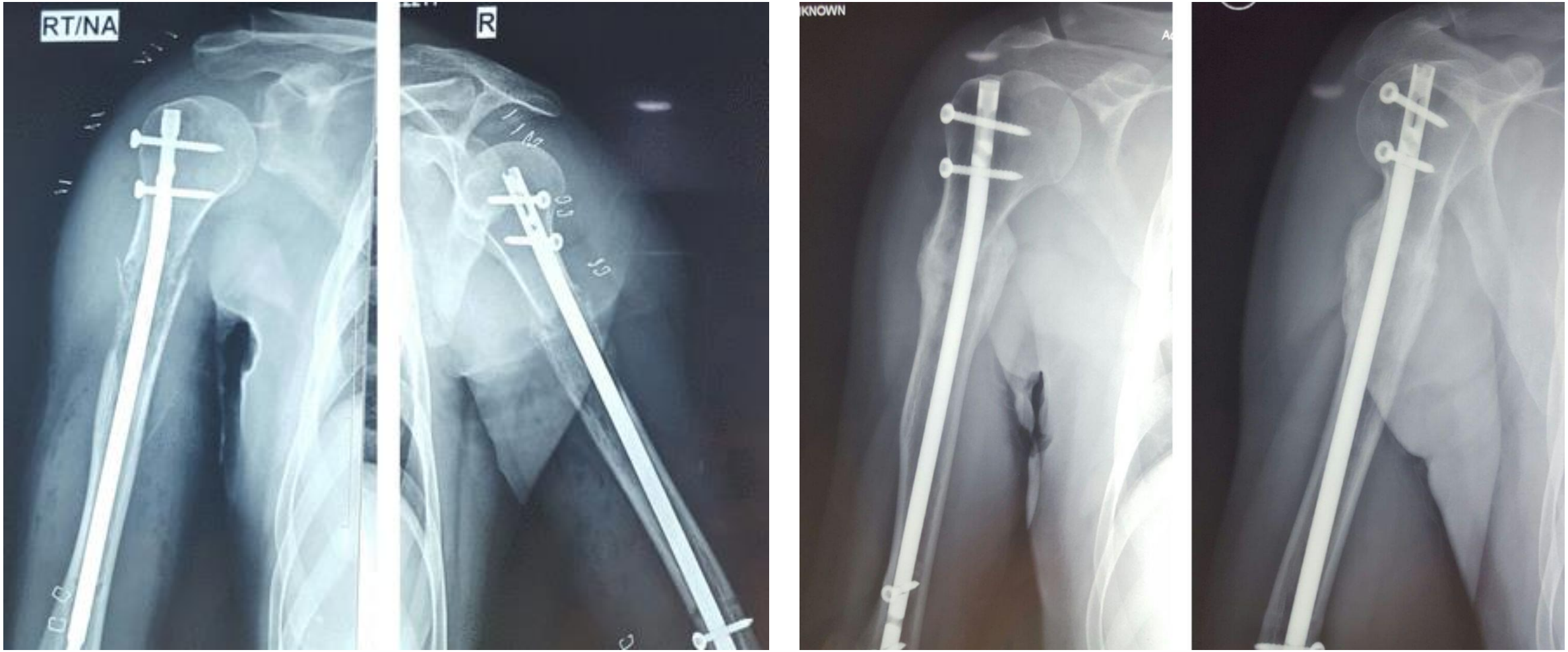
Surgery or Radiation (or both!?)



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Vaishya R, Vijay V, Agarwal AK, Healing of pathological fracture in a case of multiple myeloma *Case Reports* 2017;**2017**:bcr2016218672.

What medications are used to treat the bones?

- Bone Working Group of the International Myeloma Working Group Recommendations:
- IV Bisphosphonates : all patients regardless of active bone lesions
- RANK-L antagonists (Xgeva / Denosumab) : patients who cannot get a bisphosphonate, and only if bone disease is present
- For Smouldering MM or solitary plasmacytoma: if there is osteoporosis.

Self-care tips

- Eat plenty of vegetables
- Weight bearing / strength training exercise
- Avoid low calorie diets; consume enough protein
- Calcium, vitamin D and vitamin K
- Light aerobics / stationary bicycle
- Consider physical therapy / rehab if serious issues with bone injury or pain are limiting.
- Improved kidney health can improve bone health

Swedish Cancer Institute: Multiple Myeloma Options

Autologous stem cell transplant	**Abecma (Ide-cel, bb2121) SOC /Clinical trials**	**Carvikty / Cilta-Cel (to start this fall)**	**GPRC5D CAR-T cell therapy New combination?**
Teclistamab	Linvoseltamab	CC-93269-MM-001	Future Talquetamab approval?
Bispecifics in 2nd line therapy with combination	Bispecifics in smoldering MM	Novel immunotherapy targets: IV and oral (TTI-622, ORIC-533)	SWOG phase 3 trials for 1st line

Thank you